



U.S. Department of Health & Human Services

Food and Drug Administration

SAVE REQUEST

USER: (jsh)
FOLDER: K093775 - 1035 pages
COMPANY: ROMODEX INTERNATIONAL SRL (ROMODEX)
PRODUCT: CATHETER, INTRAVASCULAR, THERAPEUTIC, LONG-TERM GREATER THAN 30 DAYS (LJS)
SUMMARY: Product: EVGUIDE TIP LOCATION SYSTEM

DATE REQUESTED: May 4, 2011

DATE PRINTED: May 4, 2011

Note: Printed



JUL 15 2010

510(k) Summary

- Proprietary Name:** Sapiens™ Tip Location System also known as evGuide™ Tip Location System
- Device Trade name:** Sapiens™ Tip Location System (TLS)
- Product Classification:** Class II, 21 CFR §880.5970
LJS - Accessory to Percutaneous, Implanted, Long-Term Intravascular Catheters General Hospital
- Applicant name:** Romedex International Srl 58 Aleea Arubium, Bucharest, 022944 Romania, +1.650.209.4838, info@romedex.com, www.romedex.com
- Contact person:** Sorin Grunwald Ph.D., MBA. 175 Colorado Ave, Palo Alto, CA 94303, sorin@romedex.com, Tel: +1.650.209.4838, Fax: +1.650.887.0348
- Preparation Date:** June 4, 2010
- Predicate Devices:** K091324 - Sherlock 3CG Tip Positioning System
K032613 - Transvenous Pacemaker Placement Assist Device
K973371 - Conduction Anesthesia Kit
K843263 - Arrow-Johans ECG Adaptor
- Indications for Use:** The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.
- Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.
- Device Description:** The Sapiens™ TLS consists of the following elements: sterile electrical adaptor, ECG module and cable, laptop running Sapiens™ TLS software, label printer (optional), and remote control (optional). A stylet or a guidewire inserted in a central venous catheter can be connected to the Sapiens™ TLS system via the Sapiens™ TLS Electrical Adaptor establishing a direct electrical connection to the catheter distal tip for ECG signal measurement. A different ECG signal measurement method – the column of saline method – can be used by connecting the Sapiens™ TLS Electrical Adaptor to the Arrow-Johans Adaptor, by connecting the Arrow-Johans Adaptor to any central venous catheter and by injecting saline solution into the catheter lumen through the Arrow-Johans Adaptor, thus establishing electrical conductivity to the distal tip of the catheter. When the central venous catheter or its associated stylet or guidewire is connected to Sapiens™ TLS, the Sapiens™ TLS laptop screen displays skin ECG signals and endovascular electrograms acquired at the location of the distal tip of the catheter. The waveforms provided by Sapiens™ TLS can be used for guiding and positioning of the central venous catheter. These ECG waveforms can be printed using an optional label printer to document the catheter tip location for the patient's file.
- Bench Top Safety & Performance Tests:** Verification and validation tests have been performed in accordance with Design Controls per 21 CFR §820.30.

Bench top testing has been performed side-by-side with available predicate devices which has demonstrated substantial equivalence of Sapiens™ TLS to the respective predicate devices. The following tests were performed: a) electrical impedance testing and b) ECG waveform accuracy tests.

**Summary of
Non-clinical Data:**

Non-clinical studies were performed which have demonstrated safety and efficacy of Sapiens™ TLS using Electrical Adaptor, good correlation between bench top and in-vivo data, and substantial equivalence with predicate devices. The following tests were performed: a) ECG waveform accuracy comparison with a commercially available ECG monitor, b) ECG waveform accuracy comparison with the Conduction Anesthesia Kit (K973371) and c) system usability and validation testing.

**Summary of
Clinical Data:**

To date, Sapiens™ TLS has been used in Europe for central venous catheter guidance and positioning in five major hospital centers on more than 350 adult patients (ages 19-96) of both genders for placing several types of central venous catheters: PICCs, CVCs, implantable ports, hemodialysis catheters, and tunneled catheters. Several types of users including nurses and physicians have used Sapiens™ TLS for different clinical procedures, e.g., oncology, anesthesia, patient monitoring in the ICU, hemodialysis in different clinical settings: in the operating room, in outpatient clinics and at the bedside.

Side-by-side comparisons with available predicate devices were performed which demonstrated substantial equivalence of Sapiens™ TLS to the respective predicate devices.

In the two analyzed subsets of 362 patients (332 patients from a prospective, multicenter, non-controlled study and 30 patients from a human factors/ usability study), the catheter tip placement using Sapiens™ TLS at the desired location was confirmed with chest X-ray or fluoroscopy in 97% of the cases. No adverse events or complications have occurred.

**Summary of
Technological
Characteristics
Compared to
Predicate Devices**

The subject Sapiens™ TLS Electrical Adaptor combines design features, materials and technological characteristics of marketed predicate devices including the Transvenous Pacemaker Placement Assist Device (K032613) and Conduction Anesthesia Kit (K973371) such as: a) a sterile, insulated, electrically conductive wire of very low electrical resistance; b) a distal end alligator clip to connect to stylets and guidewires; c) a proximal end connector which can be connected to an ECG cable or to an ECG connection switch. When compared to the Conduction Anesthesia Kit, the Sapiens™ TLS Electrical Adaptor has simplified the design of the device by removing the switch box. When compared to Transvenous Pacemaker Placement Assist Device, the Sapiens™ TLS Electrical Adaptor has simplified the design of the device by removing the connection box.

The Sapiens™ TLS Electrical Adaptor may be connected to the ECG pin of the predicate Arrow-Johans Adaptor (K843263) using an ECG cable which allows for the saline conduction method of ECG measurement. Use of the Sapiens™ TLS Electrical Adaptor with the Arrow-Johans Adaptor does not require any modifications of design features, materials, or technological characteristics of the marketed predicate device.

Additionally, the subject Sapiens™ TLS System combines design features, components and technological characteristics of the predicate device Sherlock 3CG Tip Positioning System (K091324) but uses only cardiac electrical signal detection to provide real-time catheter tip location information. The subject Sapiens™ System does not use a passive magnet like the predicate device.

Any differences between technological features of the subject and predicate devices do not raise new questions of safety or efficacy of the subject Sapiens™ TLS device.

**Summary of
Substantial
Equivalence:**

The Sapiens™ TLS has the same intended use and similar indications for use as the commercially available Sherlock 3CG Tip Positioning System (K091324), Transvenous Pacemaker Placement Assist Device (K032613), Conduction Anesthesia Kit (K973371), and Arrow-Johans ECG Adaptor (K843263). Additionally, clinical and non-clinical performance testing has demonstrated that any differences in technological characteristics do not raise new issues of safety or effectiveness when compared to the aforementioned predicate devices. Therefore, the Sapiens™ TLS meets the requirements for substantial equivalence to the referenced predicate devices.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room - WO66-G609
Silver Spring, MD 20993-0002

JUL 15 2010

Dr. Sorin Grunwald, Ph.D.
Romodex International, Srl
175 Colorado Avenue
Palo Alto, California 94303

Re: K093775

Trade/Device Name: evGuide Tip Location System
Regulation Number: 21 CFR 880.5970
Regulation Name: Percutaneous, Implanted, Long Term Intravascular Catheter
Regulatory Class: II
Product Code: LJS
Dated: June 5, 2010
Received: June 7, 2010

Dear Dr. Grunwald:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to

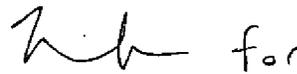
<http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm> for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,



Anthony D. Watson, B.S., M.S., M.B.A.
Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

SECTION 4: INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K093775

Not known at this time _____

Device Name: Sapiens™ TLS

Indications for Use:

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Page of

(Posted November 13, 2003)

R. C. Chang
(Division Sign-Off)

Division of Anesthesiology, General Hospital
Infection Control, Dental Devices

510(k) Number: K093775



JUL 28 2010

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room W-066-0609
Silver Spring, MD 20993-0002

Dr. Sorin Grunwald, Ph.D.
US FDA Agent for Romedex International, Srl
175 Colorado Avenue
Palo Alto, California 94303

Re: K093775

Trade/Device Name: Sapiens™ TLS
Regulation Number: 21 CFR 880.5970
Regulation Name: Percutaneous, Implanted, Long Term Intravascular Catheter
Regulatory Class: II
Product Code: LJS
Dated: June 5, 2010
Received: June 7, 2010

Dear Dr. Grunwald:

This letter corrects our substantially equivalent letter of July 15, 2010.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

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Page - Dr. Grunwald

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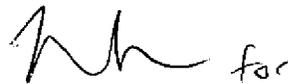
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Sincerely yours,



Anthony D. Watson, B.S., M.S., M.B.A.
Director

Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

SECTION 4: INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K093775

Not known at this time _____

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Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Page of
(Posted November 13, 2003)

RLC 7/20/10
(Division Sign-Off)

Division of Anesthesiology, General Hospital
Infection Control, Dental Devices

510(k) Number: K093775



JUL 28 2010

Food and Drug Administration
10903 New Hampshire Avenue
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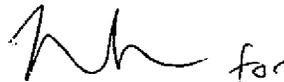
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Sincerely yours,



Anthony D. Watson, B.S., M.S., M.B.A.

Director

Division of Anesthesiology, General Hospital,

Infection Control and Dental Devices

Office of Device Evaluation

Center for Devices and

Radiological Health

Enclosure

SECTION 4: INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K093775

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(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Page of
(Posted November 13, 2003)

RHC Ch 7/20/10
(Division Sign-Off)

Division of Anesthesiology, General Hospital
Infection Control, Dental Devices

510(k) Number: K093775



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

December 09, 2009

ROMODEX INTERNATIONAL SRL
C/O SORIN GRUNWALD
175 COLORADO AVE.
PALO ALTO, CALIFORNIA 94303
UNITED STATES
ATTN: SORIN GRUNWALD

510k Number: K093775

Received: 12/8/2009

Product: EVGUIDE TIP LOCATION SYSTEM

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you when the processing of your 510(k) has been completed or if any additional information is required. **YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.**

Please remember that all correspondence concerning your submission **MUST** be sent to the Document Mail Center (DMC) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

On September 27, 2007, the President signed an act reauthorizing medical device user fees for fiscal years 2008 - 2012. The legislation - the Medical Device User Fee Amendments of 2007 is part of a larger bill, the Food and Drug Amendments Act of 2007. Please visit our website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/default.htm>

for more information regarding fees and FDA review goals. In addition, effective January 2, 2008, any firm that chooses to use a standard in the review of ANY new 510(k) needs to fill out the new standards form (Form 3654) and submit it with their 510(k). The form may be found at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm>.

We remind you that Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the PHS Act by adding new section 402(j) (42 U.S.C. § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Section 402(j) requires that a certification form <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm> accompany 510(k)/HDE/PMA submissions. The agency has issued a draft guidance titled: "Certifications To Accompany Drug, Biological

Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007”

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134034.htm>. According to the draft guidance, 510(k) submissions that do not contain clinical data do not need the certification form.

Please note the following documents as they relate to 510(k) review: 1) Guidance for Industry and FDA Staff entitled, “Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs and BLA Supplements”. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. Please refer to this guidance for information on a formalized interactive review process. 2) Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm>. In addition, the 510(k) Program Video is now available for viewing on line at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm>.

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have questions on the status of your submission, please contact DSMICA at (301)796-7100 or the toll-free number (800)638-2041, or at their internet address <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have procedural questions, please contact the 510(k) Staff at (301)796-5640.

Sincerely,

510(k) Staff

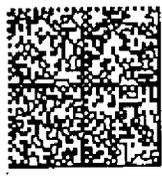
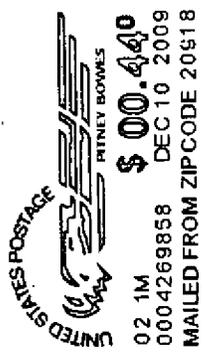
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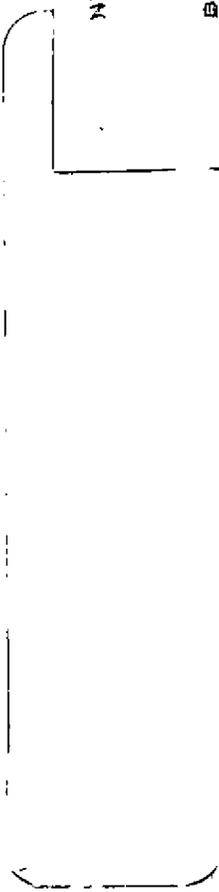
**DEPARTMENT OF
HEALTH & HUMAN SERVICES**

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room WC66-0609
Silver Spring MD 20993-0002

Official Business
Penalty for Private Use \$300



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MAILED FROM ZIP CODE 20918



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941 AC 1

70 12/17/09

RETURN TO SENDER
NO SUCH NUMBER
UNABLE TO FORWARD

BC: 20993

*0940-11370-17-2#



Document Cover Sheet:

K093775 - K8248

FSR0203-003

Date of Submission 11/15/2009
Description EVGUIDE TIP LOCATION SYSTEM
Date of Scan
Document Prep DSF4 11/3/10
Scanner DSF4 11/3/10
Image Quality Reviewer



DOCUMENTS EXPECTED	DOCUMENT DATE	PAGE# START	PAGE# END	PAGE IN DOC	INDEXER
Decision Letter	07/15/10	1	2	3	<input type="checkbox"/>
Indications for Use	07/15/10	3	3	2	<input type="checkbox"/>
Reviewer Memorandum	07/15/10	4	5	3	<input type="checkbox"/>
510K Decision Tree		6	6	2	<input type="checkbox"/>
Reviewer Notes	07/15/10	7	87	82	<input type="checkbox"/>
SUPP_001	06/05/10	88	308	222	<input type="checkbox"/>
Contents	06/05/10	88	133	47	<input type="checkbox"/>
Attachment 1 EvGuide Sapiens TLS Users Manual	06/05/10	134	154	22	<input type="checkbox"/>
Attachment 2 EvGuide Sapiens TLS Adaptor Instructions For Use	06/05/10	155	159	6	<input type="checkbox"/>
Attachment 3 Romedex Sterigenics Sterilization VALID Protocol	06/05/10	160	184	26	<input type="checkbox"/>
Attachment 4 Romedex Sterigenics Sterilization VALID Report	06/05/10	185	201	18	<input type="checkbox"/>
Attachment 5 EvGuide Sapiens Sterilization Test Results	06/05/10	202	203	3	<input type="checkbox"/>
Attachment 6 Bioburden Validation For Romedex Protocol	06/05/10	204	211	9	<input type="checkbox"/>
Attachment 7 Bioburden Validation For Romedex Report	06/05/10	212	217	7	<input type="checkbox"/>
Attachment 8 EvGuide Sapiens Shelf Life Test Protocol	06/05/10	218	228	12	<input type="checkbox"/>
Attachment 9 Biocompatibility Summary For The Arrow Johans	06/05/10	229	235	8	<input type="checkbox"/>

Document Cover Sheet:

K093775 - K8248

FSR0203-003

Date of Submission 11/15/2009
Description EVGUIDE TIP LOCATION SYSTEM
Date of Scan <i>Enter Date of Scan Here</i>
Document Prep <i>Enter Document Prep Here</i>
Scanner <i>Enter Scanner Here</i>
Image Quality Reviewer

DOCUMENTS EXPECTED	DOCUMENT DATE	PAGE# START	PAGE# END	PAGE IN DOC	INDEXER
Attachment 10 EvGuide Sapiens System Human Factors	06/05/10	236	256	22	<input type="checkbox"/>
Attachment 11 EvGuide Sapiens Post Market Clinical Study	06/05/10	257	262	7	<input type="checkbox"/>
Attachment 12 K093775 Updated Submission Cover Sheet	06/05/10	263	269	8	<input type="checkbox"/>
Attachment 13 K093775 Updated Section 4 IFU Statement	06/05/10	270	271	3	<input type="checkbox"/>
Attachment 14 EvGuide Sapiens ECG Waveform Accuracy	06/05/10	272	290	20	<input type="checkbox"/>
Attachment 15 EKG Guided Peripherally Inserted Central	06/05/10	291	299	10	<input type="checkbox"/>
Attachment 16 The ECG Method For Positioning The Tip	06/05/10	300	308	10	<input type="checkbox"/>
Correspondence	03/31/10	309	309	2	<input type="checkbox"/>
Correspondence	03/30/10	310	310	2	<input type="checkbox"/>
Correspondence	03/04/10	311	312	3	<input type="checkbox"/>
Reviewer Notes	03/03/10	313	373	62	<input type="checkbox"/>
Acknowledgement Letter	12/09/09	374	375	3	<input type="checkbox"/>
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Cover Page	11/15/09	376	376	2	<input type="checkbox"/>
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Medical Device User Fee Cover Sheet	11/15/09	383	385	4	<input type="checkbox"/>

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FSR0203-003

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Cover Letter	11/15/09	393	395	4	<input type="checkbox"/>
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Appendix A Predicate Device	11/15/09	467	482	17	<input type="checkbox"/>
Appendix B Labeling	11/15/09	483	511	30	<input type="checkbox"/>
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Appendix G System Performance Testing	11/15/09	653	689	38	<input type="checkbox"/>
Appendix H Published Paper In JAVA	11/15/09	690	698	10	<input type="checkbox"/>
Appendix I Clinical Experience	11/15/09	699	715	18	<input type="checkbox"/>
Appendix J Certifications Of Main Suppliers	11/15/09	716	742	28	<input type="checkbox"/>
Appendix K Sterilization And Biocompatibility	11/15/09	743	768	27	<input type="checkbox"/>
Appendix L FDA Forms 3654	11/15/09	769	809	42	<input type="checkbox"/>

Document Cover Sheet:

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Silver Spring, MD 20993-0002

JUL 15 2010

Dr. Sorin Grunwald, Ph.D.
Romodex International, Srl
175 Colorado Avenue
Palo Alto, California 94303

Re: K093775

Trade/Device Name: evGuide Tip Location System
Regulation Number: 21 CFR 880.5970
Regulation Name: Percutaneous, Implanted, Long Term Intravascular Catheter
Regulatory Class: II
Product Code: LJS
Dated: June 5, 2010
Received: June 7, 2010

Dear Dr. Grunwald:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

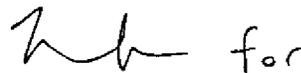
If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to

<http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm> for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,



Anthony D. Watson, B.S., M.S., M.B.A.
Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

SECTION 4: INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K093775

Not known at this time _____

Device Name: Sapiens™ TLS

Indications for Use:

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

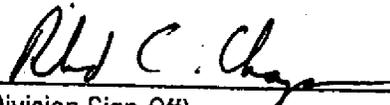
Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Page of

(Posted November 13, 2003)



(Division Sign-Off)

Division of Anesthesiology, General Hospital
Infection Control, Dental Devices

510(k) Number: K093775

evGuide-Sapiens™ TLS USER'S MANUAL

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evGuide-Sapiens™ TLS USER'S MANUAL

Note: The names evGuide™ TLS and Sapiens™ TLS will be used interchangeably in this document.

1. Overview

1.1 Indications for Use

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

1.2 The ECG Method for Catheter Guidance

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health care institutions and as documented in many papers including:

- a. *Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation*, by Nancy Moureau et al. published in the Journal of the Association for Vascular Access in 2010, JAVA Vol. 15 No. 1 2010, pp. 9-15
- b. *The ECG method for positioning the tip of PICCs: results from two preliminary studies*, by Mauro Pittiruti et al. published in the Journal of the Association for Vascular Access in 2008, JAVA Vol. 13 No. 4 2008, pp. 112-119

Figure 1 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community. The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the "red" or "right shoulder" electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode,

the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A "giant" P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface ECG, the tip of the electrode is in the superior cava vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava).

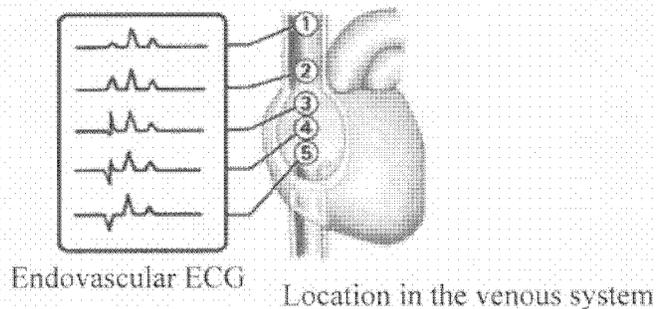


Figure 1: Changes in the ECG waveform as function of location in the vasculature

Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy.

1.3 Sapiens™ TLS Description

The Sapiens™ TLS consists of the Sapiens™ TLS Electrical Adaptor, an ECG Module and an ECG cable, a laptop, and the Sapiens™ TLS application software. The Sapiens™ TLS components excluding the Sapiens™ TLS Adaptors are also referred to as the Sapiens™ TLS System. An optional printer can be connected to the laptop for documentation purposes. The Sapiens™ TLS Saline Adaptor can be connected to an Arrow-Johans Adaptor (Teleflex) to be used according to the saline column method as described herein. The Sapiens™ TLS Saline Adaptor with the Arrow-Johans Adaptor can be connected to any commercially available central venous catheters and the Sapiens™ TLS Electrical Adaptor to any commercially available stylets or guidewires used for the placement of central venous catheters. The Sapiens™ TLS system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, or intracavitary ECG) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and

acquired in real time through the Sapiens adaptors. Thus, the waveforms presented on the Sapiens™ TLS graphical user interface can aid the placement of central venous catheters.

The Sapiens™ TLS System is shipped in two subsystems: laptop running the Sapiens™ TLS software and the Sapiens™ TLS ECG module together with the corresponding cables.

Store the Sapiens™ TLS System indoors at room temperature and condition.

Figure 2 shows the system components:

1. PC/Laptop running Sapiens™ TLS software
2. ECG module
3. USB connection cable to the ECG module
4. ECG cable
5. Sterile Sapiens™ TLS Electrical Adaptor connected to an Arrow-Johans Adaptor placed between a syringe and a catheter
6. Skin ECG electrodes
7. Optional label printer
8. Optional remote control

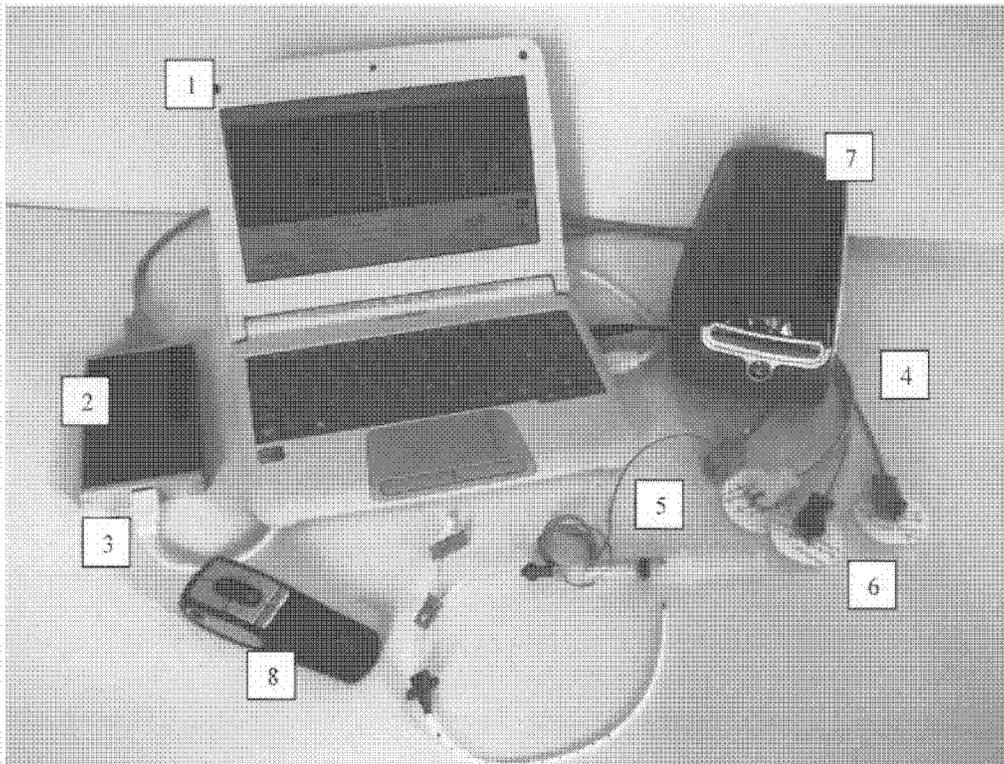


Figure 2: Sapiens TLS System Configuration

1.4 Warnings and Precautions

A Warning indicates that the personal safety of the patient or physician may be involved. Disregarding a Warning could result in injury to the patient or physician. A Caution indicates that particular service procedures or precautions must be followed to avoid possible damage to the product.

Warnings

- Warning:** Before using the Sapiens™ TLS System for the first time, be sure to read and understand all of the information in this User's Manual.
- Warning:** Failure to abide by the precautions detailed below causes the system and its use to be out of compliance with regulations and places the patient and the user at risk of injury or death.
- Warning:** When using the Sapiens™ TLS System with the Sapiens™ TLS Adaptors, always follow the Instructions for Use provided with the Sapiens™ TLS Adaptor. When using the Arrow-Johans Adaptor, always follow the Instructions for Use provided with the Arrow-Johans Adaptor.
- Warning:** The Sapiens™ TLS System should only be used by physicians and nurses trained in central lines placement procedures and in assessing the ECG information provided by the Sapiens™ TLS System.
- Warning:** The Sapiens™ TLS only works for a sinus rhythm of the heart.
- Warning:** The Sapiens™ TLS User's Manual provides information about ECG waveforms and their correspondence with specific locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** Place skin electrodes carefully at locations indicated by this User's Manual and ensure good skin-electrode contact. Failure to do so may cause unstable ECG waveforms and/or ECG waveforms which are not described in this Manual. In such a case, the use of an additional and/or different method may be required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** In patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** In patients undergoing central venous catheterization using venous access through the saphenous or the femoral veins, the catheter tip will typically not reach the right atrium and the caval atrial junction. In such a situation,

the ECG waveforms described by this manual cannot be used for catheter guidance and placement and the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In certain patients, unstable ECG waveforms may be detected because of the manipulation of the Sapiens™ TLS Adaptor by the user. Verify that the connection between the Sapiens™ TLS Adaptor and the central venous catheter and the connection between the Sapiens™ TLS Adaptor and the ECG cable are free from contact with any other material and refrain from touching the Sapiens™ TLS Adaptor and any of its connections. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In certain patients, no ECG waveforms may be detected because of very specific impedance mismatch between the patient and the ECG electrodes. Be sure to use the Instructions for Use provided by the manufacturer of the skin electrodes. Verify the connection between the patient's skin and the electrodes, between the electrodes and Sapiens™ TLS ECG cable, and between the Sapiens™ TLS Adaptor and the Sapiens™ TLS ECG cable. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In neonates, unstable ECG waveforms may be detected because of patient's movements or manipulation by the user. In such a situation, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: The Sapiens™ TLS system is not intended to diagnose or treat disease.

Warning: Monitor catheter tip placement during insertion procedure and verify catheter tip location placement using your institution's guidelines.

Warning: Do not place and/or use the Sapiens™ TLS system in the presence of strong magnetic fields such as Magnetic Resonance Imaging (MRI) devices. The high magnetic fields created by an MRI device will attract the equipment with a force sufficient to cause death or serious personal injury to persons between the equipment and the MRI device. This magnetic attraction may also damage the equipment. The magnetic and the RF fields associated with the MRI environment may interfere with the display of ECG waveforms. Consult the MRI manufacturer for more information.

Warning: Do not use the Sapiens™ TLS system at the same time with a defibrillator. Disconnect any Sapiens™ TLS Adaptor from any catheter and any Sapiens™ TLS ECG cable connection from any ECG skin electrode before using a defibrillator.

- Warning:** Always use controls, make adjustments and perform procedures with Sapiens™ TLS as specified in this User's Manual.
- Warning:** The Sapiens™ TLS system is password protected to avoid accidental changes in the software and system configuration. Do not install any software on the Sapiens™ TLS System unless instructed to do so by qualified Romedex personnel and under the guidance of qualified Romedex personnel. Failure to do so may result in patient and user harm and system damage.
- Warning:** The Sapiens™ TLS system must be powered only by the batteries provided with the Sapiens™ TLS Laptop. Batteries may not be charged while using the Sapiens™ TLS system in a medical procedure.
- Warning:** Charge the Sapiens™ TLS system only when the system is Off using a medical grade power adaptor.
- Warning:** All optional system components including the optional printer must be powered by, and only by a medical grade power adaptor if they are connected to the Sapiens™ TLS system during the clinical procedure.
- Warning:** Do not use additional cables, extension cords or outlets with the Sapiens™ TLS System.
- Warning:** This device is not to be used in the presence of combustible or flammable gases, anesthetics, or cleaners/disinfectants.
- Warning:** Do not remove system covers. To avoid electrical shock, use only the power cord supplied with the system and connect only to properly grounded wall outlets. Only Romedex qualified personnel should service the system.
- Warning:** Maximum care should be taken in checking that all connecting cables and connections, such as alligator clips, are electrically insulated and do not come into contact with other electrical cables or metal surfaces
- Warning:** No part of the body of the patient must be in direct or indirect uninsulated contact with metal surfaces.

Cautions

- Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician
- Caution:** Active electric motor driven equipment, such as pumps, may interfere with the display of the ECG waveforms. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Caution:** Equipment such as CT scanners, X-rays and fluoroscopy systems, cauterizers and diathermy equipment, operating in close proximity may emit strong electromagnetic or radio frequency interference (RFI) which

could interfere with the display of ECG waveforms by Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Caution: Electric equipment which requires direct contact with the patient may interfere with the display of ECG waveforms by Sapiens™ TLS. Do not use electric cauterization, electric scalpels, and ablation equipment while using Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

1.5 Sapiens TLS System Limitations

When using the Sapiens™ TLS Electrical Adaptor, a stylet or a guidewire typically provided with the kit of the vascular access device must be used in order to ensure an electrically conductive path between the proximal and the distal ends of the vascular access device.

When using the saline adaptor configuration of Sapiens™ TLS, the user needs to ensure that the catheter lumen is constantly filled with saline and in contact with the Arrow-Johans Adaptor, such that electrical conductivity through the catheter lumen is ensured from the proximal to the distal end of the vascular access device.

When using the saline adaptor configuration, instability of the endovascular electrical signal baseline may occur if the user makes hand contact with the proximal end connection of the Arrow-Johans Adaptor.

The Sapiens™ TLS system must be battery powered when used in a clinical case, i.e., as long as ECG electrodes are connected to the patient. The system battery lasts for approximately two hours. Recharging the battery must be done in between clinical cases.

The Sapiens™ TLS system uses data processing algorithms to enhance the quality of the endovascular ECG signal. In situations when electrodes have been disconnected and reconnected again, e.g., when the red clip electrode is connected to the sterile adaptor, it may take several seconds for the system to transition from a no-signal to a stable signal state. Please wait while the system makes this transition and do not touch the electrical connections of the adaptor during this time.

The Sapiens™ TLS system uses a serial communication protocol and a USB-Serial converter between the laptop and the ECG module. If the USB connector is not connected when the Sapiens software application starts up or if the USB connector is

disconnected before shutting down the Sapiens software application, under certain circumstances the Sapiens application must be restarted.

In order to prevent accidental installation of software on the Sapiens™ TLS laptop computer, the user does not have administrative rights to install software. Only Romedex personnel have the administrative rights to perform software installation on the Sapiens™ TLS laptop.

2. Sapiens™ TLS procedure workflow

2.1 System setup

Find an appropriate location for the system. Ensure the Sapiens™ TLS System is placed no more than 4 feet away from the patient outside the sterile field.

Ensure that all the individual power switches to the Laptop, optional printer, and medical grade power supply, where appropriate, are turned OFF. Connect the ECG module to the Laptop via the USB cable provided with the system. Connect the ECG cable to the ECG module via the ECG cable connector.

The laptop and the ECG module can run on the laptop battery. If the optional printer is not used, then there is no need to connect the medical grade power supply to the power outlet. Fully charging the laptop battery should be accomplished before any procedure if the system runs on battery. A full battery charge lasts for approximately two hours.

Turn the system on by turning on the power switches on of the individual systems in the following order:

- a. Optional printer
- b. Laptop

Once the Laptop power up sequence is finished, the Sapiens™ TLS software will be launched automatically. The startup screen is shown in Figure 3.

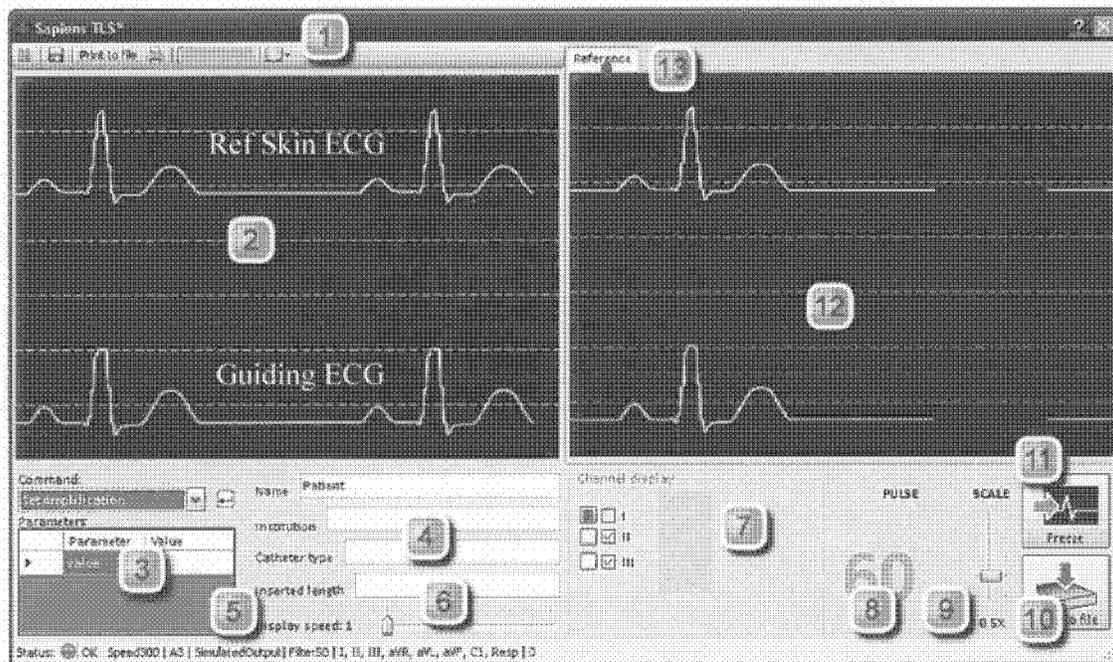


Figure 3: Sapiens™ TLS Screen Layout

- 1 - Toolbar containing controls for play / pause the data acquisition, load / save ECG files, printing to file / printer, settings and help. The following functions are available on the toolbar:
- Pause/Play the ECG waveform in acquisition and playback modes.
 - Save the case to file. When clicking the “Save” icon, all ECG waveforms for the entire duration since the beginning of the case or since last save are saved in a file. The default name of the file is the name of the patient to which the date and time are appended. The default directory is C:/Data created when installing the Sapiens™ TLS application.
 - Print to file. Click on the button to select (highlight) it, click again to unselect it. When this button is selected, the printer output will be redirected to a file using a default name and location.
 - Print. By clicking the printer icon, the print preview will be displayed. The desired information needs to be first frozen on the right hand side screen before it can be printed. The printer output will be redirected to the default printer. A default label printer is preinstalled on the system.
 - Clicking on the Help button brings up the User's manual and information about the Sapiens™ TLS software.
 - By dragging the question mark to a screen location, certain hints will be provided depending on the location.
 - Closes the Sapiens™ TLS application before turning off the computer. If the user accidentally closes it and needs to reopen it again, double click on the Sapiens TLS icon on the desktop.

- 2 - Main screen where the real-time ECG waveforms are displayed: the reference skin ECG waveform (lead III in Einthoven's reference system) and the guiding ECG waveform at the tip of the catheter (lead II in Einthoven's reference system).
- 3 - Available commands accepted by the device and respective parameters
- 4 - 'Patient name', 'institution', 'catheter type' and 'inserted length' information that will be shown on printed label.
- 5 - Status bar displaying information about the ECG module status
- 6 - Scroll bar used for changing the scroll speed of the ECG waveform display
- 7 - Color and visibility setting for channels.
- 8 - Frequency of R-Peaks measured in number of peaks / minute.
- 9 - Scale setting used to amplify the signals received from device.
- 10 - Pressing this button will save the current image shown in Main screen.
- 11 - Pressing this button will copy the current image shown in Main screen to Secondary screen.
- 12 - Secondary screen used for freezing ECG waveforms for comparison.
- 13 - Tab container displays the 'Reference' page.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

To power off the system:

- a. Close the Sapiens™ TLS application
- b. Power down the Windows operating system on the laptop
- c. Turn off the optional printer

2.2 Patient preparation and vein puncture

Connect the ECG cable to the patient:

1. Before preparing the sterile field, take the ECG cable supplied with the Sapiens™ TLS System and wipe the cable down according to hospital's guideline.
2. Locate three new off-the-shelf ECG snap electrode patches and place one on the patient's lower left abdomen, one on the patient's lower right abdomen, and one on the patient's left shoulder or arm per the ECG electrodes instructions for use.
3. Connect the green clip connector of the provided ECG cable to the electrode snap on the patient's left lower abdomen.
4. Connect the black clip connector of the provided ECG cable to the electrode snap on the patient's left lower abdomen.
5. Connect the yellow clip connector of the provided ECG cable to the electrode snap on the patient's left shoulder or arm.

6. Leave the red clip connector of the provided ECG cable in a reachable location for the connection with the sterile adaptor during the procedure.

With the Sapiens™ TLS system running, the reference skin ECG waveform should be at this time visible and stable. It should be possible to unambiguously identify the ECG waveform elements, e.g., the P-wave and the R-wave, as represented in this User's Manual. If this is not the case, do not attempt to use Sapiens™ TLS for catheter guidance and positioning and use another method for catheter tip location verification as indicated by the institutional guidelines, e.g., chest X-ray or fluoroscopy.

Prepare the patient for central venous catheterization per institution's guidelines.

Perform vein puncture and venous access per institution's guidelines, if applicable under ultrasound imaging guidance.

2.3 Connecting the Sapiens™ TLS Adaptor or the Arrow-Johans adaptor

In order to obtain ECG waveforms at the tip of the central venous catheter, the non-sterile red clip connector of the provided ECG cable must be connected to the sterile central venous catheter. This connection is achieved using the Sapiens™ TLS Electrical Adaptor and/or the Arrow-Johans Adaptor. Please refer to the Instructions for Use of these adaptors for details.

When using the Sapiens™ TLS Electrical Adaptor, connect the alligator clip end of the Sapiens™ TLS Adaptor to the proximal end of the stylet or guidewire which is packaged with your venous access device or pre-inserted in one of the lumens of your venous access device. Connect the red clip connector of the provided ECG cable to the plug end of the sterile Sapiens™ TLS Electrical Adaptor.

When using the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor, connect the Arrow-Johans Adaptor similarly to the Sapiens™ TLS Saline Adaptor. Then connect the alligator clip of the Sapiens™ TLS Electrical Adaptor to the snap nipple connector of the Arrow-Johans Adaptor and then connect the red clip connector of the provided ECG cable to the plug end of the sterile Sapiens™ TLS Electrical Adaptor.

2.4 Electrical vs. saline adaptors

The choice between using the Sapiens™ TLS Electrical Adaptor or the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor is a matter of user preference and workflow optimization and is potentially subject to institutional guidelines. Please refer also to the Instructions for Use of the respective adaptors.

Typical situations for using the Sapiens™ TLS Electrical Adaptor are:

1. Placement of open-ended PICCs with pre-inserted stylets and luer-locks which allow for stylet position control
2. Implantable ports using open vein access with over-the-guidewire catheter placement
3. Any central venous catheter inserted over a guidewire with centimeter markings

Typical situations for using the combination between the Arrow-Johans Adaptor and the Sapiens TLS Electrical Adaptor are:

1. Any post-procedural tip location verification of any central venous catheter type
2. Placement of closed-end PICCs
3. Placement of central venous catheters using the modified Seldinger technique (MST) which do not have pre-inserted stylets, e.g., tunneled catheters like Broviac catheters.
4. Any central venous catheter inserted over a guidewire without centimeter markings, e.g., CVCs.
5. Hemodialysis catheters which may require tip location verification for both ends: the long distal end in the right atrium and the short distal end at the caval-atrial junction.

2.5 Display ECG waveforms

As soon as the Sapiens™ TLS adaptors and/or the Arrow-Johans Adaptor are connected to the catheter and to the ECG cable, the guiding ECG waveform is displayed (Figure 3).

The waveforms on the top in Figure 3 on both left and right hand side display windows represent the skin ECG or reference ECG. The waveforms on the bottom in Figure 3 on both left and right hand side display windows represent the electrical signal detected at the tip of the central venous catheter.

The right hand side window in Figure 3 is labeled "Reference". The reference window allows for saving the ECG waveforms at a desired location for further comparison. Clicking on the "Freeze" button below the Reference window or using the left arrow key on the keyboard freezes the display, such that the frozen ECG waveform can be used as a reference.

The scroll speed of the ECG waveform can be selected by using the scroll bar "Display speed" (6 in Fig 3). The amplitude scale for the ECG waveform can be manually selected by using the Scale scrollbar (9 in Fig 3) or the up/down arrow keys on the keyboard.

2.6 Document the catheter tip location

The ECG waveforms can be recorded real-time during the procedure by clicking on the "Record" button. The ECG waveforms are recorded in a file. The file name is

automatically generated by the computer if a patient ID is not input. If a patient ID is input the file name is generated based on the patient ID. The file can be copied to a USB memory stick or memory card as a removable storage device.

Clicking the "Print/Save" button sends a screen shot to the printer if attached and save the screen shot in a file in JPG format. The file name is assigned automatically if no patient ID is input and a name is assigned based on the patient ID if a patient ID is input.

Using Sapiens™ TLS it is possible to print the ECG waveforms at the chosen tip location in order to attach the print to the patient chart and document the catheter tip location. The alphanumeric information input by the user and the ECG waveforms displayed in the Reference window are printed using the print layout illustrated in Figure 4. The print layout is displayed when clicking on the printer icon on the command toolbar at the top of the screen. The reference skin ECG and the guiding ECG waveforms are displayed on the right hand side and respectively on the left hand side of the print layout. Between the two waveforms a heart symbol is printed in order to allow the user to mark with a pen on printed paper the location of tip where the corresponding ECG waveforms have been obtained.

The patient name, institution name, catheter type and length, are displayed as well as they were input in the corresponding fields of the graphical user interface.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

This information is printed out in the corresponding fields of the print layout in Figure 4.

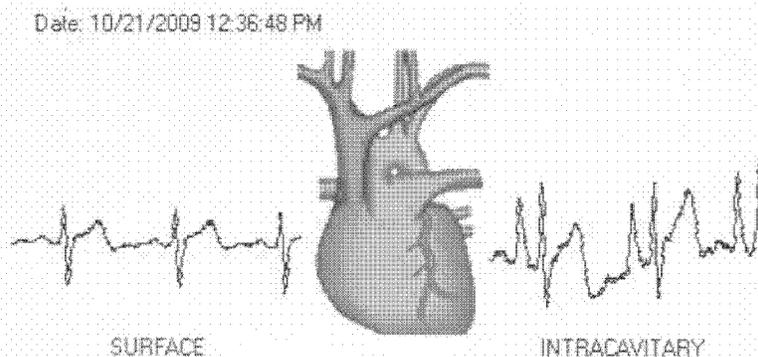


Figure 4: Print layout

To copy any file from the Sapiens™ TLS laptop to a removable storage medium, exit the Sapiens™ TLS application and use the Windows XP operating system to copy the desired file to the desired location.

3. Sapiens™ TLS Catheter Guidance

3.1 Outside the thoracic cavity

Outside the thoracic cavity the ECG signals are similar to the ones at the skin level. Figure 5 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located outside the thoracic cavity relative to the reference skin ECG.

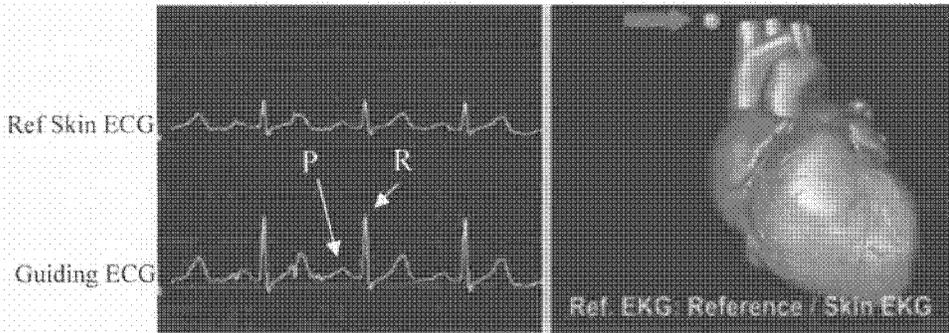


Figure 5: ECG waveform at the tip of the catheter outside the thoracic cavity.

3.2 Superior vena cava

Figure 6 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the upper superior vena cava (SVC). Compared to Figure 5 one can notice that the reference skin ECG waveform has not changed since this waveform does not depend on the location of the tip of the catheter. The amplitude and energy of the guiding ECG waveform have increase in Figure 6 when compared to Figure 5 indicating that the catheter tip is approaching the heart, i.e., a region of high electrical activity. Still, the shape of the ECG waveform has not changed significantly indicating that the catheter tip is not yet close to the sino-atrial node and the caval-atrial junction.

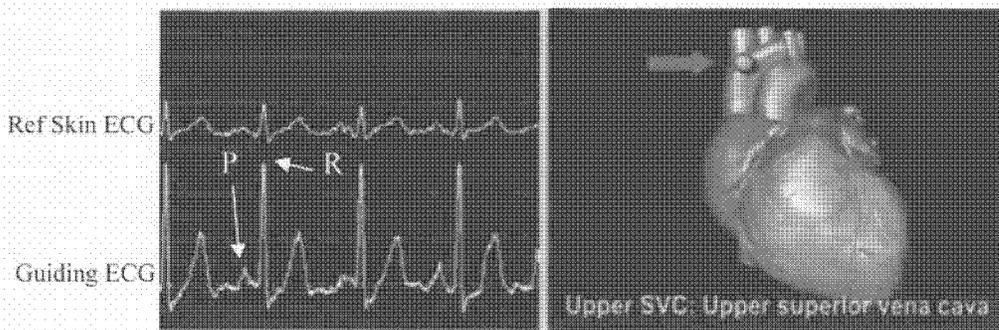


Figure 6: ECG waveform at the tip of the catheter in the upper SVC

3.3 Lower third of the superior vena cava

Figure 7 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in lower third of the upper superior vena cava. The P-wave has increased visibly when compared to Figure 6. The amplitude of the P-wave is about half size of the amplitude of the R-wave.

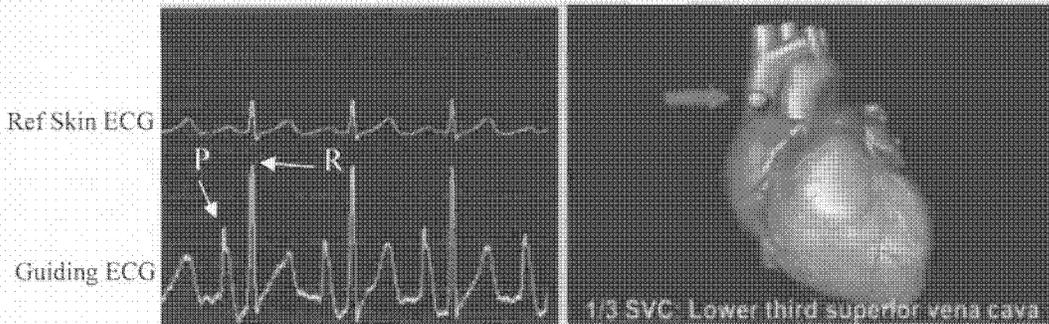


Figure 7: ECG waveform at the tip of the catheter in the lower third of the SVC

3.4 Caval-atrial junction

Figure 8 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located at the caval-atrial junction (CAJ) right below the sino-atrial node (SAN). The P-wave is bi-phasic, i.e., has a negative component. A negative component of the P-wave appears when the tip of the catheter is below the sino-atrial node (SAN). Since the P-wave has a negative component but the amplitude of the P-wave has not increased much compared to Figure 7, the ECG waveform in Figure 8 is typical of the caval-atrial junction with the tip of the catheter just below the SAN.

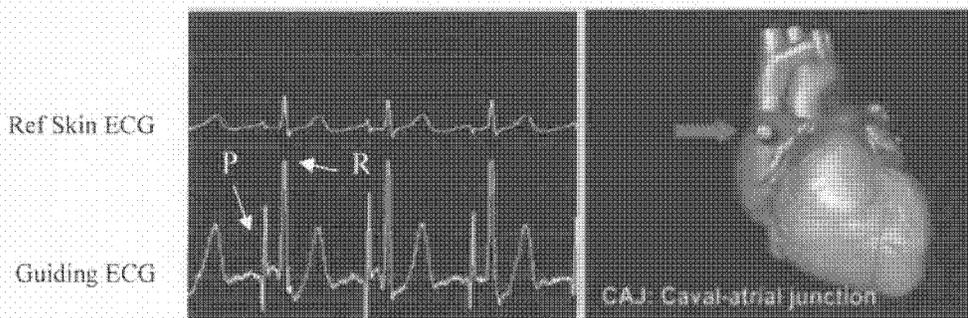


Figure 8: ECG waveform at the tip of the catheter at CAJ right below the SAN

3.5 Right atrium

Figure 9 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the right atrium (RA). The P-wave continues to have a negative component indicating that the catheter tip continues to be below the sino-atrial node. The P-wave amplitude has increased significantly when compared to Figures 7 and 8. This is an

indication that the tip of the catheter is in the middle of the right atrium where the P-wave intensity is maximal due to the right-atrial activity.

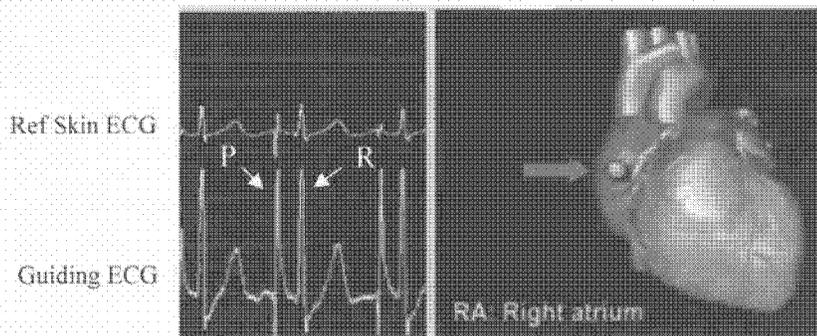


Figure 9: ECG waveform at the tip of the catheter in the RA.

3.6 Inferior Vena Cava

Figure 10 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the inferior vena cava (IVC). The P-wave has changed polarity when compared to Figure 7. In Figure 7 the P-wave is positive whereby in Figure 10 the P-wave is negative. This is an indication that the catheter tip is approaching the inferior vena cava. The relatively high negative amplitude of the P-wave compared to the positive one in Figure 7 is an indication that the tip of the catheter is just entering the inferior vena cava coming from the right atrium.

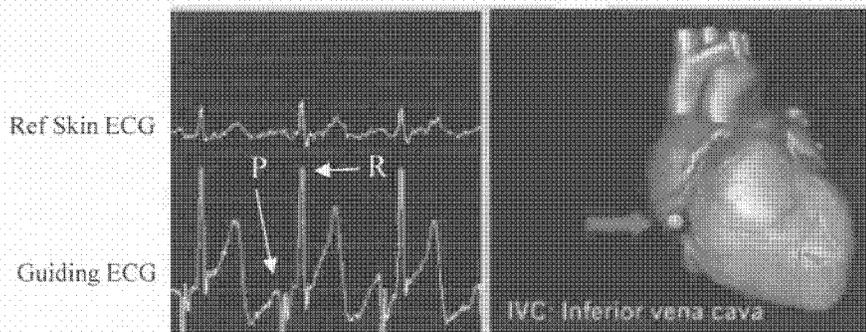


Figure 10: ECG waveform at the tip of the catheter in the IVC.

3.7 Catheter tip placement verification

As described in Section 3 of this Sapiens™ TLS User's Manual, using the Sapiens™ TLS the ECG waveforms can be unambiguously mapped to specific catheter tip locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described in Section 3.1.-3.6, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Per institutional guidelines and in accordance with clinical judgment, in indicated patients, and under the conditions described by this User's Manual, Sapiens™ TLS may be used in conjunction with ultrasound-guided vein puncture or open vein access to replace chest X-ray and fluoroscopy for intra- and post-procedural central venous catheter tip location confirmation.

Using Sapiens™ TLS, central venous catheter tip location can be documented for the patient's chart either on paper or electronically.

Using Sapiens™ TLS, the location of the central venous catheter tip can be determined and documented as required by the different types of central venous catheters and by different institutional guidelines, for example:

1. When the tip of a PICC catheter must be placed in the lower third of the superior vena cava, the ECG waveforms illustrated in Figure 7 must be detected and documented at the tip of the PICC catheter.
2. When during intra-procedural catheter insertion or, at later times, during periodical post-procedural catheter tip verification, the long end of a hemodialysis catheter must be placed in the right atrium while its short end must be placed at the caval-atrial junction, then the ECG waveform in Figure 9 must be detected and documented at the long tip and, respectively, the ECG waveform in Figure 8 must be detected and documented at the short tip of the hemodialysis catheter.
3. When the tip of a central venous catheter (CVC) or of an implantable port must be placed at the caval-atrial junction, then an ECG waveform like the one in Figure 8 must be detected and documented at the tip of the catheter.

4. Error Messages and Troubleshooting

1. Electrodes not connected
If Sapiens™ TLS does not detect any connection of electrodes to the patient, a message is displayed on the status bar (5) in Figure 3. In such a case, verify that the skin electrodes are well attached to the patient's skin, that the ECG cable clips are well attached to the snap nipple on the electrodes and that the Sapiens™ TLS Adaptors are well connected to the red clip of the ECG cable. Verify that the ECG cable is well attached to the ECG module. If the error situation persists, you may replace the ECG skin electrodes with new ones. If the problem persists, contact your Romedex representative.
2. ECG module not connected
If Sapiens™ TLS does not detect the presence of an ECG module, a message is displayed on the status bar (5) in Figure 3. In such a case, verify that the USB cable between the ECG module and the laptop is well connected. Close and reopen the Sapiens™ TLS software. If the problem persists, contact your Romedex representative.
3. Battery status

The battery status is displayed on the task bar of the Windows operating system. To check battery status, close the Sapiens™ TLS software and point the mouse cursor to the battery icon on the Windows task bar. When finished, reopen the Sapiens™ TLS software.

4. Printer error

A printer error message is displayed when printing if the printer is not connected or if it is out of paper. Check the printer connection and paper status and try again. If the problem persists, contact your Romedex representative.

5. Cleaning and Disinfection

To clean the Sapiens™ TLS system:

1. Turn off the system
2. Dampen a nonabrasive cloth with either warm water or rubbing alcohol
3. Gently wipe the dampened cloth over the exterior surfaces of the ECG module and of the laptop.

For a list of disinfectants recommended for use please contact Romedex International.

Warning: Do not submerge the Sapiens™ TLS ECG module or the laptop or allow fluid to enter any of the connectors.

6. Warranty

The manufacturer, Romedex International Srl, warrants this product against defects in material and workmanship for a period of one year from the date of original purchase, and during such period agrees to repair, or at Romedex International's discretion, replace any defective unit free of charge. The warranty on the repaired or replaced unit continues from the purchase date of the original unit. This warranty does not cover damages resulting from misuse, abuse, modification, or alteration of the Sapiens™ TLS.

The following actions void the warranty of the Sapiens™ TLS:

1. Opening or servicing the ECG module or the laptop
2. Removal of system labels by anyone other than by Romedex authorized service personnel
3. Connecting the ECG module to any unauthorized laptop
4. Connecting any unauthorized peripheral to the laptop
5. Installing software on the laptop other than by authorized Romedex personnel or under authorized Romedex personnel guidance.

7. Service and Repair

For servicing information or to return your Sapiens™ TLS for repair, please contact Romedex International's technical support at service@romedex.com.

Warning: Only qualified personnel should attempt to service the Sapiens™ TLS system.

8. Technical Specifications

1. Laptop: ASUS Eee 900HA or better, 100-240V, 50/60 Hz
2. Laptop power consumption: Less than 40W
3. Operating system: Windows XP or later
4. ECG module: 4-lead, full patient isolation, defibrillation protected
5. Dimensions ECG module: 0.8" x 2.4" x 4" (2 cm x 6 cm x 10 cm)
6. Connector type: USB
7. ECG cable: 4-lead, 10 ft (3 m)
8. IEC 60601-1: Type CF Applied Part when used with the Sapiens TLS or Arrow-Johans Adaptors

9. Disposal Information

To return the Sapiens™ TLS for end of life recycling please contact your nearest Romedex sales or distributor office in the country of purchase.

10. Contact Information

For additional information and training materials, please go to the Romedex International web site: www.romedex.com.

If you have any questions or comments regarding the use of this product please contact:

*Romedex International Srl
58 Aleea Arubium Str
Bucharest, 022944 Romania
Tel: +40.743.490.892
Fax: +40.317.107.048
Email: info@romedex.com*

11. References

- a. *Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation*, by Nancy Moureau et al. published in the Journal of the Association for Vascular Access in 2010, JAVA Vol. 15 No. 1 2010, pp. 9-15
- b. *The ECG method for positioning the tip of PICCs: results from two preliminary studies*, by Mauro Pittiruti et al. published in the Journal of the Association for Vascular Access in 2008, JAVA Vol. 13 No. 4 2008, pp. 112-119

evGuide-Sapiens™ TLS ADAPTOR

INSTRUCTIONS FOR USE

DESCRIPTION:

- Sapiens™ TLS Adaptor is a family of sterile adaptors made of medical grade materials to facilitate placement of central venous access devices. Sapiens™ TLS adaptors are packaged in sterile individual pouches. Alternatively, the Sapiens™ TLS adaptors can be included in venous access device kits by the corresponding manufacturer of market available devices, e.g., PICC, CVC, hemodialysis catheters, implantable ports, and other central lines.
- The Sapiens™ TLS Adaptor must be used with the Sapiens™ Tip Location System. The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients. Limiting but not contraindicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous veins which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location. Please refer to the Sapiens™ TLS system User's Manual.
- The Sapiens™ TLS Electrical Adaptor, the adaptor is a sterile 39" long isolated stainless steel wire with a plug connector at one end and an alligator clip at the other end. The alligator clip is used to attach the Sapiens™ TLS adaptor to any commercially available stylet or guidewire used for central venous catheter placement. The plug connector is used to connect the adaptor to the ECG cable provided with the Sapiens™ TLS system.
- The Sapiens™ TLS Electrical Adaptor can also be used in combination with the Arrow-Johans Adaptor (Teleflex). In such a situation, the alligator clip of the Electrical Adaptor must be connected to the snap connector of the Arrow-

Johans Adaptor.

CONTRAINDICATIONS:

- All contraindications of central venous catheters apply as specified by the central venous catheter manufacturer.
- There are no contraindications specific to the Sapiens™ TLS Adaptor

POSSIBLE COMPLICATIONS:

- All complications indicated by the manufacturer of the central venous catheter should be considered when using the Sapiens™ TLS adaptor.
- There are no complications specific to the Sapiens™ TLS Adaptor.

WARNINGS:

- Refer to the Sapiens™ TLS User's Manual, its warnings and precautions when considering using Sapiens™ TLS for catheter tip placement confirmation.
- Monitor catheter tip placement per institutional policy.
- Release the central venous catheter after insertion according to your institution's guidelines.
- The Sapiens™ TLS only works for a sinus rhythm of the heart.
- Do not release the central venous catheter based on Sapiens™ TLS information if the signal on the screen is unstable or does not show the ECG waveforms as illustrated in Figures 4 through 9 and according to the Sapiens™ TLS User's Manual. In such a case, use a different method for guiding the placement of your central line as indicated by the institutional guidelines and clinical judgement, e.g., chest X-ray or fluoroscopy.
- If the Sapiens™ TLS Adaptor becomes damaged, remove the adaptor with caution as to not change the position of the catheter.
- The Sapiens™ TLS Adaptor is for Single Use Only.
- Sapiens™ TLS Adaptor is sterilized by ethylene oxide (ETO).
- Do not re-sterilize the adaptor or accessories by any method.
- The manufacturer shall not be liable for any damages caused by reuse or re-sterilization of this adaptor or accessories.
- Contents are sterile in an unopened, undamaged package.

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- Do not use adaptor or accessories if package is opened or damaged.
- The Sapiens™ TLS Adaptor is not intended to diagnose or treat disease.

PRECAUTIONS:

- Do not use sharp instruments near the adaptor.
- Adaptor may be damaged if clamps other than what is provided are used.
- Examine adaptor before each insertion for damage.
- Read instructions carefully before using this device. The adaptor should be manipulated by a qualified, licensed physician or other qualified health care professional.
- The medical techniques and procedures described in these instructions for use do not represent all medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgment in treating any specific patient.
- Use standard hospital protocols when applicable.
- Discard gloves and change to a new pair of sterile gloves after connecting the Adaptor to the Sapiens™ TLS System and completing the setup of the Sapiens™ TLS System per User's Manual.
- Beware of the adaptor wire. Tripping over the adaptor might cause malfunction of the adaptor, detachment of the adaptor connectors from the system or injuries for the user.

Note: After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations

Note: For detailed central venous catheter preparation and insertion information, follow the instructions stated in the catheter's Instruction for Use provided by the catheter manufacturer.

ELECTRICAL VS. SALINE ADAPTORS

The choice between using the Sapiens™ TLS Electrical Adaptor or the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor is a matter of user preference and workflow optimization and is potentially subject to institutional guidelines. Please refer also to the Instructions for Use of the respective adaptors.

Typical situations for using the Sapiens™ TLS Electrical Adaptor are:

1. Placement of open-ended PICCs with pre-inserted stylets and luer-locks which allow for stylet position control
2. Implantable ports using open vein access with over-the-guidewire catheter placement
3. Any central venous catheter inserted over a guidewire with centimeter markings

Typical situations for using the combination between the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor are:

1. Any post-procedural tip location verification of any central venous catheter type
2. Placement of closed-end PICCs
3. Placement of central venous catheters using the modified Seldinger technique (MST) which do not have pre-inserted stylets, e.g., tunneled catheters like Broviac catheters.
4. Any central venous catheter inserted over a guidewire without centimeter markings, e.g., CVCs.
5. Hemodialysis catheters which may require tip location verification for both ends: the long distal end in the right atrium and the short distal end at the caval-atrial junction.

WORKFLOW

1. Attach ECG skin electrodes as indicated by the Sapiens™ TLS User's Manual.
2. Prepare patient and insert the central venous access device according to institutional protocols and the device instructions for use.
3. When using the Sapiens™ TLS Electrical Adaptor, Figure 1, expose the stylet pre-inserted in the catheter at the distal end close to the touyh borst. Open the Adaptor package and take out the Sapiens™ TLS Adaptor wire. Attach the mini-grabber connector to the exposed stylet close to the touyh borst. Follow the catheter manufacturer's instructions regarding the use of the stylet during procedure. Place the catheter onto the patient where sterile field is established. Clip the Sapiens™ TLS Adaptor wire to the sterile drape to ensure the catheter stays in the sterile field.
4. When using the Sapiens™ TLS Electrical Adaptor in combination with the Arrow-Johans Adaptor, Figure 3, attach the alligator clip of the Electrical Adaptor to the snap clip of the Arrow-Johans Adaptor.
5. In either configuration, attach the plug connector of the Sapiens™ TLS Adaptor wire

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to the red lead of the ECG cable provided with the Sapiens™ TLS System according to User's Manual.

6. The ECG patterns provided by the Sapiens™ TLS Adaptor and System, Figures 4 through 9, may be considered in assessing catheter tip location. Please refer to the Sapiens™ TLS User's Manual for detail information, warnings and precautions regarding tip location confirmation.

WARNING: Failure to verify catheter placement may result in serious trauma or fatal complications.

7. When using the Electrical Adaptor, disconnect the alligator clip from the stylet or guidewire. Remove stylet according to the manufacturer's instructions.
8. Record catheter length, catheter lot number, adaptor's lot number and tip position on patient's chart.
9. Record patient name, catheter length on the Sapiens™ TLS graphical user interface
10. Document tip location by printing using Sapiens™ TLS.

CATHETER TIP PLACEMENT VERIFICATION

As described herein and in the Sapiens™ TLS User's Manual, using the Sapiens™ TLS the ECG waveforms can be unambiguously mapped to specific catheter tip locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment. Per institutional guidelines and in accordance with clinical judgment, in indicated patients, and under the conditions described by this User's Manual, Sapiens™ TLS may be used in conjunction with ultrasound-guided vein puncture or open vein access to replace chest X-ray and fluoroscopy for intra- and post-procedural central venous catheter tip location confirmation.

Using Sapiens™ TLS, central venous catheter tip location can be documented for the patient's chart either on paper or electronically.

Using Sapiens™ TLS, the location of the central venous catheter tip can be determined and documented as required by the different types of central venous catheters and by different institutional guidelines, for example:

1. When the tip of a PICC catheter must be placed in the lower third of the superior vena cava, the ECG waveforms illustrated in Figure 7 must be detected and documented at the tip of the PICC catheter.
2. When during intra-procedural catheter insertion or, at later times, during periodical post-procedural catheter tip verification, the long end of a hemodialysis catheter must be placed in the right atrium while its short end must be placed at the caval-atrial junction, then the ECG waveform in Figure 9 must be detected and documented at the long tip and, respectively, the ECG waveform in Figure 8 must be detected and documented at the short tip of the hemodialysis catheter.
3. When the tip of a central venous catheter (CVC) or of an implantable port must be placed at the caval-atrial junction, then an ECG waveform like the one in Figure 8 must be detected and documented at the tip of the catheter.

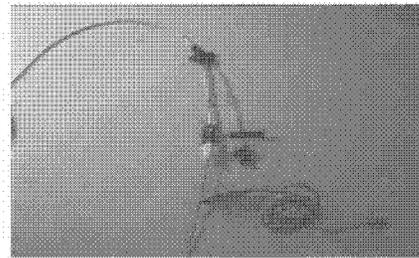


Figure 1: SAPIENS™ TLS Electrical Adaptor

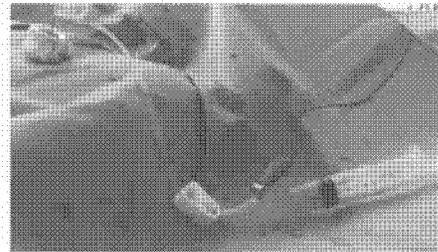


Figure 3: Sapiens™ TLS Electrical Adaptor in combination with Arrow-Johans Adaptor

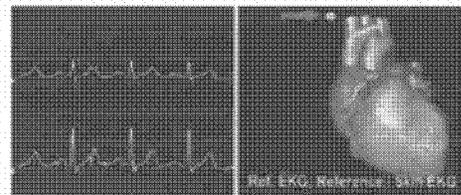


Figure 4: Tip outside thoracic cavity

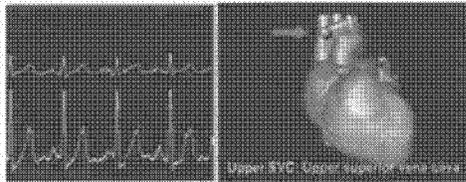


Figure 5: Tip in upper SVC

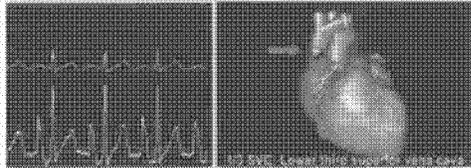


Figure 6: Tip in lower third of SVC

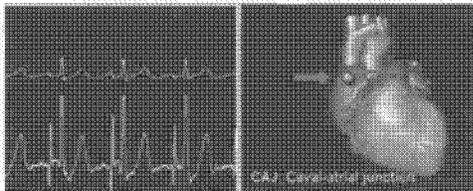


Figure 7: Tip at caval-atrial junction

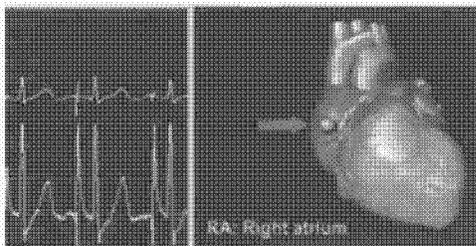


Figure 8: Tip in the right atrium



Figure 9: Tip in the inferior vena cava

If you have any questions or comments regarding this product, contact

Romedex International Srl
58 Aleea Arubium Str
Bucharest, 022944 Romania
Tel: +40.743.490.892
Fax: +40.317.107.048
Email: info@romedex.com

CONTACT INFORMATION

For additional information, please go to the Romedex International web site:
www.romedex.com.



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

March 31, 2010

ROMEDEX INTERNATIONAL SRL
C/O SORIN GRUNWALD
175 COLORADO AVENUE
PALO ALTO, CALIFORNIA 94303
UNITED STATES
ATTN: SORIN GRUNWALD

510k Number: K093775

Product: EVGUIDE TIP LOCATION SYSTEM

Extended Until: 06/29/2010

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and Radiological Health

ROMEDEX INTERNATIONAL SRL

Aleea Arubium, nr.58, sector.2, Bucharest, 022944, ROMANIA
Tel: +1.650.209.4838 Fax: +1.650.887.0348 email: info@romedex.com
www.romedex.com

FDA CDRH DMC

MAR 31 2010,

Received

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002

RE: K093775 – Response to Request for Additional Information

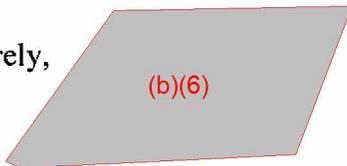
Attention: Mr.Nikhil Thakur, Lead Reviewer

March 30th, 2010

Dear Mr. Thakur,

In regard to your email of 3/4/10 requesting additional information for the Romedex International 510(k), K093775, we have determined that we require additional time to fully respond to the Agency's questions. Therefore we respectfully request an extension of 90 days from the date of this letter. We intend to submit the full response by June 29, 2010. Please contact me at the email address below if you should have any questions or concerns.

Sincerely,



(b)(6)

Sorin Grunwald Ph.D.
Romedex International, Srl
sorin@romedex.com

K44



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

March 04, 2010

ROMEDEX INTERNATIONAL SRL
C/O SORIN GRUNWALD
175 COLORADO AVENUE
PALO ALTO, CALIFORNIA 94303
UNITED STATES
ATTN: SORIN GRUNWALD

510k Number: K093775

Product: EVGUIDE TIP LOCATION SYSTEM

We are holding your above-referenced Premarket Notification (510(k)) for 30 days pending receipt of the additional information that was requested by the Office of Device Evaluation. Please remember that all correspondence concerning your submission MUST cite your 510(k) number and be sent in duplicate to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>.

The deficiencies identified represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceProvisionsofFDAModernizationAct/ucm136685.htm>.

If after 30 days the additional information (AI), or a request for an extension of time, is not received, we will discontinue review of your submission and proceed to delete your file from our review system (21 CFR 807.87(l)). Please note our guidance document entitled, "Guidance for Industry and FDA Staff, FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm>. Pursuant to 21 CFR 20.29, a copy of your 510(k) submission will remain in the Office of Device Evaluation. If you then wish to resubmit this 510(k) notification, a new number will be assigned and your submission will be considered a new premarket notification submission.

Please remember that the Safe Medical Devices Act of 1990 states that you may not place this device into commercial distribution until you receive a decision letter from FDA allowing you to do so.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,



Marjorie Shulman

Consumer Safety Officer

Premarket Notification Section

Office of Device Evaluation

Center for Devices and Radiological Health



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

December 09, 2009

ROMODEX INTERNATIONAL SRL
C/O SORIN GRUNWALD
175 COLORADO AVE.
PALO ALTO, CALIFORNIA 94303
UNITED STATES
ATTN: SORIN GRUNWALD

510k Number: K093775

Received: 12/8/2009

Product: EVGUIDE TIP LOCATION SYSTEM

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act(Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you when the processing of your 510(k) has been completed or if any additional information is required. **YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.**

Please remember that all correspondence concerning your submission **MUST** be sent to the Document Mail Center (DMC) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

On September 27, 2007, the President signed an act reauthorizing medical device user fees for fiscal years 2008 - 2012. The legislation - the Medical Device User Fee Amendments of 2007 is part of a larger bill, the Food and Drug Amendments Act of 2007. Please visit our website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/default.htm>

for more information regarding fees and FDA review goals. In addition, effective January 2, 2008, any firm that chooses to use a standard in the review of ANY new 510(k) needs to fill out the new standards form (Form 3654) and submit it with their 510(k). The form may be found at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm>.

We remind you that Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the PHS Act by adding new section 402(j) (42 U.S.C. § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Section 402(j) requires that a certification form <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm> accompany 510(k)/HDE/PMA submissions. The agency has issued a draft guidance titled: "Certifications To Accompany Drug, Biological

Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007”
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134034.htm>. According to the draft guidance, 510(k) submissions that do not contain clinical data do not need the certification form.

Please note the following documents as they relate to 510(k) review: 1) Guidance for Industry and FDA Staff entitled, “Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs and BLA Supplements”. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. Please refer to this guidance for information on a formalized interactive review process. 2) Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm>. In addition, the 510(k) Program Video is now available for viewing on line at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm>.

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have questions on the status of your submission, please contact DSMICA at (301)796-7100 or the toll-free number (800)638-2041, or at their internet address <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have procedural questions, please contact the 510(k) Staff at (301)796-5640.

Sincerely,

510(k) Staff

K093115

510(k) Premarket Notification

evGUIDE™ TIP LOCATION SYSTEM

Romedex International Srl

43

November 15th, 2009

58 Aleea Arubium
Bucharest, 022944 Romania
Tel: 650.209.4838
Fax: 650.887.0348
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sorin@romedex.com

FDA establishment registration number: 3007923075

Received
DEC 08 2009
FDA CDRH DMC

Romedex International Srl - Confidential Information

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II

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B	<p>Labeling</p> <ol style="list-style-type: none"> 1. evGuide TLS User's Manual 2. evGuide TLS Saline and Electrical Adaptors Instructions for Use 3. evGuide TLS System product label 4. evGuide TLS Saline and Electrical Adaptors product labels 5. Predicate Device Labeling (where available)
C	<p>Software Documentation</p> <ol style="list-style-type: none"> 1. Software Design Control SOP 2. Off-the-Shelf Software Validation SOP 3. Software Requirements Specification 4. Software Risk and Hazard Analysis Matrix 5. Software Design Description 6. Software bill of materials 7. Software installation instructions
D	<p>EMC & Electrical Safety Testing</p> <ol style="list-style-type: none"> 1. EMC: Radiated emissions (EN 55011, 2007) 2. EMC: Radiated RF Immunity IEC/EN 60601-1-2 (EN 61000-4-3 2003/2006) 3. Electrostatic discharge IEC/EN 60601-1-2 (EN 61000-4-2 2003/2006) 4. Hi-pot testing (IEC/EN 60601-1-1 2000/2001) 5. Leakage currents testing (IEC/EN 60601-1-1 2000/2001)
E	<p>Product and Design Specification</p> <ol style="list-style-type: none"> 1. Marketing requirements 2. Product requirements specifications 3. Adaptor design specifications and drawings 4. ECG module design overview

F	Risk Management <ol style="list-style-type: none"> 1. Risk and Hazard Analysis Matrix – evGuide TLS system 2. Risk and Hazard Analysis Matrix – evGuide TLS adaptors (saline and electrical) 3. Risk and Hazard Analysis Matrix – evGuide TLS software
G	System Performance Testing (software and system) <ol style="list-style-type: none"> 1. System and software verification testing protocols and reports 2. System and software validation testing protocols and reports 3. Adapter test protocols 4. Adapter test reports 5. Traceability analysis
H	Published Paper Regarding Catheter Placement Under ECG Guidance <ol style="list-style-type: none"> 1. Paper by Dr. Pittiruti, published in JAVA 2008
I	Clinical Experience <ol style="list-style-type: none"> 1. Clinical experience
J	Certifications of main suppliers <ol style="list-style-type: none"> 1. Romedex International – Supplier approval SOP 2. Incerplast 3. Modenplast 4. Medlab 5. OTMD 6. OICPE
K	Sterilization and Biocompatibility <ol style="list-style-type: none"> 1. Sterilization batch release results 2. Biocompatibility – Certificates of Conformance 3. Sterilization validation protocol
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1. MEDICAL DEVICE USER FEE COVER SHEET

DEC 08 2009

Approved: OMB No. 0910-511 Expiration Date: January 31, 2010. See Instructions for OMB Statement.

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION MEDICAL DEVICE USER FEE COVER SHEET		PAYMENT IDENTIFICATION NUMBER: MD6046572-956733 Write the Payment Identification number on your check.	
A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: http://www.fda.gov/oc/mdufma/cover-sheet.html			
1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code) ROMEDEX INTERNATIONAL SRL 58 Aleea Arubium Bucharest 022944 RO 1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)		2. CONTACT NAME Sorin Grunwald 2.1 E-MAIL ADDRESS sorin@romedex.com 2.2 TELEPHONE NUMBER (include Area code) 16502094838 2.3 FACSIMILE (FAX) NUMBER (Include Area code) 16508870348	
3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/oc/mdufma)			
Select an application type: <input checked="" type="checkbox"/> Premarket notification(510(k)); except for third party <input type="checkbox"/> 513(g) Request for Information <input type="checkbox"/> Biologics License Application (BLA) <input type="checkbox"/> Premarket Approval Application (PMA) <input type="checkbox"/> Modular PMA <input type="checkbox"/> Product Development Protocol (PDP) <input type="checkbox"/> Premarket Report (PMR) <input type="checkbox"/> Annual Fee for Periodic Reporting (APR) <input type="checkbox"/> 30-Day Notice		3.1 Select a center <input checked="" type="checkbox"/> CDRH <input type="checkbox"/> CBER 3.2 Select one of the types below <input checked="" type="checkbox"/> Original Application Supplement Types: <input type="checkbox"/> Efficacy (BLA) <input type="checkbox"/> Panel Track (PMA, PMR, PDP) <input type="checkbox"/> Real-Time (PMA, PMR, PDP) <input type="checkbox"/> 180-day (PMA, PMR, PDP)	
4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status) <input type="checkbox"/> YES, I meet the small business criteria and have submitted the required qualifying documents to FDA <input checked="" type="checkbox"/> NO, I am not a small business 4.1 If Yes, please enter your Small Business Decision Number:			
5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA? <input checked="" type="checkbox"/> YES (All of our establishments have registered and paid the fee, or this is our first device, and we will register and pay the fee within 30 days of FDA's approval/clearance of this device.) <input type="checkbox"/> NO (If "NO," FDA will not accept your submission until you have paid all fees due to FDA. This submission will not be processed; see http://www.fda.gov/cdrh/mdufma for additional information)			
6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.			
<input type="checkbox"/> This application is the first PMA submitted by a qualified small business, including any affiliates <input type="checkbox"/> This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only		<input type="checkbox"/> The sole purpose of the application is to support conditions of use for a pediatric population <input type="checkbox"/> The application is submitted by a state or federal government entity for a device that is not to be distributed commercially	
7. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA). <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO			
8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION \$4,007.00		27-Nov-2009	

Form FDA 3601 (01/2007)

"Close Window" Print Cover sheet

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
DEVICE FACILITY USER FEE

PAYMENT IDENTIFICATION NUMBER: **50016777**
Include the Payment Identification Number (PIN) with payment.

The following actions must be taken to properly submit your payment:

1. To submit payment, please select one of the following options:

A. To pay electronically using ACH (electronic check from a US bank) or a credit card, please select the "Pay Now" option.

B. To pay using a check drawn on a US bank in US dollars, please follow these instructions:

- Make check payable to the Food and Drug Administration
- Write the payment identification number (PIN) on the check
- Mail check and a printed copy of the order to:
Food and Drug Administration
P.O. Box 70961
Charlotte, NC 28272-0961

OR

- For checks sent by courier, mail the check and printed copy of the order to:
Wachovia Bank
Attn: Food and Drug Administration Lockbox 70961
1525 West WT Harris Blvd., Room D1113-022
Charlotte, NC 28262

Note: This Wachovia Bank address is for courier delivery only; do not send mail to this address.

C. To pay by wire transfer, please read the following:

You are responsible to pay any administrative costs associated with the processing of a wire transfer. Contact your bank or financial institution regarding the additional fees.

US Department of Treasury
TREAS NYC
33 Liberty Street
New York, NY 10045

FDA Deposit Account Number: 75060099
Beneficiary: Food and Drug Administration, 1350 Piccard Drive, Suite 200A, Rockville, MD 20850
US Department of Treasury routing/transit number: 021030004
SWIFT Number: FRNYUS33

You must include the user fee payment identification number (PIN), and ensure that the fee that your bank will charge for the wire transfer is added to your fee payment.

2. Company Name and Address

ROMEDEX INTERNATIONAL SRL
58 Aleea Arubium
Bucharest 022944
RO

2.1 Employer Identification Number (EIN)

3. Contact Name

Sorin Grunwald

3.1 E-mail Address

sorin@romedex.com

3.2 Telephone Number

16502094838

3.3 Fax Number

16508870348

4. PIN-PCN (Payment Identification Number-Payment Confirmation Number):

50016777-10119756

5. Amount Due:

\$2,008.00

01-Oct-2009

[Close](#)

[Print Order](#)

2. CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number (if known)
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SECTION A					TYPE OF SUBMISSION				
PMA <input type="checkbox"/> Original Submission <input type="checkbox"/> Premarket Report <input type="checkbox"/> Modular Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment <input type="checkbox"/> Licensing Agreement	PMA & HDE Supplement <input type="checkbox"/> Regular (180 day) <input type="checkbox"/> Special <input type="checkbox"/> Panel Track (PMA Only) <input type="checkbox"/> 30-day Supplement <input type="checkbox"/> 30-day Notice <input type="checkbox"/> 135-day Supplement <input type="checkbox"/> Real-time Review <input type="checkbox"/> Amendment to PMA & HDE Supplement <input type="checkbox"/> Other	PDP <input type="checkbox"/> Original PDP <input type="checkbox"/> Notice of Completion <input type="checkbox"/> Amendment to PDP	510(k) <input checked="" type="checkbox"/> Original Submission: <input checked="" type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated (Complete section I, Page 5) <input type="checkbox"/> Additional Information <input type="checkbox"/> Third Party	Meeting <input type="checkbox"/> Pre-510(K) Meeting <input type="checkbox"/> Pre-IDE Meeting <input type="checkbox"/> Pre-PMA Meeting <input type="checkbox"/> Pre-PDP Meeting <input type="checkbox"/> Day 100 Meeting <input type="checkbox"/> Agreement Meeting <input type="checkbox"/> Determination Meeting <input type="checkbox"/> Other (specify):	IDE <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	Humanitarian Device Exemption (HDE) <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment	Class II Exemption Petition <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Evaluation of Automatic Class III Designation (De Novo) <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Other Submission <input type="checkbox"/> 513(g) <input type="checkbox"/> Other (describe submission):
IDE <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	Humanitarian Device Exemption (HDE) <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment	Class II Exemption Petition <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Evaluation of Automatic Class III Designation (De Novo) <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Other Submission <input type="checkbox"/> 513(g) <input type="checkbox"/> Other (describe submission):					

Have you used or cited Standards in your submission? Yes No (If Yes, please complete Section I, Page 5)

SECTION B				SUBMITTER, APPLICANT OR SPONSOR			
Company / Institution Name Romedex International Srl			Establishment Registration Number (if known) 3007923075				
Division Name (if applicable)			Phone Number (including area code) 650.209.4838				
Street Address 58 Alcea Arubium			FAX Number (including area code) 650.887.0348				
City Bucharest		State / Province		ZIP/Postal Code 022944		Country ROMANIA	
Contact Name Sorin GRUNWALD PhD							
Contact Title Managing Director			Contact E-mail Address sorin@romedex.com				

SECTION C				APPLICATION CORRESPONDENT (e.g., consultant, if different from above)			
Company / Institution Name							
Division Name (if applicable)			Phone Number (including area code) 650.209.4838				
Street Address 175 Colorado Av.			FAX Number (including area code) 650.887.0348				
City Palo Alto		State / Province CA		ZIP Code 94303		Country USA	
Contact Name Sorin GRUNWALD PhD							
Contact Title US FDA Agent for Romedex International Srl			Contact E-mail Address sorin@romedex.com				

SECTION D1

REASON FOR APPLICATION - PMA, PDP, OR HDE

<input type="checkbox"/> New Device <input type="checkbox"/> Withdrawal <input type="checkbox"/> Additional or Expanded Indications <input type="checkbox"/> Request for Extension <input type="checkbox"/> Post-approval Study Protocol <input type="checkbox"/> Request for Applicant Hold <input type="checkbox"/> Request for Removal of Applicant Hold <input type="checkbox"/> Request to Remove or Add Manufacturing Site	<input type="checkbox"/> Change in design, component, or specification: <input type="checkbox"/> Software / Hardware <input type="checkbox"/> Color Additive <input type="checkbox"/> Material <input type="checkbox"/> Specifications <input type="checkbox"/> Other (<i>specify below</i>)	<input type="checkbox"/> Location change: <input type="checkbox"/> Manufacturer <input type="checkbox"/> Sterilizer <input type="checkbox"/> Packager
<input type="checkbox"/> Process change: <input type="checkbox"/> Manufacturing <input type="checkbox"/> Packaging <input type="checkbox"/> Sterilization <input type="checkbox"/> Other (<i>specify below</i>)	<input type="checkbox"/> Labeling change: <input type="checkbox"/> Indications <input type="checkbox"/> Instructions <input type="checkbox"/> Performance Characteristics <input type="checkbox"/> Shelf Life <input type="checkbox"/> Trade Name <input type="checkbox"/> Other (<i>specify below</i>)	<input type="checkbox"/> Report Submission: <input type="checkbox"/> Annual or Periodic <input type="checkbox"/> Post-approval Study <input type="checkbox"/> Adverse Reaction <input type="checkbox"/> Device Defect <input type="checkbox"/> Amendment
<input type="checkbox"/> Response to FDA correspondence:		<input type="checkbox"/> Change in Ownership <input type="checkbox"/> Change in Correspondent <input type="checkbox"/> Change of Applicant Address
<input type="checkbox"/> Other Reason (<i>specify</i>):		

SECTION D2 REASON FOR APPLICATION - IDE

<input type="checkbox"/> New Device <input type="checkbox"/> New Indication <input type="checkbox"/> Addition of Institution <input type="checkbox"/> Expansion / Extension of Study <input type="checkbox"/> IRB Certification <input type="checkbox"/> Termination of Study <input type="checkbox"/> Withdrawal of Application <input type="checkbox"/> Unanticipated Adverse Effect <input type="checkbox"/> Notification of Emergency Use <input type="checkbox"/> Compassionate Use Request <input type="checkbox"/> Treatment IDE <input type="checkbox"/> Continued Access	<input type="checkbox"/> Change in: <input type="checkbox"/> Correspondent / Applicant <input type="checkbox"/> Design / Device <input type="checkbox"/> Informed Consent <input type="checkbox"/> Manufacturer <input type="checkbox"/> Manufacturing Process <input type="checkbox"/> Protocol - Feasibility <input type="checkbox"/> Protocol - Other <input type="checkbox"/> Sponsor	<input type="checkbox"/> Response to FDA Letter Concerning: <input type="checkbox"/> Conditional Approval <input type="checkbox"/> Deemed Approved <input type="checkbox"/> Deficient Final Report <input type="checkbox"/> Deficient Progress Report <input type="checkbox"/> Deficient Investigator Report <input type="checkbox"/> Disapproval <input type="checkbox"/> Request Extension of Time to Respond to FDA <input type="checkbox"/> Request Meeting <input type="checkbox"/> Request Hearing
<input type="checkbox"/> Report submission: <input type="checkbox"/> Current Investigator <input type="checkbox"/> Annual Progress Report <input type="checkbox"/> Site Waiver Report <input type="checkbox"/> Final		
<input type="checkbox"/> Other Reason (<i>specify</i>):		

SECTION D3 REASON FOR SUBMISSION - 510(k)

<input checked="" type="checkbox"/> New Device	<input type="checkbox"/> Additional or Expanded Indications	<input type="checkbox"/> Change in Technology
<input type="checkbox"/> Other Reason (<i>specify</i>):		

Section 2 14

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed				Summary of, or statement concerning, safety and effectiveness information	
1	LJS	2	LDF	3	DQY
4		5		6	DQY
7		8		9	
				<input checked="" type="checkbox"/> 510 (k) summary attached <input type="checkbox"/> 510 (k) statement	

Information on devices to which substantial equivalence is claimed (if known)					
	510(k) Number		Trade or Proprietary or Model Name		Manufacturer
1	K091324	1	Sherlock 3CG TPS	1	Bard Access Systems
2	K032613	2	Transvenous Pacemaker Placement Assist Device	2	Peter Rothenberg
3	K973371	3	Conduction Anesthesia Kit - Certodyn	3	B. Braun Medical
4	K843263	4	Arrow-Johans ECG Adaptor	4	Teleflex/Arrow International
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name
 Vascular Access Catheter Accessories

	Trade or Proprietary or Model Name for This Device	Model Number
1	evGuide Tip Location System (TLS)	1
2		2
3		3
4		4
5		5

FDA document numbers of all prior related submissions (regardless of outcome)					
1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission
 Laboratory Testing Animal Trials Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code LJS	C.F.R. Section (if applicable) 880.5970	Device Class <input type="checkbox"/> Class I <input checked="" type="checkbox"/> Class II <input type="checkbox"/> Class III <input type="checkbox"/> Unclassified
Classification Panel General Hospital		

Indications (from labeling)
 The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide™ Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.

FDA Document Number (if known)

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

<input checked="" type="checkbox"/> Original <input checked="" type="checkbox"/> Add <input checked="" type="checkbox"/> Delete		Facility Establishment Identifier (FEI) Number		<input checked="" type="checkbox"/> Manufacturer <input checked="" type="checkbox"/> Contract Sterilizer <input checked="" type="checkbox"/> Contract Manufacturer <input checked="" type="checkbox"/> Repackager / Relabeler	
Company / Institution Name (b)(4)			Establishment Registration Number (b)(4)		
Division Name (if applicable)			Phone Number (including area code) (b)(4)		
Street Address (b)(4)			FAX Number (including area code) (b)(4)		
City (b)(4)		State / Province		ZIP Code	Country (b)(4)
Contact Name (b)(4)		Contact Title (b)(4)		Contact E-mail Address (b)(4)	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		Facility Establishment Identifier (FEI) Number		<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer <input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler	
Company / Institution Name			Establishment Registration Number		
Division Name (if applicable)			Phone Number (including area code)		
Street Address			FAX Number (including area code)		
City		State / Province		ZIP Code	Country
Contact Name		Contact Title		Contact E-mail Address	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		Facility Establishment Identifier (FEI) Number		<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer <input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler	
Company / Institution Name			Establishment Registration Number		
Division Name (if applicable)			Phone Number (including area code)		
Street Address			FAX Number (including area code)		
City		State / Province		ZIP Code	Country
Contact Name		Contact Title		Contact E-mail Address	

Section 2 13

Note: Complete this section if your application or submission cites standards or includes a "Declaration of Conformity to a Recognized Standard" statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
(b)(4)	(b) 13485	ANSI/AAMI/ISO	Medical devices - quality management systems - requirements for regulatory devices (b)(4)	2003	
(b)(4)	14971	ANSI/AAMI/ISO	(b)(4) Medical devices - application of risk management to medical devices (b)(4)	2007	
(b)(4)	11135-1	ISO	Sterilization of health care products - ethylene oxide - part 1: Requirements for development, validation, and routing control of a sterilization process for medical devices (b)(4)	2007	(b)(4)
(b)(4)	10993 -4, -5, -6, -7, -10	ISO	Biological evaluation of medical devices - Part 1: Evaluation and testing	2002, 1999, 1994, 2008, 2002	
(b)(4)	60601-1-1 60601-1-2	IEC/EN	Safety standards for electrical medical equipment	2000/2001 2003/2006	
(b)(4)	594-2	ISO	Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment - Part 2: Lock fittings	1998	
(b)(4)	1041	BS EN	Information supplied by the manufacturer of medical devices	2008	

Please include any additional standards to be cited on a separate page.

Public reporting burden for this collection of information is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of the Chief Information Officer (HFA-710)
5600 Fishers Lane
Rockville, Maryland 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

CDHR PREMARKET REVIEW SUBMISSION COVER SHEET**Romedex International Srl****EvGuide Tip Location System****SECTION I - ADDITIONAL STANDARDS CITED IN THE SUBMISSION**

FDA forms 3654 are attached in Appendix L

8	Standards No.	Standards Organization	Standards Title	Version	Date
	980	EN	Graphical symbols for use in labeling of medical devices	2008	
9	Standards No.	Standards Organization	Standards Title	Version	Date
	55011	EN	Industrial, scientific and medical RF equipment – radio disturbances characteristics – limits and methods	2007	
10	Standards No.	Standards Organization	Standards Title	Version	Date
	730	IEEE	Software Quality Assurance	1998	
11	Standards No.	Standards Organization	Standards Title	Version	Date
	829	IEEE	Software test documentation	1998	
12	Standards No.	Standards Organization	Standards Title	Version	Date
	830	IEEE	Recommended practices for software requirements specification	1993	
13	Standards No.	Standards Organization	Standards Title	Version	Date
	1058	IEEE	Software Project management	1998	
14	Standards No.	Standards Organization	Standards Title	Version	Date
	1074	IEEE	Developing software life cycle	1997	
15	Standards No.	Standards Organization	Standards Title	Version	Date
	J-STD-06	IEEE	Software development plan	1995	

3. 510(K) COVER LETTER

November 15-th, 2009

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

CONFIDENTIAL & PROPRIETARY

Re: **TRADITIONAL 510(k)**

Device Trade name:	evGuide™ Tip Location System
Common and Usual Name:	Vascular Access Catheter Accessories
Classification Name:	Percutaneous, Implanted, Long-Term Intravascular Catheter
	21 CFR §880.5970, Class II
Classification Code:	LJS
Classification Panel :	General Hospital

Dear Sir/Madam,

In accordance with section 510(k) of the Federal Food, Drug and Cosmetic Act, amended by the FDA Modernization Act, Romedex International Srl (www.romedex.com) is notifying the FDA of its intent to introduce into interstate commerce the evGuide™ Tip Location System (TLS). The evGuide™ Tip Location System (TLS) also known under the trade name Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as peripherally inserted central catheters (PICCs), central venous catheters (CVCs), implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

The evGuide™ TLS also known under the trade name Sapiens™ Tip Location System (TLS) has obtained the CE mark and is currently commercialized in Europe.

The evGuide™ TLS consists of three components:

- 1) The evGuide™ TLS Saline Adaptor is a sterile, single-use disposable device that connects the proximal end hub of any commercially available central venous catheter with the evGuide™ TLS System to provide cardiac electrical signals using the column of saline method.
- 2) The evGuide™ TLS Electrical Adaptor is a sterile, single-use disposable that connects the proximal end of any commercially available guidewire or stylet used in the placement of central venous catheters with the evGuide™ TLS System to provide cardiac electrical signals.

- 3) The evGuide™ TLS system contains an ECG module, a laptop, connection cables and software with capabilities to acquire and display cardiac electrical signals.

Contained in the subject 510(k) is the information to support a substantial equivalence rationale for each of the evGuide™ TLS components and Romedex International Srl hereby submits this Traditional Premarket Notification for the evGuide™ TLS as a whole.

Romedex International Srl believes that the evGuide™ TLS System is substantially equivalent to the following currently marketed predicate devices:

- (1) Sherlock 3CG Tip Positioning System marketed by Bard Access Systems (K091324, cleared Aug 7, 2009, product code LJS, regulation number 880.5970)
- (2) Transvenous Pacemaker Placement Assist Device by Peter Rothenberg (K032613, cleared Nov 20, 2003, product code LDF, regulation number 870.3680)
- (3) Conduction Anesthesia Kit marketed by B. Braun Medical (K973371, cleared Nov 24, 1997, product code DQY, regulation number 870.1250)
- (4) Arrow-Johans ECG Adaptor marketed by Teleflex/Arrow International (K843263, cleared Sep 20, 1984, product code DQY, regulation number 870.1250).

This Premarket Notification is submitted in duplicate along with the basis for the substantial equivalency determination. A brief comparison of the subject device with the currently marketed predicate device along with a summary of verification and validation activities are included to support substantial equivalence of the subject and predicate device.

Romedex International Srl considers the information described in this Premarket Notification and its appendices to be confidential commercial information, and therefore exempt from public disclosure. We request that this notification be treated as confidential commercial information in accordance with 21 CFR Section 20.61(b).

If there are any questions concerning this 510(k) Premarket Notification, please contact me by desk phone at Tel: 650.209.4838, by email at: sorin@romedex.com, or by fax at: 650.887.0348.

Sincerely,

(b)(6)

Sorin Grunwald Ph.D., Managing Director, Romedex International Srl

Enclosures

- Traditional 510(k) – in duplicate
- CDRH Premarket Review Submission Cover Sheet (Included in submission binder)
- Medical Device User Fee Confirmation and Cover Sheet (Included in submission binder)



4. INDICATIONS FOR USE STATEMENT

510(k) Number (if known): ___ Not known at this time ___ ___

Device Name: evGuide™ TLS

Indications for Use:

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide™ Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

Prescription Use (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Page ___ of ___
(Posted November 13, 2003)

5. 510(K) SUMMARY

510(k) SUMMARY

Proprietary Name: evGuide™ Tip Location System

Device Name: evGuide™ Tip Location System

Device Trade name:	evGuide™ Tip Location System
Common and Usual Name:	Vascular Access Catheter Accessories
Classification Name:	Percutaneous, Implanted, Long-Term Intravascular Catheter
Classification Code:	21 CFR §880.5970, Class II
Classification Panel :	LJS General Hospital

Manufacturer: Romedex International Srl
58 Aleea Arubium
Bucharest, 022944 Romania
Tel: 650.209.48.38
www.romedex.com
FDA establishment registration number: 3007923075

Contact: Sorin Grunwald
175 Colorado Ave
Palo Alto, CA 94303
Tel: 650.209.4838
Fax: 650.887.0348

Preparation Date: November 15th, 2009

Intended Use:

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

Predicate Devices:

The evGuide TLS is substantially equivalent to the following currently marketed predicate device:

- (1) Sherlock 3CG Tip Positioning System marketed by Bard Access Systems (K091324, cleared Aug 7, 2009, product code LJS, regulation number 880.5970)
- (2) Transvenous Pacemaker Placement Assist Device by Peter Rothenberg (K032613, cleared Nov 20, 2003, product code LDF, regulation number 870.3680)
- (3) Conduction Anesthesia Kit marketed by B. Braun Medical (K973371, cleared Nov 24, 1997, product code DQY, regulation number 870.1250)

- (4) Arrow-Johans ECG Adaptor marketed by Teleflex/Arrow International (K843263, cleared Sep 20, 1984, product code DQY, regulation number 870.1250).

System Description:

The evGuide TLS consists of the following elements:

1. Sterile evGuide TLS Electrical Adaptor
2. Sterile evGuide TLS Saline Adaptor
3. Skin ECG electrodes (supplied by user)
4. evGuide TLS ECG module
5. ECG cable
6. PC/Laptop running evGuide TLS software
7. USB connection cable to the cardiac electrical signal (ECG) module
8. Label printer (optional)

System Use:

When a central venous catheter or its associated stylet is connected to the evGuide TLS system via the evGuide TLS Saline or Electrical Adaptors, the evGuide TLS PC/Laptop screen displays cardiac electric or endovascular ECG signals acquired at the location of the tip of the catheter. The waveforms provided by evGuide TLS can be used for guiding the placement of the central venous catheter. The evGuide TLS must be used in accordance to the evGuide TLS User's Manual and the Instructions for Use. The central venous catheter must be used in accordance to the manufacturer's Instructions for Use.

Technological Characteristics of Substantial Equivalence:

The evGuide Tip Location System (TLS) consists of a sterile electrical adaptor, a sterile saline adaptor (connection assemblies), an ECG module and data acquisition and display software running on a laptop. Optionally, a printer can be attached to evGuide TLS. The system is designed to aid in central venous catheter tip positioning through ECG signal information. The evGuide TLS detects and displays a cardiac electrical signal from three ECG electrodes, including the evGuide electrical or saline adaptor and two body electrodes, which provide catheter tip positioning information.

Performance Data:

Bench and laboratory test results, preclinical tests results and the clinical experience support the performance characteristics of evGuide TLS and show that evGuide TLS is safe and effective. These results validate the performance of all the components of evGuide TLS and of the system as a whole.

Summary of Substantial Equivalence:

The evGuide TLS has the same combined intended use and utilizes the same fundamental scientific technology as that of the referenced predicate devices. The results of performance testing demonstrate substantial equivalence of the evGuide TLS to the legally marketed predicate devices. Any differences between the subject and predicate devices do not raise new issues of safety and effectiveness.



6. TRUTHFUL AND ACCURACY STATEMENT

PREMARKET NOTIFICATION

TRUTHFUL AND ACCURACY STATEMENT

[As Required by 21 CFR 807.87(k)]

I certify that, in my capacity as Managing Director of *Romedex International Srl.*, I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

(b)(6)



(Signature)

Sorin Grunwald

(Typed Name)

(Date)

12 / 5 / 2009

7. CLASS III SUMMARY AND CERTIFICATION

This section is not applicable. The evGuide TLS (Adaptors and System) fall under the FDA's Classification for a Class II device.



8. FINANCIAL CERTIFICATION OR DISCLOSURE STATEMENT

This section is not applicable.

9. DECLARATIONS OF CONFORMITY AND SUMMARY REPORTS

This section is not applicable.

10. EXECUTIVE SUMMARY

Background:

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health care institutions and as documented in many papers including the one attached in **Appendix H**: "The ECG method for positioning the tip of PICCs: results from two preliminary studies" by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008.

Figure 10.1 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community (**Appendix H**).

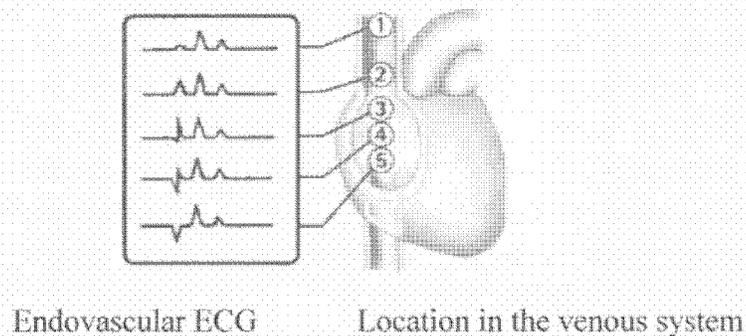


Figure 10.1: Changes in the ECG waveform as function of location in the vasculature (from Dr. M. Pittiruti, **Appendix H**)

The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the "red" or "right shoulder" electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A "giant" P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface ECG, the tip of the electrode is in the superior vena cava vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava). Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, which are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Indications for Use

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

evGuide™ TLS Overview

The evGuide TLS consists of the evGuide Saline Adaptor, the evGuide Electrical Adaptor, an ECG Module and an ECG cable, a laptop, and the evGuide TLS application software. The evGuide TLS components excluding the evGuide Adaptors are also referred to as the evGuide TLS System. An optional printer can be connected to the laptop for documentation purposes. The evGuide TLS Saline Adaptor can be connected to any commercially available central venous catheters and the evGuide TLS Electrical Adaptor to any commercially available stylets or guidewires used for the placement of central venous catheters. The evGuide system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, or intracavitary ECG) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and acquired in real time through the evGuide adaptors. Thus, the waveforms presented on the evGuide TLS graphical user interface can aid the placement of central venous catheters.

The components of the evGuide TLS are illustrated in Figure 10.2:

1. Sterile evGuide TLS Electrical Adaptor (6)
2. Sterile evGuide TLS Saline Adaptor
3. Skin ECG electrodes (supplied by user) (7)
4. evGuide TLS ECG module (1)
5. ECG cable (5)
6. PC/Laptop running evGuide TLS software (2)
7. USB connection cable to the cardiac electrical signal (ECG) module (3)
8. Label printer (optional) (4)

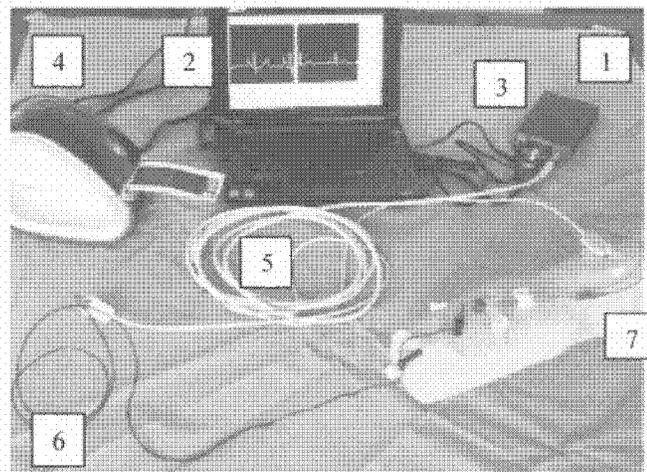


Figure 10.2: evGuide TLS – system configuration

The evGuide TLS software displays on the screen (Figure 10.3) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated below, the user can estimate the location of the catheter tip. For example, in the Figure 10.3 the large waveform on the bottom of the right hand side of the screen is representative of a location very close to the sino-atrial node (the pacemaker of the heart) and the large waveform on the bottom left hand side of the screen shows a waveform representative of the lower third of the superior vena cava. The smaller waveforms in the upper half of both screens shows the skin ECG signal used for comparison.

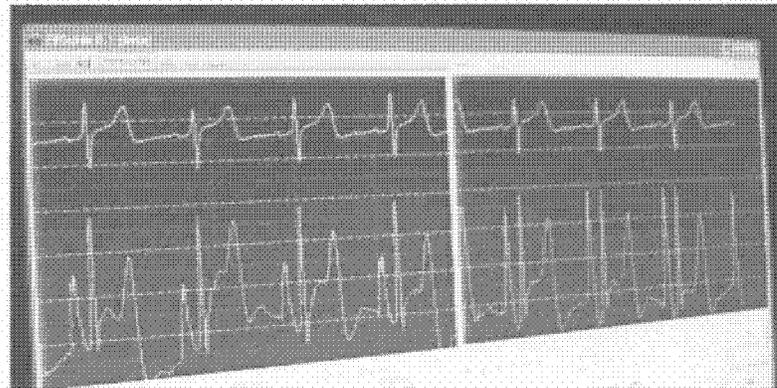


Figure 10.3: Typical evGuide TLS display with reference screen and waveforms

The evGuide TLS Saline Adaptor (Figure 10.4) is a sterile device which can be used with the “column of saline” endovascular technique. In this technique, saline is injected from a syringe into the catheter lumen providing a conductive path between the catheter hub (proximal end) and the catheter tip (distal end). The evGuide TLS saline adaptor (1) is connected between the proximal end of a commercially available catheter (3) and the saline filled syringe (2), commercially available. An electrical wire (4) is integrated by construction in the adaptor (1) in such a way as to provide electrical conductivity between the saline solution inside the adaptor and the electrical connector at the other end of the wire (5). The electrical wire is an isolated multi-threaded stainless steel wire, 39 inches long.

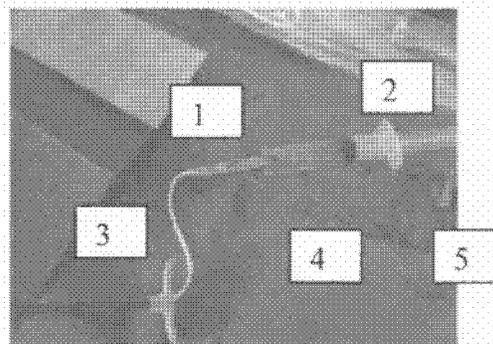


Figure 10.4: evGuide TLS Saline Adaptor

The evGuide TLS Electrical Adaptor is a sterile device and is shown in Figure 10.5. The device consists of a 39 inches isolated electrical wire (3) having an alligator or a clip connector at one end (1) and a nipple connector (2) at the other end. In use, the alligator/clip connector is connected to a commercially available stylet or guidewire inserted in the central venous catheter to be placed and the nipple connector (2) is connected to the red (Right Arm) clip of the standard ECG cable provided with the evGuide TLS system. Through this electrical connection, the evGuide TLS system can measure and display endovascular ECG waveforms at the distal end of the catheter tip. The electrical wire (3) is an isolated multi-threaded stainless steel wire, 39 inches long.

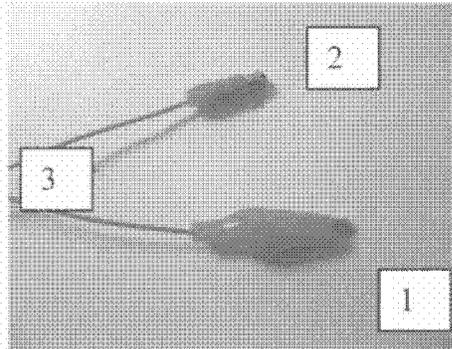


Figure 10.5: evGuide TLS Electrical Adaptor

Substantial Equivalence Discussion:

Romedex International Srl believes that evGuide TLS is substantially equivalent to the following currently marketed predicate devices:

- (1) Sherlock 3CG Tip Positioning System marketed by Bard Access Systems (K091324, cleared Aug 7, 2009, product code LJS, regulation number 880.5970)
- (2) Transvenous Pacemaker Placement Assist Device by Peter Rothenberg (K032613, cleared Nov 20, 2003, product code LDF, regulation number 870.3680)
- (3) Conduction Anesthesia Kit marketed by B. Braun Medical (K973371, cleared Nov 24, 1997, product code DQY, regulation number 870.1250)
- (4) Arrow-Johans ECG Adaptor marketed by Teleflex/Arrow International (K843263, cleared Sep 20, 1984, product code DQY, regulation number 870.1250).

Tables 10.1, 10.2, and 10.3 summarize the device comparison between evGuide TLS and the selected predicate devices.

Table 10.1: Comparison of evGuide TLS – Electrical Adaptor with predicate devices

No	Characteristic	Subject Device evGuide TLS – Electrical Adaptor	Predicate Device Conduction Anesthesia Kit Certodyn	Predicate Device Transvenous Pacemaker Placement Assist Device
1	510(k) Clearance	Subject 510(k)	K973371	K032613
2	Classification	Class II	Class II	Class II
3	Indication Statement	<i>The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.</i>	<i>To aid in the accurate placement of central venous catheters using the RAECG technique</i>	<i>This device is designed to connect an intravascular electrode to a monitor through a standard EKG patient lead for the purpose of displaying an intravascular signal in real-time. Only the black pinjack is "active". The red pinjack is electrically blind and designed to isolate the proximal electrode from inadvertent stimulation</i>
4	Design1	Wire length: 39"	Wire length: 39"	Wire length: 24"
5	Design2	Electrical resistance < 10 Ohm	Electrical resistance < 10 Ohm	Electrical resistance < 10 Ohm
6	Materials1	PVC Isolated stainless steel threaded wire	Isolated stainless steel threaded wire	Isolated stainless steel threaded wire
7	Materials2	PVC Isolated stainless steel alligator clip	Isolated stainless steel alligator clip	Isolated stainless steel grabber
8	Materials3	Solder paste	Solder paste	Solder paste
9	Materials4	Stainless steel ECG cable connector	Stainless steel ECG cable connector	Stainless steel ECG cable connector

Table 10.2: Comparison of evGuide TLS – Saline Adaptor with predicate devices

Item No	Characteristic	Subject Device evGuide TLS – Saline Adaptor	Predicate Device Arrow-Johans ECG Adaptor
1	510(k) Clearance	Subject 510(k)	K843263
2	Classification	Class II	Class II
3	Indication for Use Statement	<i>The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.</i>	<i>The adaptor is to be used in the placement of central venous catheters and more accurately diagnosing atrial dysrhythmias.</i>
4	Design 1	Adaptor with a female Luer Lock fitting at one end and a cone fitting at the other end	Adaptor with a female Luer Lock fitting at one end and a male Luer Lock fitting at the other end
5	Design2	Wire length: 39"	N/A
6	Design3	Electrical resistance < 10 Ohm	Electrical resistance < 10 Ohm
7	Materials1	(b)(4)	(b)(4)
8	Materials2	(b)(4)	(b)(4)
9	Materials3	(b)(4)	(b)(4)
10	Materials4	Solder paste	Adhesive
11	Materials5	Stainless steel ECG cable connector	Gold plated stainless steel ECG cable connector

Table 10.3: Comparison of evGuide TLS – System with predicate devices

Item No	Characteristic	Subject Device evGuide TLS	Predicate Device Sherlock 3CG TPS
1	510(k) Clearance	Subject 510(k)	K091324
2	Classification	Class II	Class II
3	Indication for Use Statement	<i>The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.</i>	<i>The Sherlock 3CG™ Tip Positioning System (TPS) is indicated for central venous catheter guidance and positioning during catheter placement. The Sherlock 3CG™ TPS provides real-time catheter tip location information through the use of passive magnet and cardiac electrical signal detection.</i>
4	Design 1	PC-based design	PC-based design
5	Design 2	Graphical User Interface with real-time and reference display windows	Graphical User Interface with real-time and reference display windows
6	Design 3	Stand-alone ECG data acquisition module connected to skin electrodes via an ECG cable and to a central venous catheter through a sterile electrical wire (Electrical or Saline Adaptor)	Integrated ECG data acquisition module connected to skin electrodes via an ECG cable and to a central venous catheter through a sterile electrical wire
7	Design 4	Print current image to a printer if connected	Print current image to a printer if connected
8	Design 5	External storage device for patient and case data: memory stick	External storage device for patient and case data: memory stick
9	Design 6	Battery operated	Battery operated
10	Design 7	Operating/Storage Humidity Parameters (unpackaged) 5%-85%	Operating/Storage Humidity Parameters (unpackaged) 5%-85%
11	Design 8	Operating temperature 59-100 degrees F	Operating temperature 59-100 degrees F
12	Design 9	Storage temperature (unpackaged) 50-100 degrees F	Storage temperature (unpackaged) 50-100 degrees F

Summary of Device Performance

Sections 14-18 of this submission summarize the various testing activities (Sterilization and shelf life, EMC and Electrical Safety, Performance, Software verification) performed for evGuide TLS and the results of testing. A risk assessment was performed to identify verification and validation activities to ensure that evGuide TLS met the acceptance criteria for durability and performance. The evGuide TLS met all acceptance criteria of the verification testing.

Additionally through validation testing, the evGuide TLS demonstrated that it can successfully meet the requirement for its intended use.

Section 19 includes a summary of an animal study that was conducted to demonstrate that the evGuide TLS provides an aid in the placement of peripherally inserted central catheters by providing real-time catheter tip location information by making use of endovascular ECG waveforms. It also demonstrated that the evGuide TLS is comparable to its predicate as noted above.

Section 20 provides a summary of the clinical experience obtained using evGuide TLS at the Catholic University Hospital Center in Rome, Italy. evGuide TLS also known as Sapiens TLS is CE-marked and has been in use on the market at selected sites in Europe. The clinical experience obtained using evGuide TLS validates that evGuide TLS can be safely and effectively used for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The clinical experience validates that the evGuide Tip Location System can provide real-time catheter tip location information by using the patient's cardiac electrical activity.

waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated below, the user can estimate the location of the catheter tip. For example, in the Figure 11.4 the yellow waveform on the right hand side of the screen is representative of a location very close to the sino-atrial node (the pacemaker of the heart) and the yellow waveform on the left hand side of the screen shows a waveform representative of the lower third of the superior vena cava. The white waveforms on both screens shows the skin ECG signal used for comparison.



Figure 11.4: evGuide TLS reference screen and waveform

The construction and functionality of evGuide TLS is viewed by Romedex International as substantially equivalent to "Sherlock 3CG" manufactured by Bard Access Systems (K091324).

Saline adaptor description:

(b)(4)

As it can be seen in Figure 11.5 and as it results from the Instructions for Use, evGuide TLS Saline Adaptor (1) is never in direct contact with blood. For the short duration of the procedure, sterile saline (crystalloid) solution 0.9% is flushed from a syringe through the Adaptor into one of the lumens of the central venous catheters placed in the patient's vasculature. The saline column flowing from the syringe through the evGuide Adaptor into the catheter is in contact with the patient's blood at the distal tip of the catheter. In this context, Romedex International Srl is providing in Section 15 biocompatibility data

11. DEVICE DESCRIPTION

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health institutions and as documented in many papers including the one attached in **Appendix H**: "The ECG method for positioning the tip of PICCs: results from two preliminary studies" by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008.

The relationship between the ECG waveform and the location around the sino-atrial node of the heart has been extensively documented in the literature and is in use in many clinical institutions world-wide. The paper "The ECG method for positioning the tip of PICCs: results from two preliminary studies" by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008 is attached in **Appendix H** of this submission. Figure 11.1 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community (**Appendix H**).

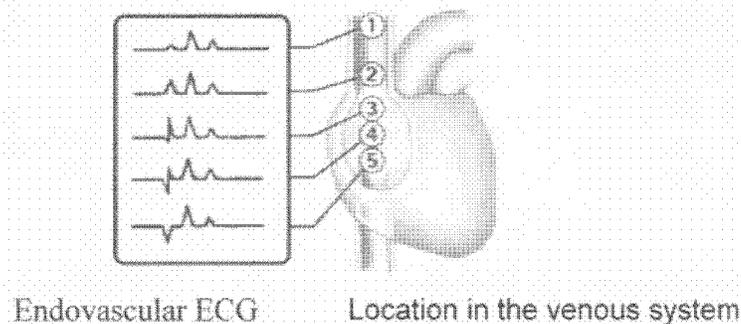


Figure 11.1 Changes of the signal waveform as a function of location according to Dr. Mauro Pittiruti (**Appendix H**)

The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the "red" or "right shoulder" electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A "giant" P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface ECG, the tip of the electrode is in the superior cava vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava). Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients

where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, the use of an additional method is required to confirm catheter tip location.

Several predicate devices including the ones selected for this submission (K091324, K973371, K032613) make use of the above mentioned method for the same guidance purpose. The evGuide™ Tip Location System (TLS) is designed for the same use as the predicate devices with which it is believed to be substantially equivalent.

The evGuide™ Tip Location System (TLS) also known as Sapiens™ Tip Location System (TLS) has obtained the CE mark and is currently commercialized in Europe.

Figure 11.2 (b)(4)

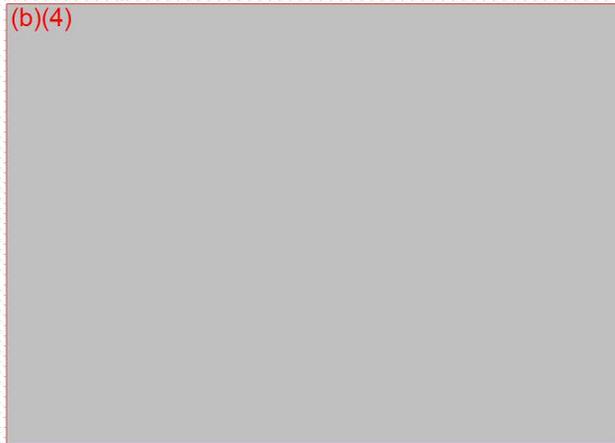


Figure 11.2: (b)(4)

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity. The evGuide TLS system consists of the evGuide Saline Adaptor, the evGuide Electrical Adaptor, an ECG Electronic Module and an ECG cable, a laptop, and the evGuide TLS application software. An optional printer can be connected to the laptop for documentation purposes. The evGuide TLS Saline Adaptor can be connected to any commercially available central venous catheters and the evGuide TLS Electrical Adaptor to any commercially available stylets or guidewires used for the placement of central venous catheters. The evGuide system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, intracavitary ECG, and intravascular ECG or endovascular electrograms) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and acquired in real time through the evGuide adaptors. The endovascular ECG technique currently in use worldwide shows that the endovascular ECG waveform has distinctive shapes in accordance with the location in the

patient's vasculature. Thus, the waveforms presented on the evGuide TLS system graphical user interface can aid the placement of central venous catheters.

The evGuide TLS consists of the following elements seen in the Figure 11.3:

1. Sterile evGuide TLS Electrical Adaptor (6)
2. Sterile evGuide TLS Saline Adaptor
3. Skin ECG electrodes (supplied by user) (7)
4. evGuide TLS ECG module (1)
5. ECG cable (5)
6. PC/Laptop running evGuide TLS software (2)
7. USB connection cable to the cardiac electrical signal (ECG) module (3)
8. Label printer (optional) (4)

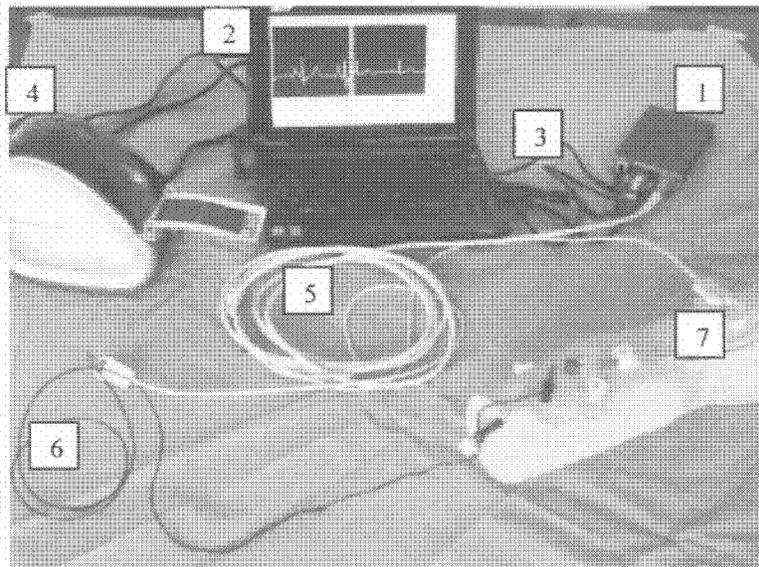


Figure 11.3 evGuide TLS system configuration

During the catheter placement procedure, one or several electrodes (7) are connected to the patient's skin using non-sterile off-the-shelf electrodes and the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the patient's central veins per the institution's guidelines, an evGuide TLS adaptor either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. The sterile evGuide TLS adaptor transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (Figure 11.4) endovascular ECG

for the evGuide Adaptor PVC plastic piece which is in contact with the saline column which is in contact with the patient's blood.

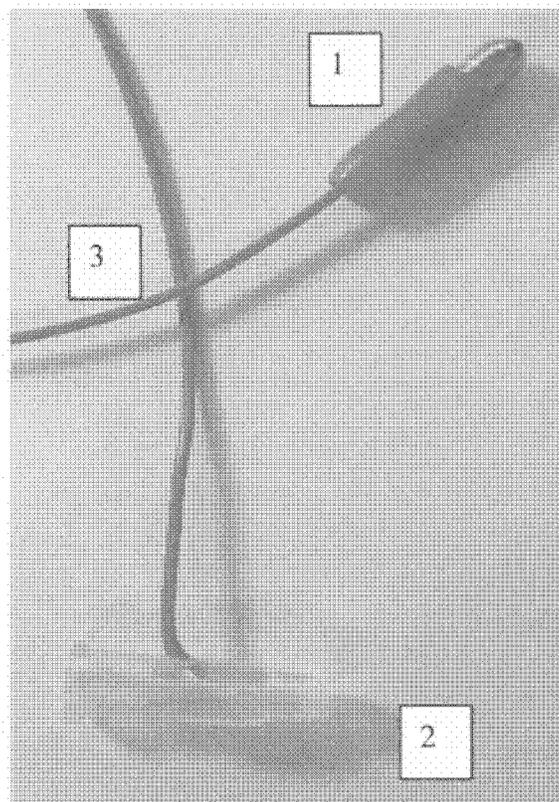


Figure 11.5 evGuide TLS Saline Adaptor

In a typical clinical setting, the evGuide TLS Saline adaptor is connected between a syringe and a central venous catheter hub as shown in Figure 11.6.

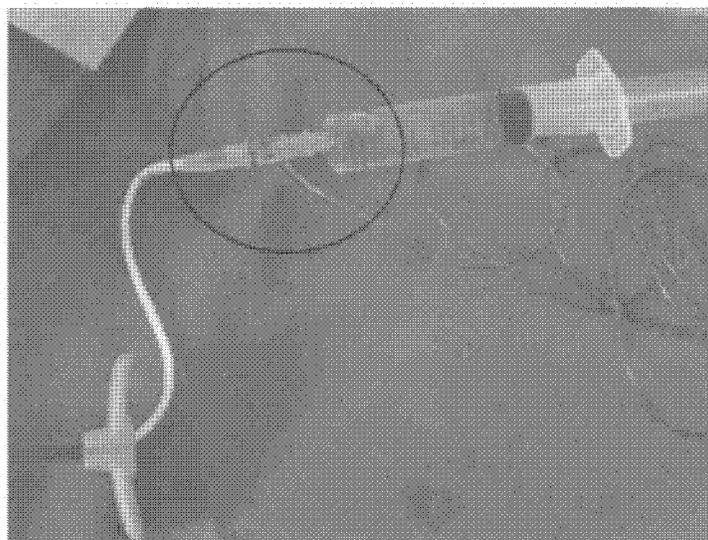


Figure 11.6 evGuide TLS Saline Adaptor in clinical use

(b)(4)



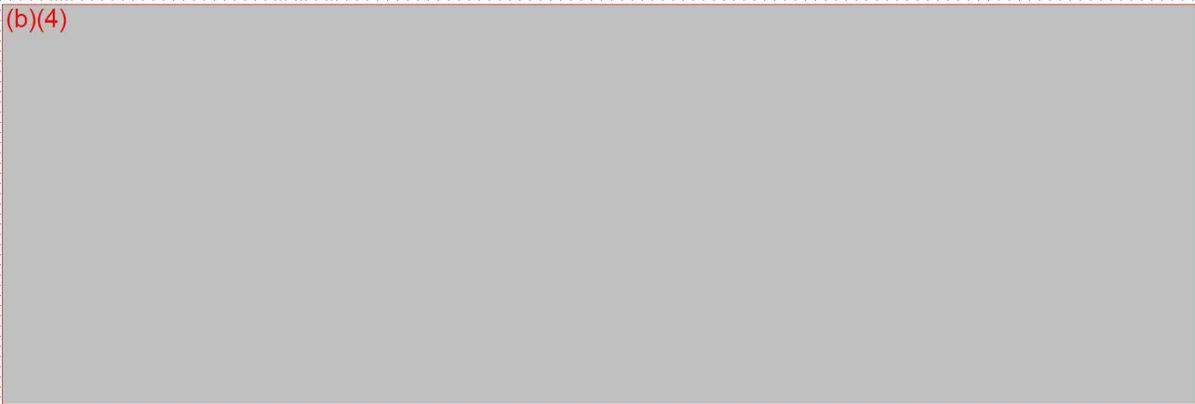
Figure 11.7: evGuide Saline Adaptor - Detail

The construction and functionality of the evGuide TLS Saline Adaptor is viewed by Romedex International as substantially equivalent to the device “Certodyn” manufactured by B.Braun Medical (K973371) and to the device “Johans-Arrow” manufactured by Teleflex/Arrow (K843263).

Electrical adaptor description:

The evGuide TLS Electrical Adaptor in Figure 11.8 makes the connection between a stylet or a guidewire using the alligator clip end (1) and a standard ECG cable using the nipple connector end (2).

(b)(4)



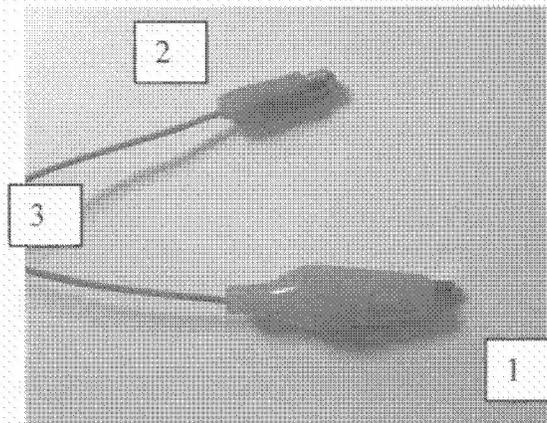


Figure 11.8: evGuide TLS Electrical Adaptor

The construction and functionality of the evGuide TLS Electrical Adaptor is viewed by Romedex International as substantially equivalent to “Conduction Anesthesia Kit Certodyn” manufactured by B.Braun Medical (K973371) and to the “Transvenous Pacemaker Placement Assist Device” by Peter Rothenberg (K032613).

Hardware description:

The evGuide TLS system hardware consists of an ECG acquisition module and a laptop. A standard ECG cable delivered with the evGuide TLS system is used to connect the ECG module to the patient. A USB cable is used to power the ECG module and to ensure data communication between the laptop, i.e., the evGuide TLS software and the ECG module. An optional printer can be connected to the laptop to document to print out ECG waveforms. The laptop is battery powered during the clinical case. Batteries are recharged between clinical cases.

The evGuide TLS software and hardware have been verified and validated at system level according to the requirements for Moderate Level of Concern using the Romedex International procedures and test protocols including the FDA Off-the-Shelf software guidance. The hardware configuration currently used with evGuide TLS and used for evGuide verification and validation testing was an Acer Netbook Inspire One and an Asus Netbook EeePC with the following minimum requirements: (b)(4)

(b)(4)

(b)(4) System verification and validation testing will be performed according to the Romedex protocols each time that the above mentioned software and/or hardware configuration changes.

(b)(4)

(b)(4)



Software description:

(b)(4)



(b)(4)



(b)(4)



(b)(4)



(b)(4)



Figure 11.10: evGuide TLS software: component interaction

Graphical User Interface description:

The graphical user interface of the evGuide TLS system is shown in Figure 11.11.

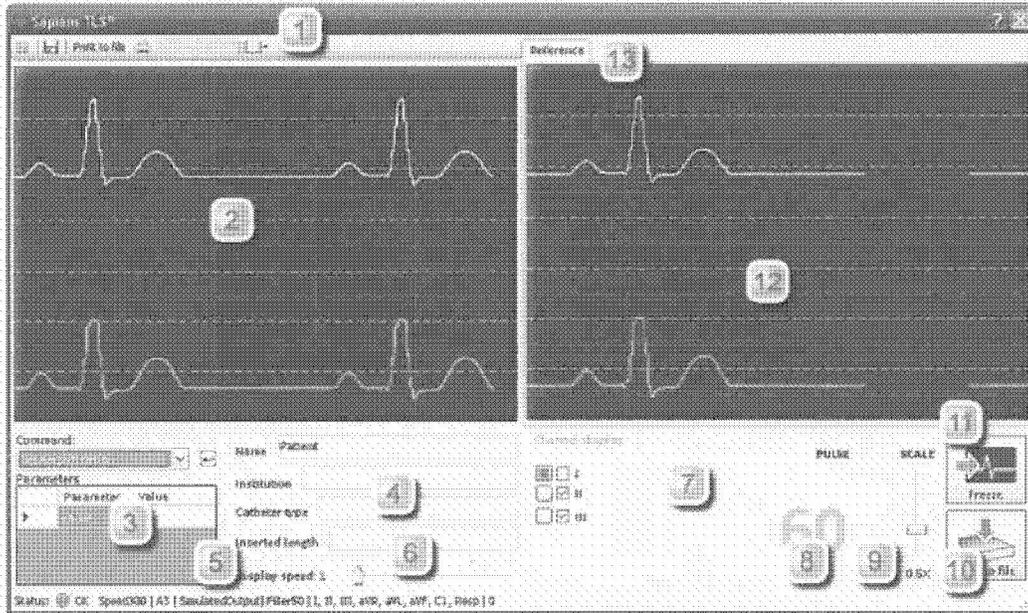


Figure 11.11: evGuide TLS Graphical User Interface

The graphic elements on interface are:

- 1 - Toolbar containing controls for play / pause the data acquisition, load / save ECG files, printing to file / printer, settings and help. The following functions are available on the toolbar:
 - a) Pause/Play the ECG waveform in acquisition and playback modes.
 - b) Save the case to file. When clicking the "Save" icon, all the ECG waveforms (lead I, II, and III) are save in a file. The default name of the file the name of the patient to which the date and time are appended. The default directory is C:/Data created when installing the evGuide TLS application.
 - c) Print to file. Click on the button to select (highlight) it, click again to unselect it. When this button is selected, the printer output will be redirected to a file using a default name and location.
 - d) Print. By clicking this button, the print preview will be displayed. You need to freeze the desired information on the right hand side screen before you can print. The printer output will be redirected to the default printer. A default label printer is preinstalled on your system.
 - e) Clicking on the Help button brings up the User's manual and information about the evGuide TLS software.
 - g) By dragging the question mark to a screen location, certain hints will be provided depending on the location.
 - h) Closes the evGuide TLS application before turning off the computer. If the user accidentally closes it and needs to reopen it again, double click on the evGuide TLS icon on the desktop.
- 2 - Main screen where the graphics are drawn.
- 3 - Available commands accepted by the device and respective parameters
- 4 - 'Patient name', 'institution', 'catheter type' and 'inserted length' information that will be shown on printed label.
- 5 - Status bar displaying various information about ECG module status
- 6 - Scroll bar used for scaling the graphics.
- 7 - Color and visibility setting for channels.
- 8 - Frequency of R-Peaks measured in number of peaks / minute.
- 9 - Scale used to amplify the signals received from device.
- 10 - Pressing this button will save the current image shown in Main screen.
- 11 - Pressing this button will copy the current image shown in Main screen to Secondary screen.
- 12 - Secondary screen used for comparison.
- 13 - Tab container displays the 'Reference' page.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

This information is printed out in the corresponding fields of the print layout in Figure 11.12:

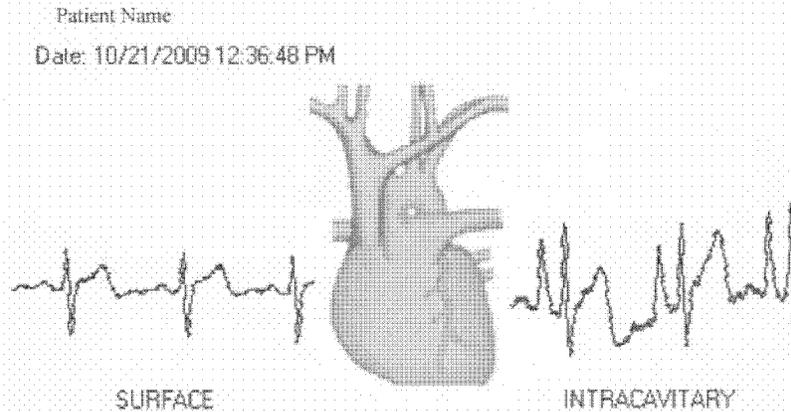


Figure 11.12: Print layout

In Figure 11.12, the SURFACE waveform represents the reference skin ECG lead and the INTRACAVITARY waveform represents the cardiac electrical signal detected at the distal tip of the catheter. The user can mark with a pen on the heart icon on the printout where the user has estimated the tip of catheter to be located at the end of the placement procedure.

The patient name, institution name, catheter type and length, are displayed as well as they were input in the corresponding fields of the graphical user interface.

A Configuration File is stored under C:/Program files/Romedex/EvGuide TLS/EVGuide.exe. The file can be edited with any editor and the parameters manually changed. Only Romedex personnel can edit this file.

In accordance with the FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices from May 11, 2005 the evGuide TLS software level of concern has been evaluated as being MODERATE before mitigating any hazard. The table below documents this assessment. Software documentation is included in this submission in **Appendix C** as required by the Table 3 of the FDA Software Guidance document mentioned above.

The decision making process to assess substantial equivalence has been applied for each of the evGuide TLS elements with respect to the corresponding predicate devices: Saline Adaptor, Electrical Adaptor, and System.

evGuide TLS Electrical Adaptor

Figure 12.2a shows the evGuide TLS Electrical Adaptor, Figure 12.2b shows the Conduction Anesthesia Kit (K973371) and the Figures 12.2c and 12.2d show the Transvenous Pacemaker Placement Assist Device (TPPAD) (K032613). Detailed product specifications for the subject device are provided in **Appendix E**.

The evGuide TLS Electrical Adaptor in Figure 12.2a makes the connection between a stylet or a guidewire using the alligator clip end (1) and a standard ECG cable using the nipple connector end (2). Similarly, the alligator clip (1) in Figure 12.2b connects to a stylet or guidewire, the other end of the wire connects to the switch box (3) and the switch box is connected to a standard ECG cable (2). Also similarly, the grabber in Figure 12.2c (1) connects to a stylet or guidewire, the cable connects to the connection box and the connections box connects to a standard ECG cable (2).

The use of the evGuide TLS Electrical Adaptor as discussed in the Instructions for Use (attached in **Appendix B**) is similar to the use of the predicate devices in clinical practice and as described on their corresponding Web sites.

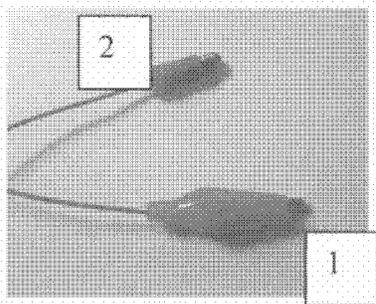


Figure 12.2a: evGuide TLS Electrical Adaptor

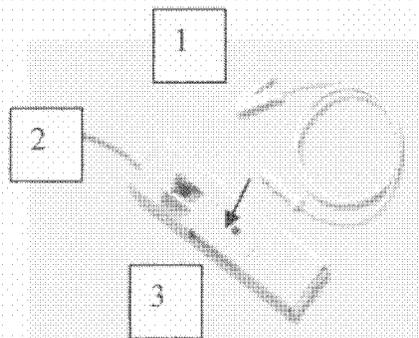


Figure 12.2b: Certodyn RAECG Universal Adaptor (Conduction Anesthesia Kit, K973371)

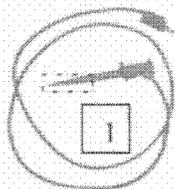


Figure 12.2c: The "Grabber" of the TPPAD (K032613)

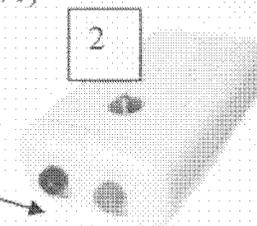


Figure 12.2d: The housing of the TPPAD (K032613)

A list of relevant features for the subject device (evGuide TLS Electrical Adaptor) and the predicate devices (Conduction Anesthesia Kit and Transvenous Pacemaker Placement Assist Device) is contained in Table 12.1. This list is useful in comparing technical characteristics between the subject device and predicate device for determining substantial equivalence.

Table 12.1 evGuide TLS Electrical Adaptor - Comparison of Relevant Features for Substantial Equivalence Determination

No	Characteristic	Subject Device evGuide TLS – Electrical Adaptor	Predicate Device Conduction Anesthesia Kit Certodyn	Predicate Device Transvenous Pacemaker Placement Assist Device
1	510(k) Clearance	Subject 510(k)	K973371	K032613
2	Classification	Class II	Class II	Class II
3	Indication for Use Statement	<i>The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.</i>	<i>To aid in the accurate placement of central venous catheters using the RAECG technique</i>	<i>This device is designed to connect an intravascular electrode to a monitor through a standard EKG patient lead for the purpose of displaying an intravascular signal in real-time. Only the black pinjack is "active". The red pinjack is electrically blind and designed to isolate the proximal electrode from inadvertent stimulation</i>
4	Design1	Wire length: 39"	Wire length: 39"	Wire length: 24"
5	Design2	Electrical resistance < 10 Ohm	Electrical resistance < 10 Ohm	Electrical resistance < 10 Ohm
6	Materials1	PVC insulated stainless steel threaded wire	Isolated stainless steel threaded wire	Isolated stainless steel threaded wire
7	Materials2	PVC insulated stainless steel alligator clip	Isolated stainless steel alligator clip	Isolated stainless steel grabber
8	Materials3	Solder paste	Solder paste	Solder paste
9	Materials4	Stainless steel ECG cable connector	Stainless steel ECG cable connector	Stainless steel ECG cable connector

Substantial Equivalence Decision Making Summary

(b)(4)



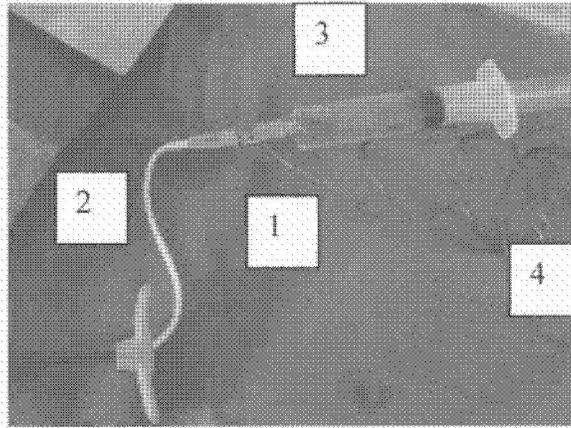


Figure 12.3c: The evGuide TLS Saline adaptor connected to a catheter and a syringe

A list of relevant features for the subject device (evGuide TLS Saline Adaptor) and the predicate device (Arrow-Johans ECG Adaptor) is contained in Table 12.2. This list is useful in comparing technical characteristics between the subject device and predicate device for determining substantial equivalence.

Table 12.2 evGuide TLS Saline Adaptor - Comparison of Relevant Features for Substantial Equivalence Determination

No	Characteristic	Subject Device evGuide TLS – Saline Adaptor	Predicate Device Arrow-Johans ECG Adaptor
1	510(k) Clearance	Subject 510(k)	K843263
2	Classification	Class II	Class II
3	Indication for Use Statement	<i>The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.</i>	<i>The adaptor is to be used in the placement of central venous catheters and more accurately diagnosing atrial dysrhythmias.</i>
4	Design 1	Adaptor with a female Luer Lock fitting at one end and a cone fitting at the other end	Adaptor with a female Luer Lock fitting at one end and a male Luer Lock fitting at the other end
5	Design2	Wire length: 39"	N/A
6	Design3	Electrical resistance < 10 Ohm	Electrical resistance < 10 Ohm
7	Materials1	(b)(4)	(b)(4)

evGuide TLS Saline Adaptor

Figure 12.3a shows the evGuide TLS Saline Adaptor and Figure 12.3b shows the predicate device Arrow-Johans ECG Adaptor (K843263). Detailed product specifications for the subject device are provided in **Appendix E**. The evGuide TLS Saline Adaptor in figure 12.3a consists of a plastic adaptor (2) having a lumen between its two ends and a stainless steel wire (3) inserted in the lumen such that it can provide electrical contact between the wire and saline solution flushed through the adaptor lumen. The stainless steel wire has a nipple connector (1) at its other end in order to be connected to a standard ECG cable.

The Arrow-Johans Adaptor in Figure 12.3b consists of a plastic adaptor (2) having a lumen between its two ends and a gold plated stainless steel piece inserted in the lumen such that it can provide electrical contact between the wire and saline solution flushed through the adaptor lumen. The gold plated stainless steel piece wire has a nipple connector (1) at its other end in order to be connected to a standard ECG cable.

Figure 12.3c shows how the evGuide TLS Saline Adaptor (1) is connected to a catheter (2) and a syringe (3). Similarly, the Arrow-Johans ECG Adaptor can be connected to a catheter and a syringe. In the case of the evGuide TLS Saline Adaptor, the electrical wire (4) attached to the plastic connection piece (2 in Figure 12.3a) between the catheter and the syringe can be connected to a standard ECG cable using the nipple connector (1) in Figure 12.3a. In the case of the Arrow-Johans Adaptor, the plastic connection piece (2 in Figure 12.3b) can be connected between a catheter and a syringe and the nipple connector (1) in Figure 12.3b can be connected to a standard ECG cable. The metal piece (3) ensures electrical connectivity between the inner lumen of (2) and the connector (1).

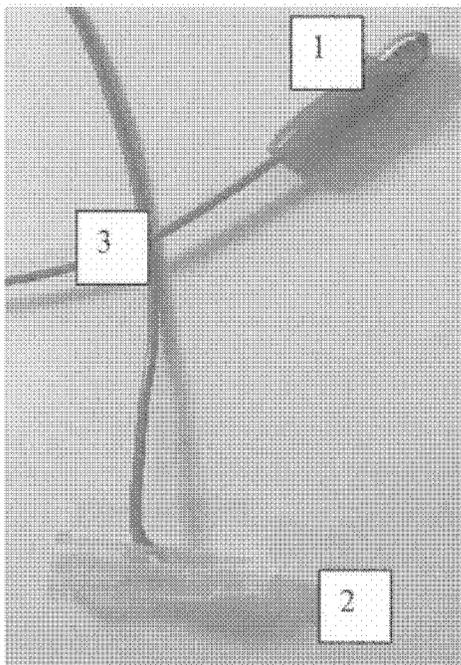


Figure 12.3a: evGuide TLS Saline Adaptor

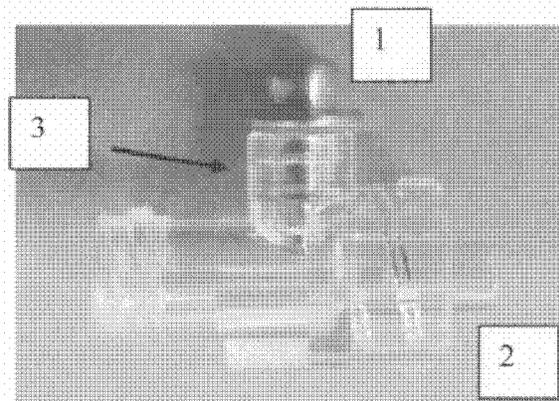


Figure 12.3b: Arrow-Johans ECG Adaptor (K843263)

			(b)(4)
8	Materials2	(b)(4)	(b)(4)
9	Materials3	(b)(4)	(b)(4)
10	Materials4	Solder paste	Adhesive
11	Materials5	Stainless steel ECG cable connector	Gold plated stainless steel ECG cable connector

Substantial Equivalence Decision Making Summary

(b)(4)

proposed evGuide TLS Saline Adaptor is substantially equivalent to the Arrow-Johans ECG Adaptor (K843263).

evGuide TLS System

Figure 12.4a shows the evGuide TLS system and Figure 12.4c its user interface. Figure 12.4b shows the Sherlock 3CG Tip Positioning System (TPS) and Figure 12.4d its user interface. Detailed product specifications for the subject device are provided in **Appendix E** and detailed software documentation for the subject device is provided in **Appendix C**.

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In Figure 12.4a, the evGuide TLS System components are as follows:

1. The User Interface running on a laptop and the ECG data acquisition module (black box)
2. A standard ECG cable (non-sterile)
3. The sterile evGuide TLS Electrical or Saline Adaptor connecting the ECG cable (non-sterile) with the central venous catheter in the sterile field.
4. The sterile insertion site of a central venous catheter to which the evGuide Electrical or Saline Adaptor is connected.

In Figure 12.4b, the Sherlock 3CG TPS System components are as follows:

1. The Integrated User Interface running on the Sherlock 3CG System containing an ECG data acquisition module, an ultrasound imaging system, and a magnetic tip locator device.
2. The ECG cable (non-sterile) connects the detection sensor placed beneath the sterile drape with the Sherlock 3CG System
3. A sterile electrical wire connecting the detection sensor placed beneath the sterile drape with the central venous catheter in the sterile field.
4. The sterile insertion site of a central venous catheter to which the sterile wire is connected.

In the working configuration, the evGuide TLS System provides exactly the same function as the ECG component of the Sherlock 3CG TPS system, which is to provide real-time catheter tip location information using cardiac electrical signals.

In Figure 12.4c, the evGuide TLS graphical user interface illustrates a display window (A) which shows real-time signals as detected by the evGuide TLS System and a display window (B) with frozen waveforms which can be used for comparison.

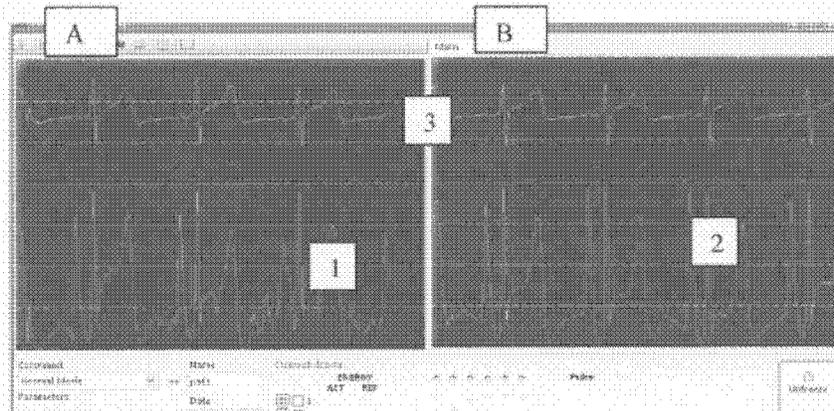


Figure 12.4c: evGuide TLS Graphical User Interface

In Figure 12.4c, the waveform (1) in the current display window (A) shows the real-time cardiac electrical signal detected at the tip of the central venous catheter placed in a patient's vasculature in its current position. The waveform (2) in display window (B) shows the frozen cardiac electrical signal detected at the tip of the central venous catheter placed in a patient's vasculature at a reference location. The differences between the frozen signal (2) and the current real-time signal (1) can be used to assess catheter tip location. The waveform (3) represents a reference skin ECG lead obtained through 2 skin ECG electrodes.

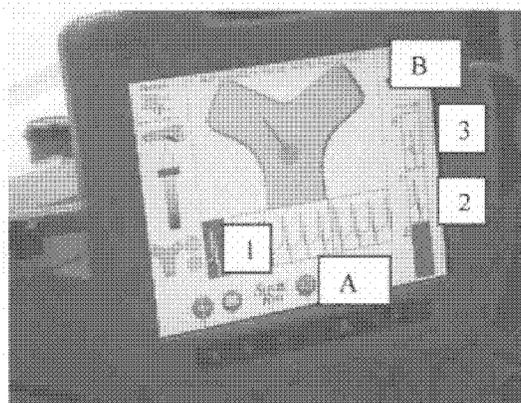


Figure 12.4d Sherlock 3CG TPS Graphical User Interface (K091324)

In Figure 12.4d, the Sherlock 3CG TPS graphical user interface illustrates a display window (A) which shows real-time electrical signals as detected by Sherlock 3CG TPS and a display window (B) with frozen waveforms which can be used for comparison. In Figure 12.4d, the waveform (1) in the current display window (A) shows the real-time cardiac electrical signal detected at the tip of the central venous catheter placed in a patient's vasculature in its current position. The waveform (2) in display window (B) shows the frozen cardiac electrical signal detected at the tip of the central venous catheter placed in a patient's vasculature at a reference location. The differences between the frozen signal (2) and the current real-time signal (1) can be used to assess catheter tip location. The waveform (3) in display window (B) represents a frozen reference skin ECG lead obtained through 2 skin ECG electrodes.

A detailed list of relevant features for the subject device (evGuide TLS System) and the predicate device (Sherlock 3CG TPS) is contained in Table 12.3. This list is useful in comparing technical characteristics between the subject device and predicate device for determining substantial equivalence.

Table 12.3 evGuide TLS System - Comparison of Relevant Features for Substantial Equivalence Determination

Item No	Characteristic	Subject Device evGuide TLS	Predicate Device Sherlock 3CG TPS
1	510(k) Clearance	Subject 510(k)	K091324
2	Classification	Class II	Class II
3	Indication for Use Statement	<i>The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.</i>	<i>The Sherlock 3CG™ Tip Positioning System (TPS) is indicated for central venous catheter guidance and positioning during catheter placement. The Sherlock 3CG™ TPS provides real-time catheter tip location information through the use of passive magnet and cardiac electrical signal detection.</i>
4	Design 1	PC-based design	PC-based design
5	Design 2	Graphical User Interface with real-time and reference display windows	Graphical User Interface with real-time and reference display windows
6	Design 3	Stand-alone ECG data acquisition module connected to skin electrodes via an ECG cable and to a central venous catheter through a sterile	Integrated ECG data acquisition module connected to skin electrodes via an ECG cable and to a central venous catheter through a sterile

		electrical wire (Electrical or Saline Adaptor)	electrical wire
7	Design 4	Print current image to a printer if connected	Print current image to a printer if connected
8	Design 5	External storage device for patient and case data: memory stick	External storage device for patient and case data: memory stick
9	Design 6	Battery operated	Battery operated
10	Design 7	Operating/Storage Humidity Parameters (unpackaged) 5%-85%	Operating/Storage Humidity Parameters (unpackaged) 5%-85%
11	Design 8	Operating temperature 59-100 degrees F	Operating temperature 59-100 degrees F
12	Design 9	Storage temperature (unpackaged) 50-100 degrees F	Storage temperature (unpackaged) 50-100 degrees F

Substantial Equivalence Decision Making Summary

(b)(4)



Statement as the predicate devices and the same Intended Use Statement as the predicate devices. *In vitro* and *in vivo* testing further qualified the equivalence between the subject device and the predicate devices and verified that no safety or effectiveness issues arise when using the subject device for its intended use. The results of this testing are included in the Performance section of this Premarket Notification (Sections 18-20).

Conclusion

Based on the analysis of the new characteristics, on test performed on the subject device, and on the comparison table with the predicate device, Romedex International Srl has concluded that the new characteristics of the subject device do not affect the safety or effectiveness of the subject device as compared to the predicate device. Romedex International Srl believes that the proposed evGuide TLS System is substantially equivalent to Sherlock 3CG Tip Positioning System (K091324).

13. PROPOSED LABELING

Users Manual and Product Labels

The evGuide TLS Saline Adaptor and the evGuide TLS Electric Adaptor are intended and labeled only for single patient use and only by prescription by a physician. The devices shall not be reused or resterilized. A draft evGuide TLS Saline and Electrical Adaptors Instructions for Use is provided in **Appendix B**.

The draft of product label for Saline Adaptor is shown below:

**ROMEDEX INTERNATIONAL SRL
EVGUIDE™ TLS SALINE ADAPTOR**

LOT XXXX-XXXXXX  XXXX-XX
QTY: 1  XXXX-XX



See IFU

Latex Free

Non-Pyrogenic

Rx_{only} Caution: Federal USA Law restricts this device to sale by or on the order of a physician

CE₁₈₆₈



Manufactured by SC Incerplast SA For:
Romedex International Srl
58 Aleea Arubium, 022944 Bucharest, Romania
Tel: +1.650.209.4838, Fax: +1.650.887.0348

The draft of product label for evGuide TLS Electrical Adaptor is shown below:

**ROMEDEX INTERNATIONAL SRL
EVGUIDE™ TLS ELECTRICAL ADAPTOR**

LOT XXXX-XXXXXX  XXXX-XX
QTY: 1  XXXX-XX



See IFU

Latex Free

Rx_{only} Caution: Federal USA Law restricts this device to sale by or on the order of a physician

CE 1868



Manufactured by SC Incerplast SA For:
Romedex International Srl
58 Aleea Arubium, 022944 Bucharest, Romania
Tel: +1.650.209.4838, Fax: +1.650.887.0348

A representative draft User's Manual for evGuide TLS is provided in **Appendix B**. Draft evGuide TLS labels are also provided in **Appendix B**. However, warning labels that will be applied to evGuide TLS labels are provided in the User's Manual.

The draft of product label for the evGuide TLS system is shown below:

ROMEDEX INTERNATIONAL SRL
EVGUIDE™ TLS



XXXX-XXXXXX



XXXX-XX



See User's Manual

CE



Manufactured by SC Incerplast SA For:
Romedex International Srl
58 Aleea Arubium
022944 Bucharest, Romania
Tel: +1.650.209.4838
Fax: +1.650.887-0348

A list of warnings and precautions included in the **evGuide TLS System draft User's Manual** is shown below.

Warnings

1. Monitor catheter tip placement during insertion procedure using your institution's guidelines.
2. This device is not to be used in the presence of combustible or flammable gases, anesthetics, or cleaners/disinfectants.
3. Electrical Shock Hazard: Do not remove system covers. To avoid electrical shock, use only the power cord supplied with the system and connect only to properly grounded wall outlets.
4. Failure to follow the guidelines described in the Users's Manual and in the Instructions for Use provided with the evGuide TLS Adapters may result in injury to patients and damage to the evGuide TLS System.
5. The evGuide TLS is not intended to diagnose or treat disease.
6. The Sapiens TLS system must be powered **ONLY** by the batteries provided with the Sapiens TLS Laptop. Batteries may **NOT** be charged while using the Sapiens TLS

- system in a medical procedure. The batteries can only be charged from the power outlet using the provided charger while the system is NOT in clinical use.
7. All optional system components including the optional printer except the medical grade power supply itself **MUST** be powered by, and only by a medical grade power supply.
 8. Failure to abide by the precautions detailed below causes the system and its use to be out of compliance with regulations and places the patient and the operator at risk of injury or death.
 9. Do NOT install any software on the evGuide TLS PC. This may result in patient and operator harm and system damage.
 10. The evGuide TLS Adapter is provided sterile in a sterile pouch. Handle the sterile evGuide TLS pouch and adapter only with sterile gloves and pay attention not to compromise the sterile field.
 11. Release the central venous catheter after insertion according to your institution's guidelines.
 12. Do not release the central venous catheter if the ECG signal on the screen is unstable or does not show the waveforms according to the User's Manual. Use a different method for guiding the placement of your central line.

Precautions

1. The evGuide TLS should only be used by physicians and nurses trained in central lines placement procedures and in assessing the ECG information provided by evGuide TLS.
2. Before using the evGuide TLS for the first time, be sure to read and understand all of the information in this Manual.

A list of warnings and precautions included in the **evGuide TLS Adaptor draft Instructions for Use** is shown below.

Warnings

1. Monitor catheter tip placement during insertion procedure per institutional policy.
2. Release the central venous catheter after insertion according to your institution's guidelines.
3. Do not release the central venous catheter based on evGuide information if the signal on the screen is unstable or does not show the waveform according to the evGuide User's Manual. In such a case, use a different method for guiding the placement of your central line.
4. If the evGuide adaptor becomes damaged, remove the adaptor with caution as to not change the position of the catheter.
5. The evGuide TLS adaptor is for Single Use Only.
6. Do not re-sterilize the adaptor or accessories by any method.
7. The manufacturer shall not be liable for any damages caused by reuse or re-sterilization of this adaptor or accessories.
8. Contents are sterile in an unopened, undamaged package. Sterilized by Ethylene Oxide.
9. Do not use adaptor or accessories if package is opened or damaged.
10. Do not use adaptor or accessories if any sign of product damage is visible.

11. The evGuide TLS adaptor is not intended to diagnose or treat disease.
12. Failure to verify catheter placement may result in serious trauma or fatal complications.

Precautions

1. Do not use sharp instruments near the adaptor.
2. Adaptor may be damaged if clamps other than what is provided are used.
3. Examine adaptor before each insertion for damage.
4. Read instructions carefully before using this device. The adaptor should be manipulated by a qualified, licensed physician or other qualified health care professional.
5. The medical techniques and procedures described in these instructions for use do not represent all medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgment in treating any specific patient.
6. Use standard hospital protocols when applicable.
7. Discard gloves and change to a new pair of sterile gloves after connecting the Adaptor to the evGuide TLS System and completing the setup of the evGuide TLS System per User's Manual.
8. Beware of the adaptor wire. Tripping over the adaptor might cause malfunction of the adaptor, detachment of the adaptor connectors from the system or injuries for the user.

Service Manual and Installation Guide

There are no user serviceable parts therefore no Service Manual will be provided. Installation instructions are provided in the Users Manual.

Predicate Device Labeling

If available, labeling for the predicated devices is provided in **Appendix B**.

14. STERILIZATION AND SHELF LIFE

The evGuide TLS System is a programmed electronic medical system that does not contact the patient. The system is non-sterile and may be wiped down by using a soft, damp cloth to remove dust and foreign matter. The evGuide TLS System does not have a shelf life.

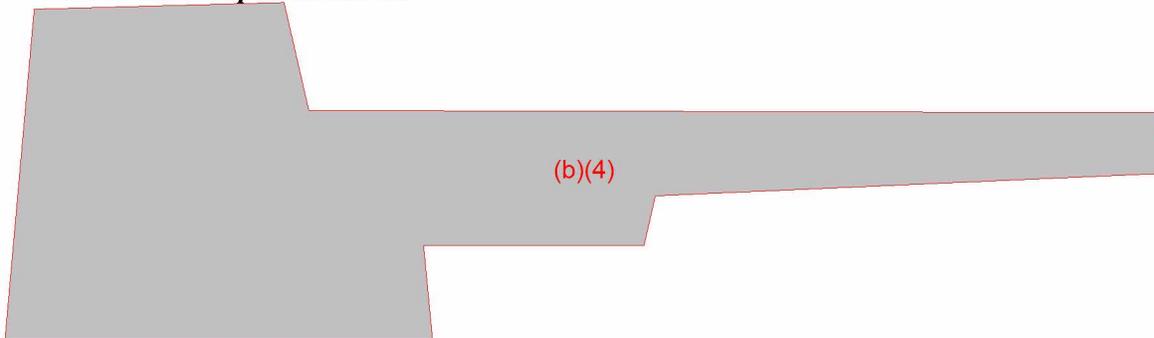
The evGuide TLS Saline Adaptor and the evGuide TLS Electric Adaptor (evGuide TLS Adaptor) are sterilized using ethylene oxide gas. The evGuide TLS Adaptors are STERILE if unit package is unopened and undamaged; for duration of time as specified by the expiration date. The evGuide TLS Adaptors will remain sterile as long as its package is unopened and undamaged. The evGuide TLS Adaptors shelf life is 12 months.

The evGuide TLS Saline Adaptor and the evGuide TLS Electric Adaptor are intended and labeled only for single patient use and only by prescription by a physician. The devices shall not be reused or resterilized.

14.1 Method of Sterilization – evGuide TLS Electrical and Saline Adaptors

Each lot of evGuide TLS Adaptor in either Electrical or Saline configuration (evGuide Adaptor) is sterilized using Ethylene Oxide sterilization. Sterilization is performed according to ANSI-AAMI-ISO 11135-1:2007 guidelines by a contract sterilizer qualified by Romedex International Srl.

Sterilization is performed at:



Sterilization results and sterilization validation results are attached in **Appendix K** of this submission. Additional sterilization validation test results are on file at Romedex International Srl and are available for review upon request.

14.2 Sterility Assurance Level – evGuide TLS Electrical and Saline Adaptors

The 100% ethylene oxide sterilization cycle used in the sterilization of the evGuide TLS Saline and Electrical Adaptors provides a minimum sterility assurance level (SAL) of 10^{-6} .

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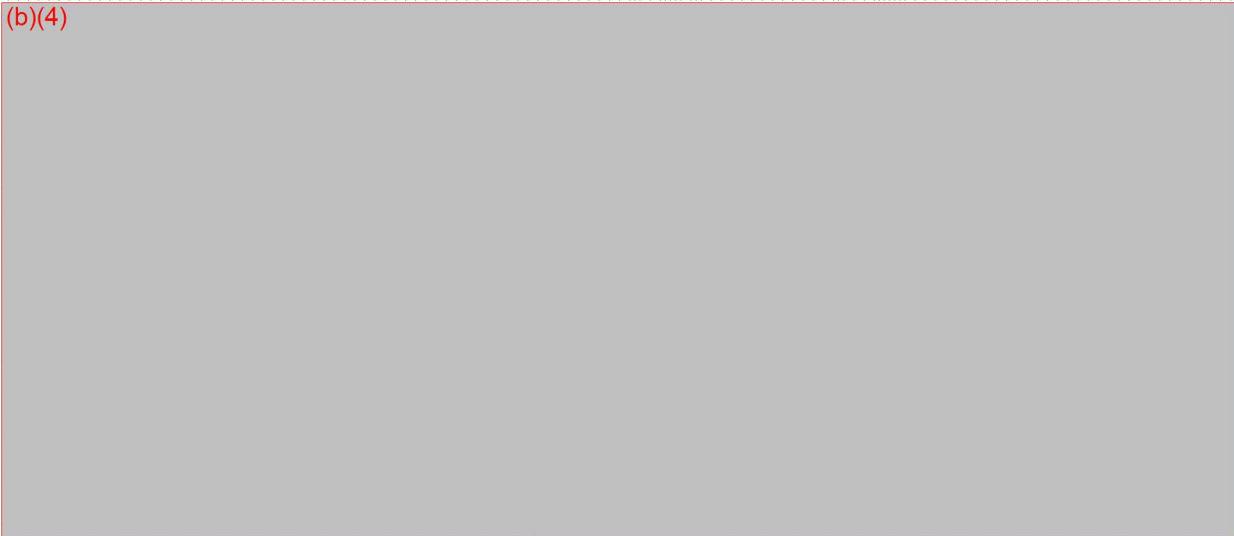
15. BIOCOMPATIBILITY

The evGuide TLS System is a non-patient contacting instrument system and does not require biocompatibility testing.

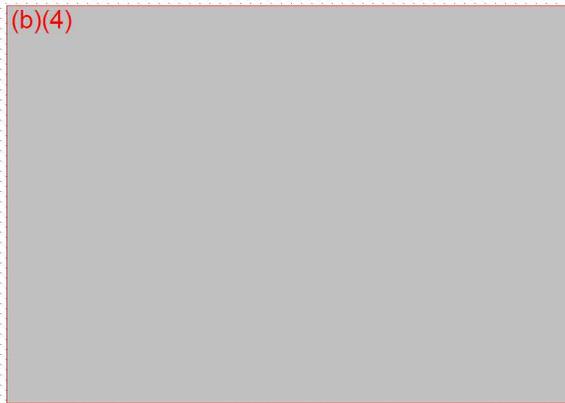
The evGuide TLS Electric Adaptor is a non-patient contacting device and does not require biocompatibility testing.

15.1 Biocompatibility Background

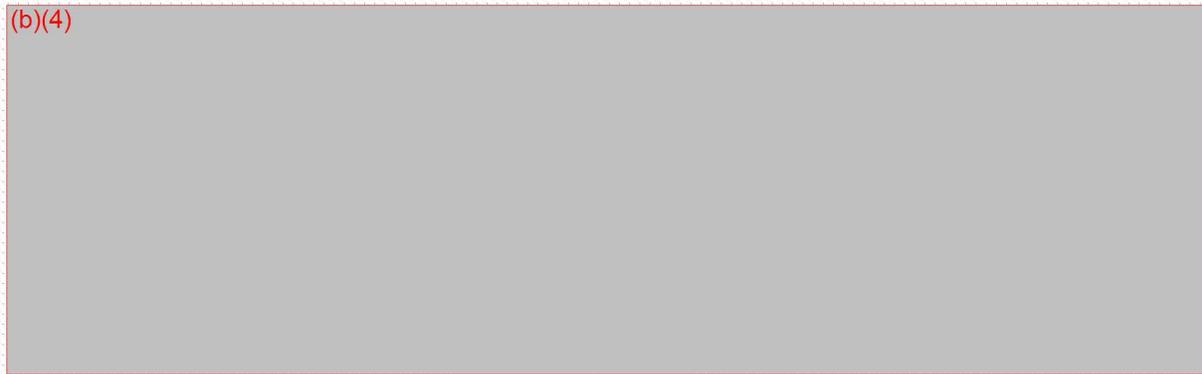
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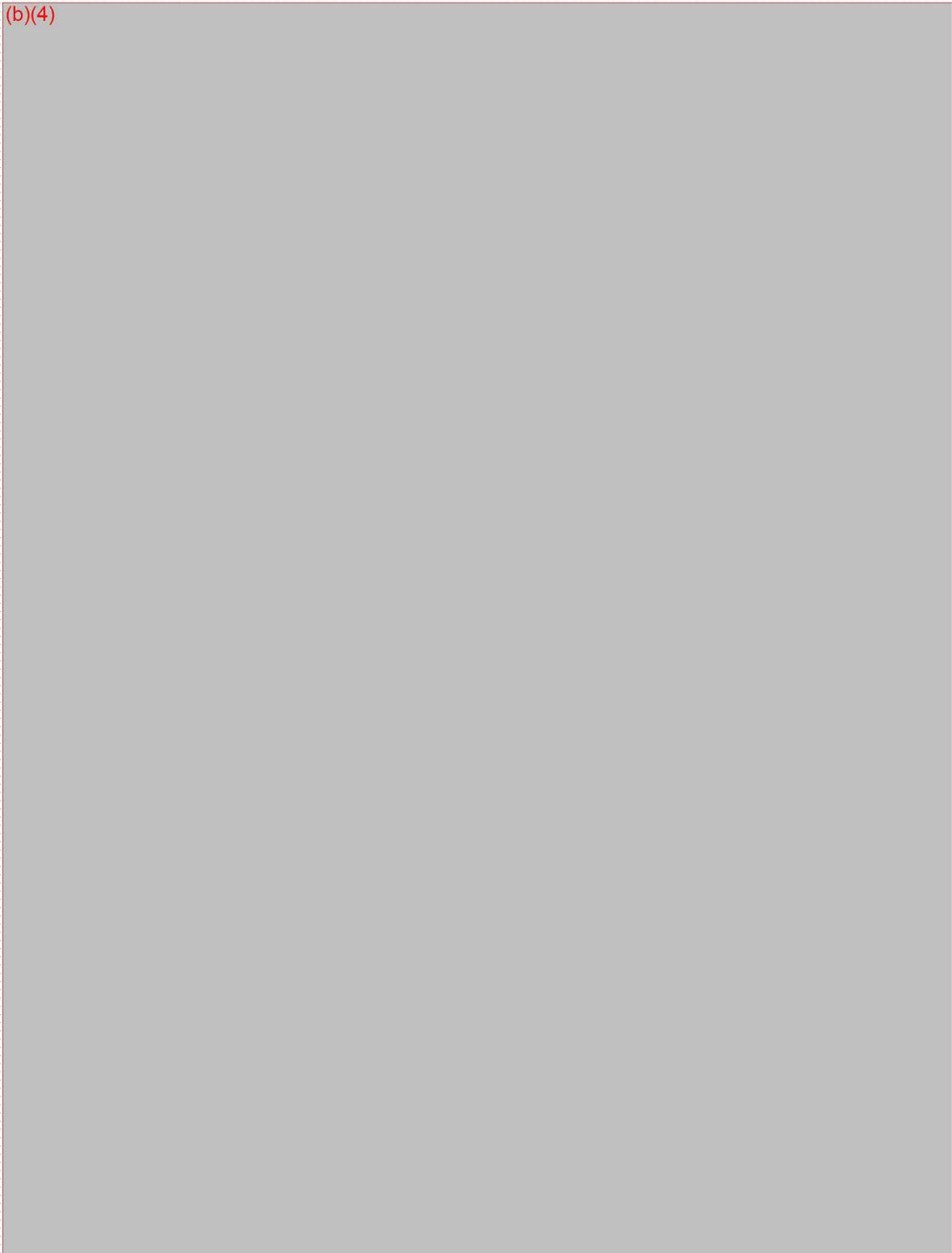


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15.2 Biocompatibility test results

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Conclusion

In conclusion, based the on the test results obtained, the good performance of the evGuide TLS Saline Adaptor in clinical studies and the long successful history of the materials used, Romedex Internatinal Srl believes that the evGuide TLS Saline Adaptor is biocompatible and safe for its intended use in humans.

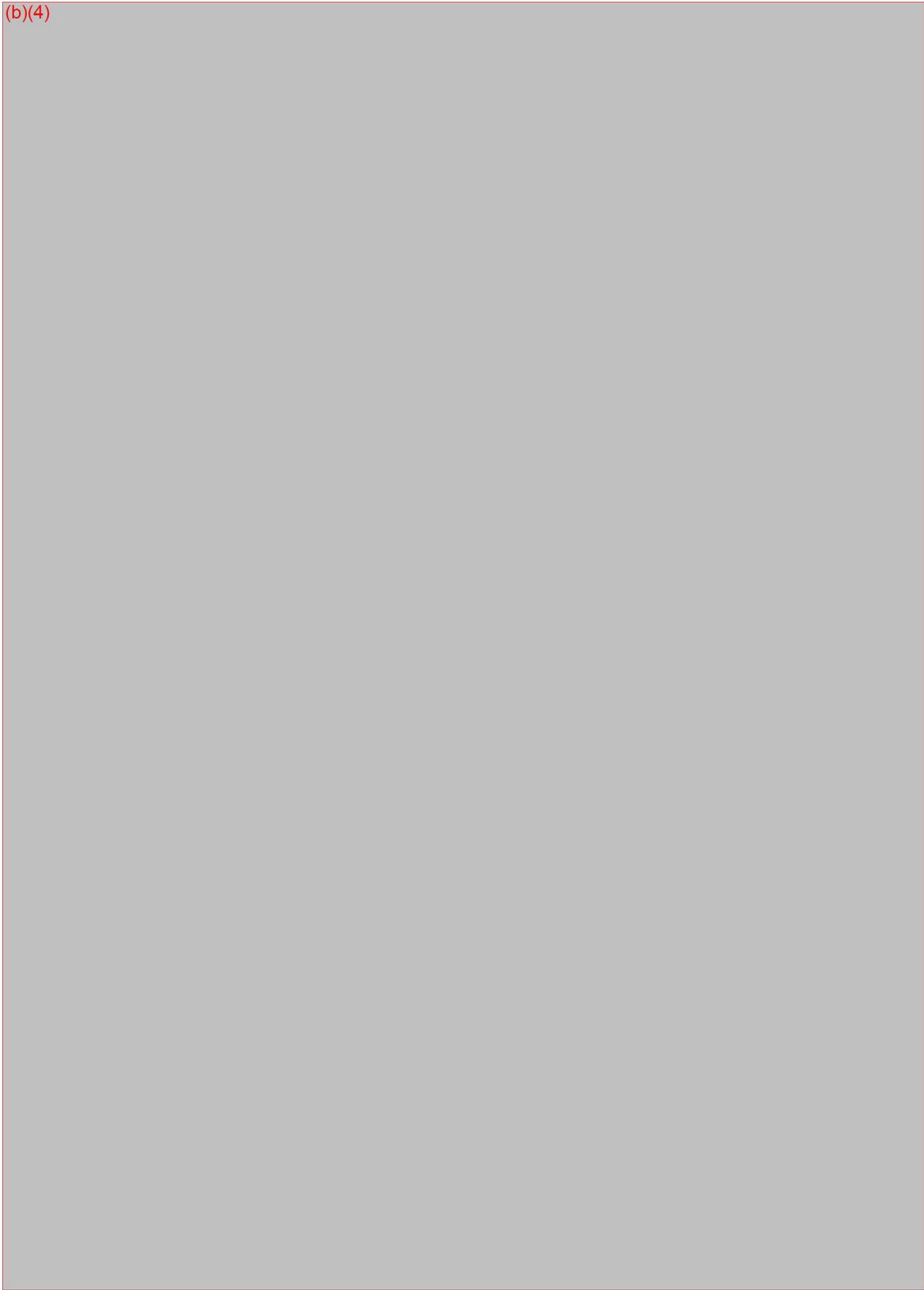


16.SFTWARE

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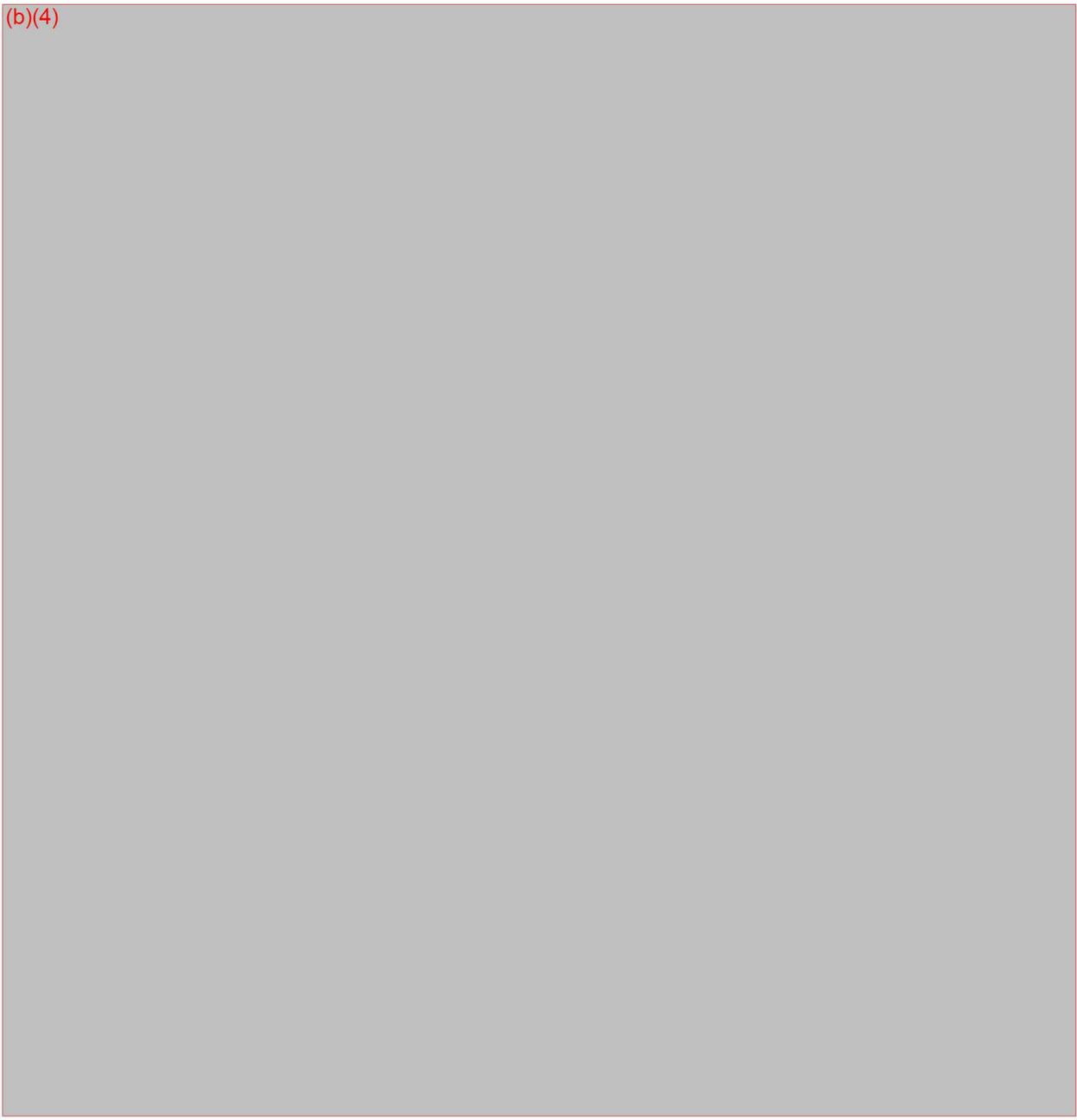
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16.2 Software Description

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Figure 16.1 – Software Development and Lifecycle

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16.3 Revision level History

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16.4 Software Device Hazard Analysis

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16.5 Software Requirements Specification

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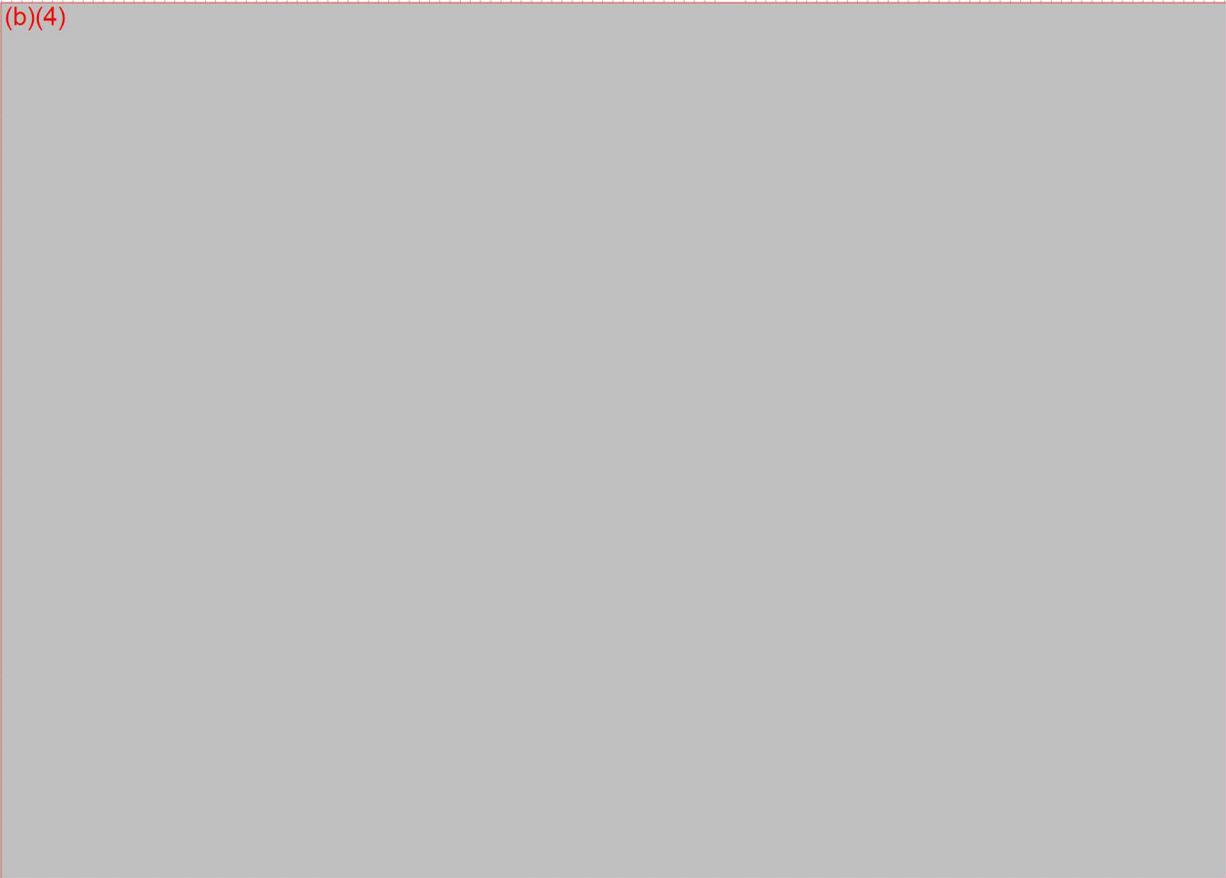


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Figure 16.2: evGuide TLS software configuration

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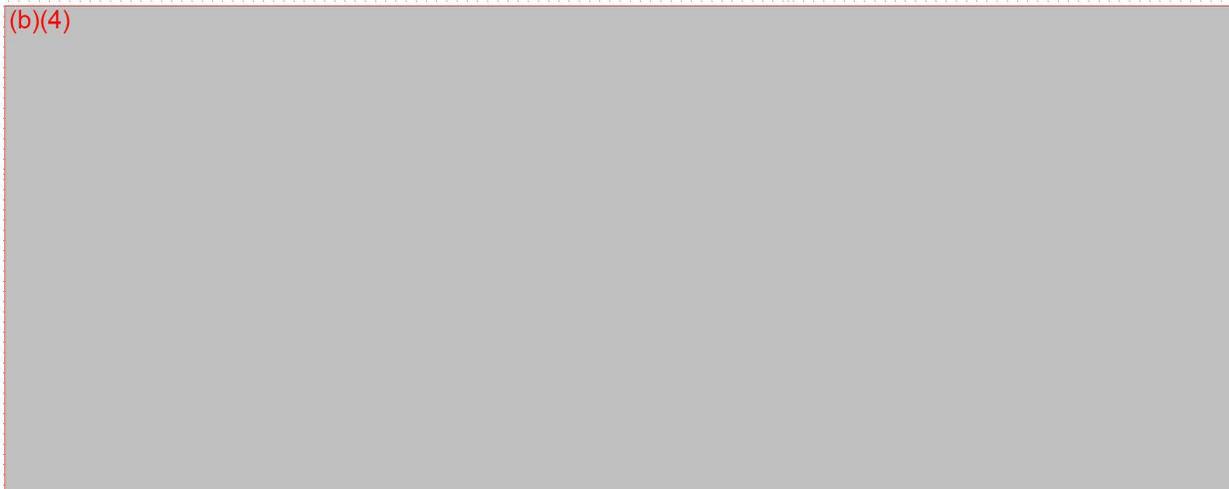


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Figure 16.3: evGuide TLS software: component interaction

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Graphical User Interface description:

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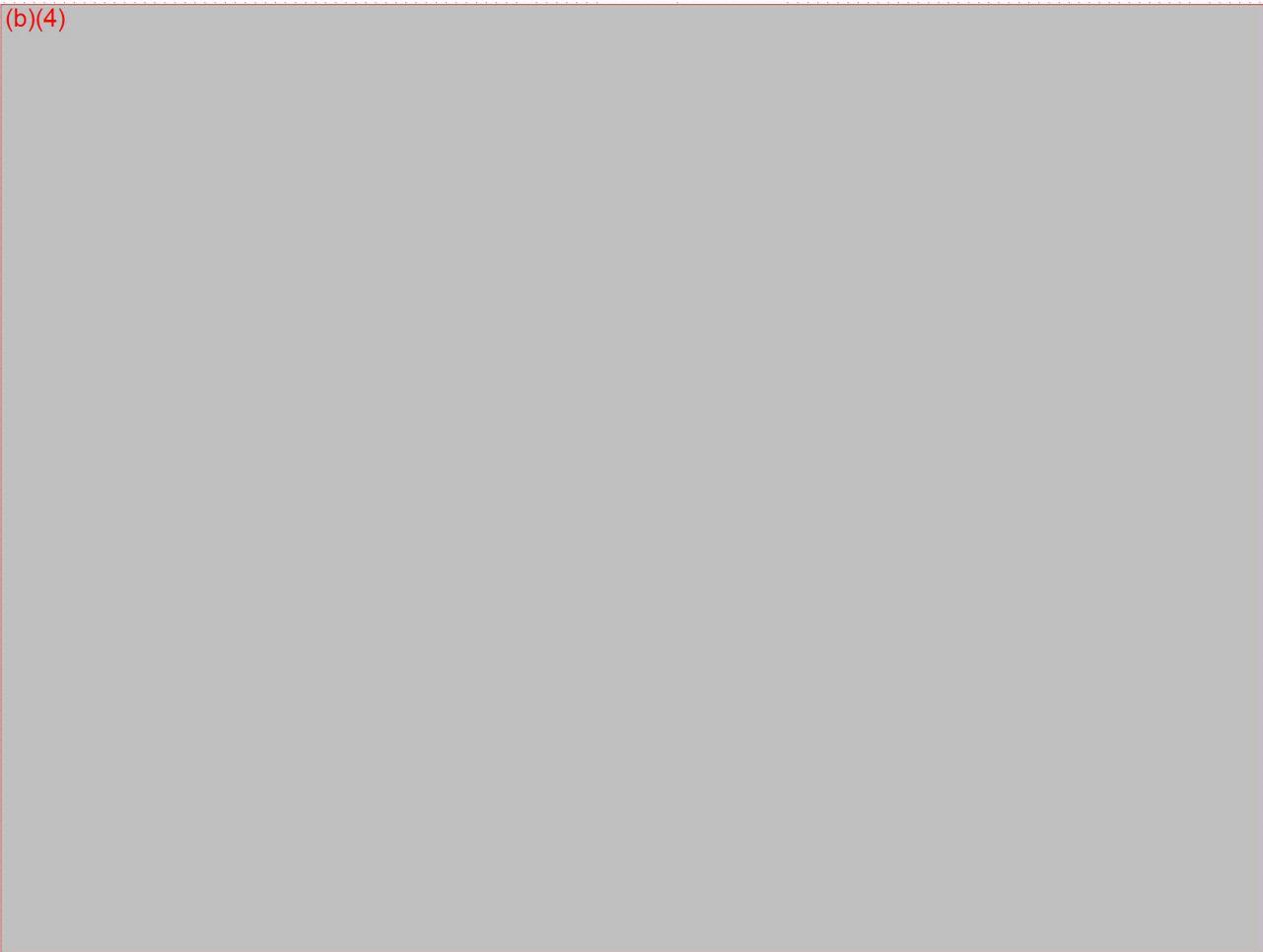


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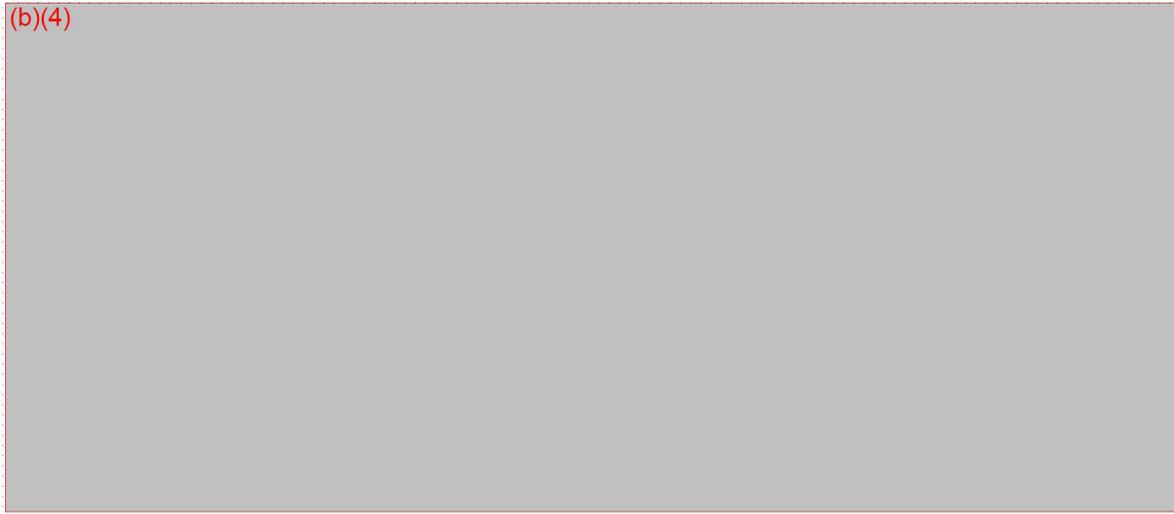


Figure 16.4: evGuide TLS Graphical User Interface

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16.6 Architecture Design Chart

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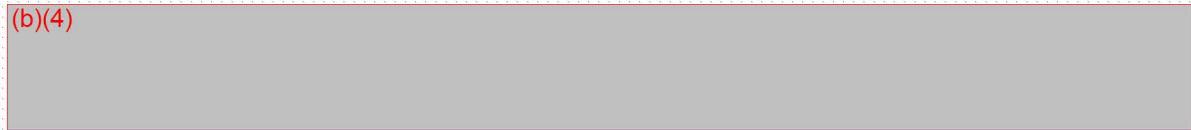
16.7 Software Design Specification

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16.8 Software Development Environment Description

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16.9 Traceability Analysis

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17. ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

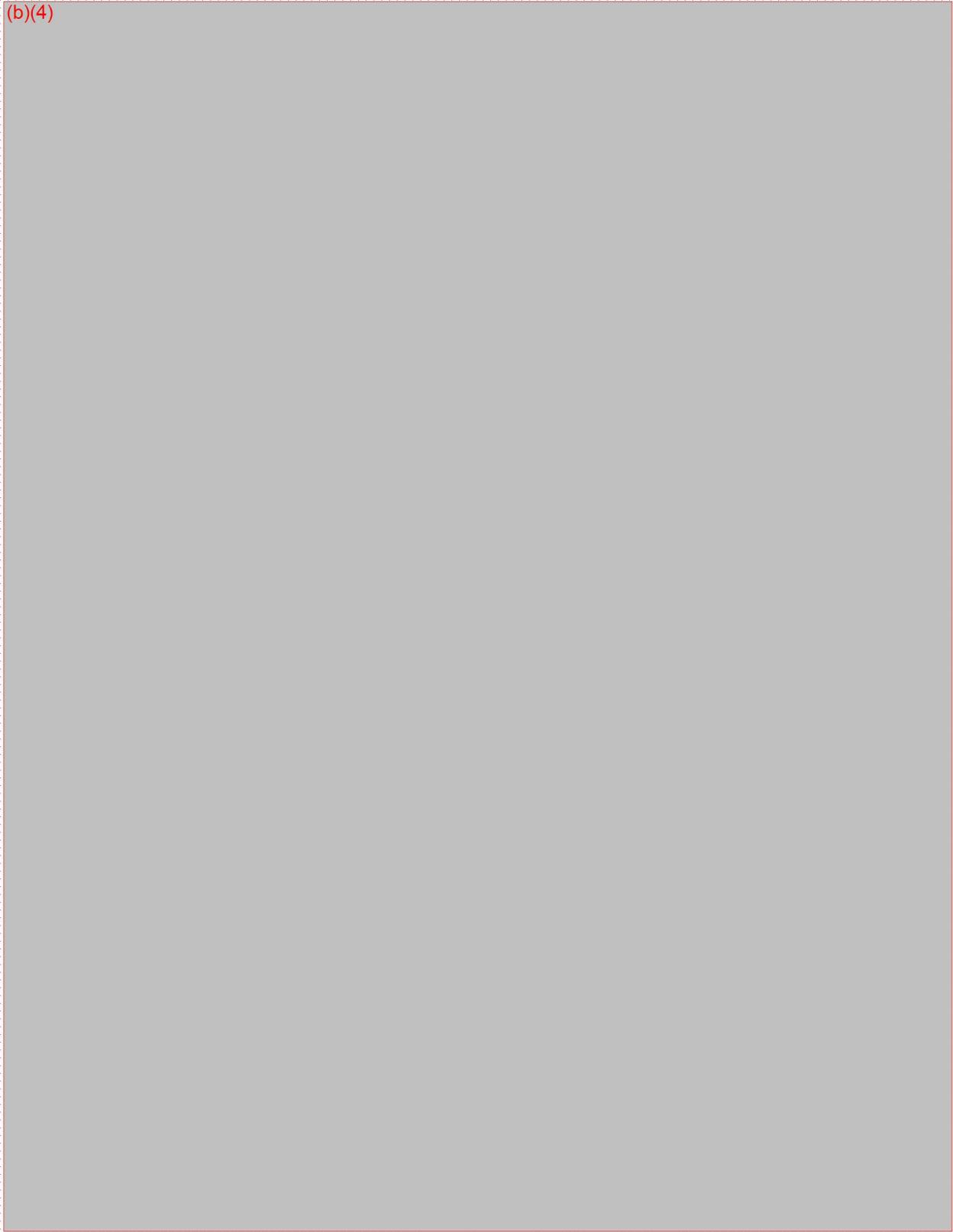
The evGuide TLS system has undergone testing and met the acceptance criteria for the following applicable requirements form electromagnetic compatibility and electrical safety standards:

- Radiated emission: EN55011, 2007, section 5.2
- Radiated RF immunity: EN 61000-4-3 (IEC/EN 60601-1-1)
- Electrical discharge: EN 61000-4-2 (IEC/EN 60601-1-2)
- Electrical Safety: IEC/EN 60601-1-1 for leakage currents (Section 19) and hi-pot (Section 20.2)

Copies of the test results are provided in **Appendix D**.

18. PERFORMANCE TESTING – BENCH

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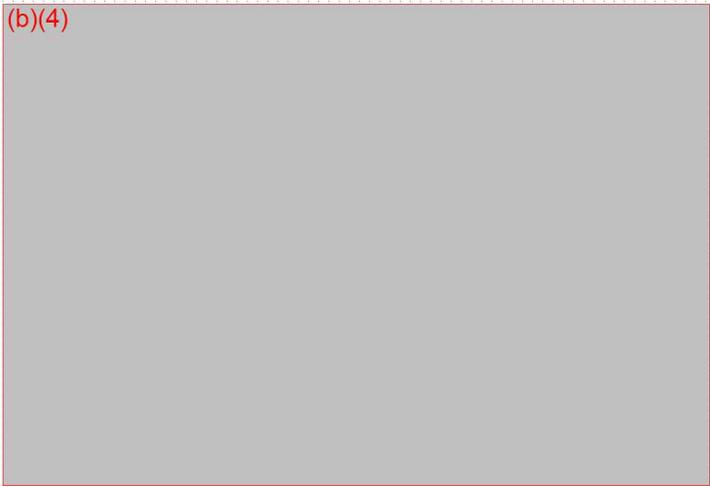


19. PERFORMANCE TESTING – ANIMAL

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Conclusion

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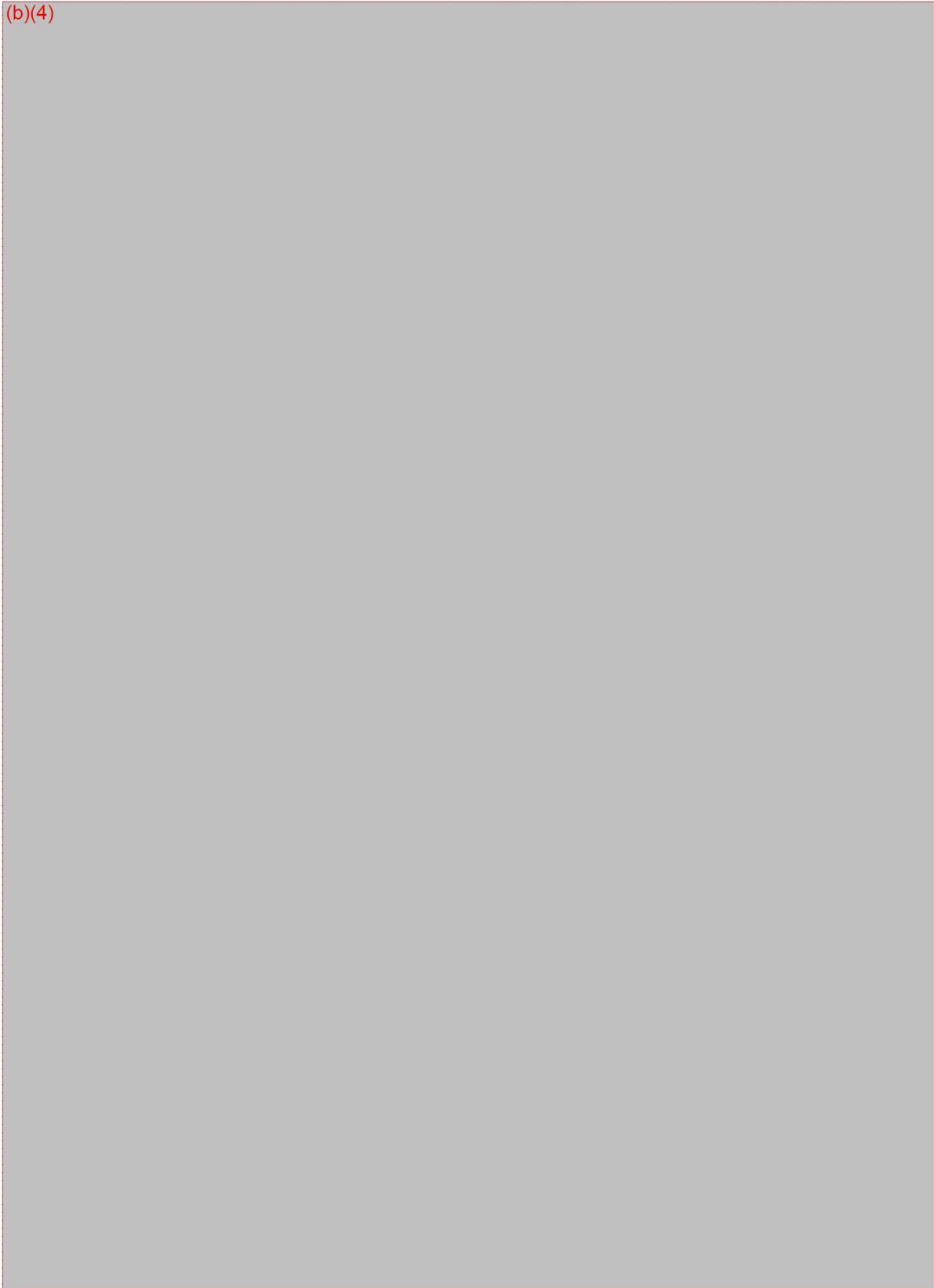
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20. PERFORMANCE TESTING – CLINICAL

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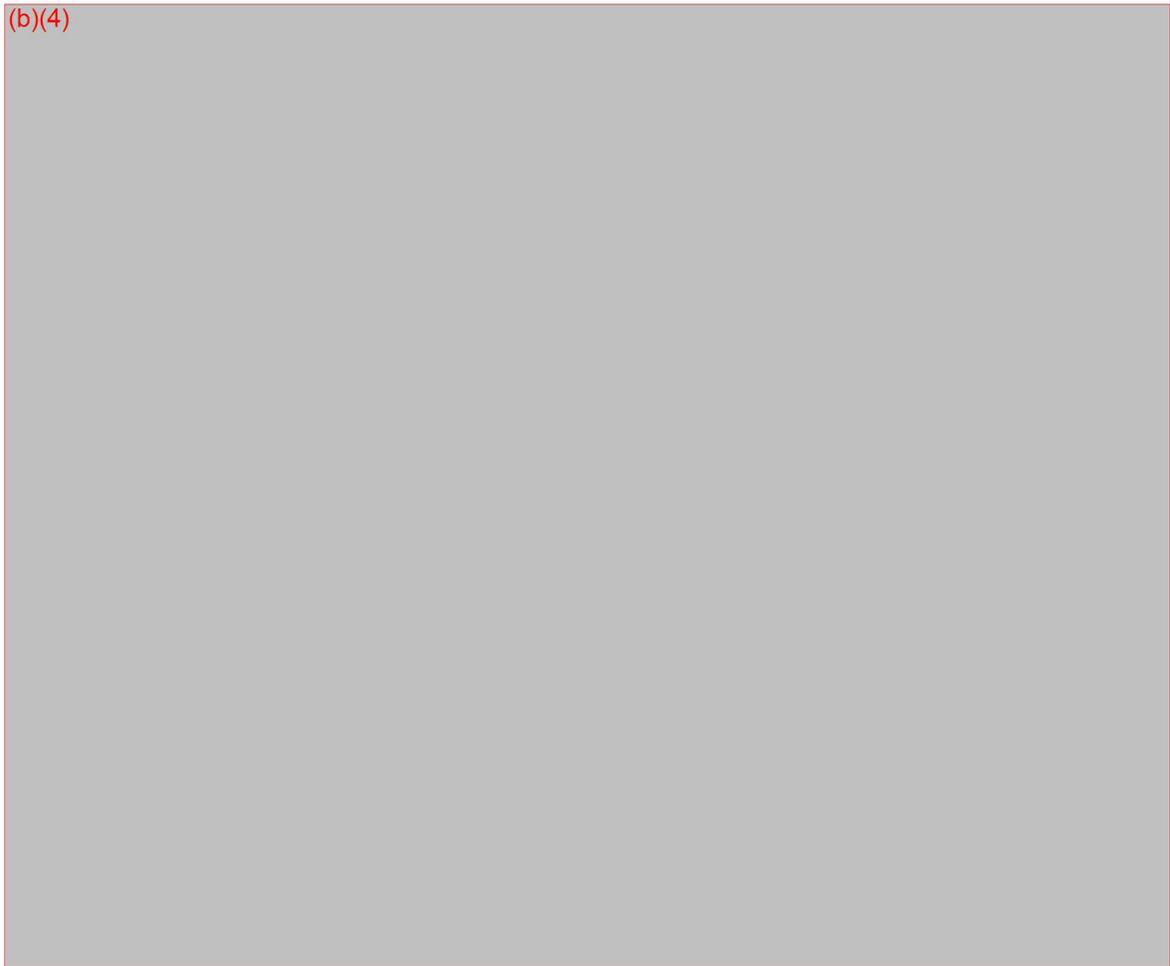
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Appendix A: Predicate Devices

510(k) Summary

AUG 07 2009

Device trade name: Sherlock 3CG™ Tip Positioning System Sensor
Sherlock 3CG™ Tip Positioning System Stylet

Device class and panel: Class II, 21 CFR §880.5970
LJS - Accessory to Percutaneous, Implanted, Long-Term Intravascular Catheters

Applicant name: Rick Gaykowski
Bard Access Systems, Inc. [wholly owned subsidiary of C.R. Bard, Inc.]
605 North 5600 West, Salt Lake City, UT 84116
(801) 522-0700, x5432

Predicate devices: K061240 - Sherlock™ II Tip Location System Detector
K063240 - Sherlock™ Tip Location System Stylet
K081626 - FlowPICC™ Console
K081625 - FlowPICC™ Stylet

Performance Standards: Performance standards have not been established by the FDA under §514 of the Federal Food, Drug and Cosmetic Act.

Indications for Use:
Sherlock 3CG™ Tip Positioning System Sensor: The Sherlock 3CG™ Tip Positioning System (TPS) is indicated for central venous catheter guidance and positioning during catheter placement. The Sherlock 3CG™ TPS provides real time catheter tip location information through the use of passive magnet and cardiac electrical signal detection.
Sherlock 3CG™ Tip Positioning System Stylet: Catheter stylets provide internal reinforcement to aid in catheter placement. When used with the Sherlock 3CG™ Tip Positioning System (TPS), the Sherlock 3CG™ TPS stylet also provides the placer rapid feedback on catheter tip location and orientation through the use of passive magnets and cardiac electrical signal detection.

Device description: The Sherlock 3CG™ Tip Positioning System (TPS) consists of a sensor, stylet, and connection assembly. The system is designed to aid in central venous catheter tip positioning through magnet tracking and ECG signal information. The Sherlock 3CG™ TPS System detects and displays the position of the magnet-tipped stylet relative to the sensor. In addition, the Sherlock 3CG™ TPS System detects and displays a cardiac electrical signal from the three ECG electrodes, including the Sherlock 3CG™ TPS Stylet and two body electrodes, which provide catheter tip positioning information.

Technological Characteristics: Technological similarities between the subject Sherlock 3CG™ Tip Positioning System Sensor and Sherlock 3CG™ Tip Positioning System Stylet and the predicate devices remain identical. There are no new questions raised regarding safety or efficacy of these devices.

Safety & Performance Tests: Verification and validation tests have been performed in accordance with Design Controls per 21 CFR §820.30.

Summary of Substantial Equivalence: Based on the indications for use, technological characteristics, and safety and performance testing, the subject Sherlock 3CG™ TPS System, consisting of the Sherlock 3CG™ TPS Sensor and Sherlock 3CG™ TPS Stylet met the minimum requirements that are considered adequate for its intended use and are substantially equivalent in design, materials, sterilization, principles of operation and indications for use to the current commercially available Sherlock™ II Tip Location System, which consists of the Sherlock™ II Tip Location System Detector and Sherlock™ Tip Location System Stylet; and the FlowPICC™ System, which consists of the FlowPICC™ Console and FlowPICC™ Stylet.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center - WO66-G609
Silver Spring, MD 20993-0002

Mr. Rick Gaykowski
Vice President, Regulatory Affairs
Bard Access Systems, Incorporated
C.R. Bard, Incorporated
605 North 5600 West
Salt Lake, Utah 84116

AUG 07 2009

Re: K091324
Trade/Device Name: Sherlock 3CG™ Tip Positioning System Stylet, Sherlock 3CG™
Tip Positioning System Sensor
Regulation Number: 880.5970
Regulation Name: Percutaneous Implanted Long-Term Intravascular Catheter
Regulatory Class: II
Product Code: LJS
Dated: July 6, 2006
Received: July 8, 2009

Dear Mr. Gaykowski:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

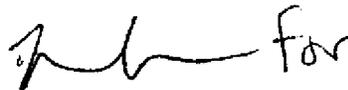
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to <http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm> for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Susan Runner" followed by a flourish and the word "for".

Susan Runner, D.D.S., M.A.
Acting Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

1 of 2

510(k) Number (if known): _____

Device Name: Sherlock 3CG™ Tip Positioning System Stylet

Indications for Use:

Catheter stylets provide internal reinforcement to aid in catheter placement. When used with the Sherlock 3CG™ Tip Positioning System (TPS), the Sherlock 3CG™ TPS Stylet also provides the placer rapid feedback on catheter tip location and orientation through the use of passive magnets and cardiac electrical signal detection.

Prescription Use
(Part 21 CFR §801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR §801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)



(Division Sign-Off)
Division of Anesthesiology, General Hospital
Infection Control, Dental Devices

510(k) Number: K091324

510(k) Number (if known): _____

Device Name: Sherlock 3CG™ Tip Positioning System Sensor

Indications for Use:

The Sherlock 3CG™ Tip Positioning System (TPS) is indicated for central venous catheter guidance and positioning during catheter placement. The Sherlock 3CG™ TPS provides real time catheter tip location information through the use of passive magnet and cardiac electrical signal detection.

Prescription Use
(Part 21 CFR §801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR §801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)



Division Sign-Off)
Division of Anesthesiology, General Hospital
Infection Control, Dental Devices

510(k) Number: K091324

K032613

PETER M. ROTHENBERG, M.D., M.A.
657 CAMINO DE LOS MARES
SUITE 137
SAN CLEMENTE, CA 92673
PHONE: (949) 489-9039
FAX: (949) 489-8136
EMAIL: PMRMDINC@SBCGLOBAL.NET

510(k) SUMMARY OF DEVICE

TRADE NAME: PACER ASSIST DEVICE (FORMAL NAME TO BE
COPYRIGHTED ON RECEIPT OF 510(K) CLEARANCE)

COMMON NAME: ACCESSORY TO EKG CABLE

CLASSIFICATION NAME: ACCESSORY TO EKG CABLE (CLASSIFICATION TO
BE DETERMINED)

CONTACT PERSON: PETER M. ROTHENBERG, M.D., M.A.

As noted in my 510 (k) application, this device is of such simplicity, there are no others *directly* comparable. Features have been incorporated into those far more technologically advanced. In essence, the subject device provides an electrically safe connection between the proximal pin of an intravascular electrode and a patient EKG lead, the signal ultimately traveling retrograde along a standard EKG cable to a bedside monitor. It would be used to facilitate placement of a transvenous pacemaker or appropriately designed intravenous catheter with *EKG* guidance rather than the more cumbersome (and expensive) fluoroscopic approach.

The device entirely consists of a pin jack (to accept the proximal pin of the electrode) connected in series via a 1000 ohm resistor to a standard EKG eyelet all encased in an appropriate housing. The snap-fit connection between the EKG lead and device eyelet completes the connection to the monitor.

DATE PREPARED: 10/27/03



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NOV 20 2003

Peter M. Rothenberg, M.D., M.A.
657 Camino De Los Mares
Suite 137
San Clemente, CA 92673

Re: K032613

Trade Name: Transvenous Pacemaker Placement Assist Device

Regulation Number: 21 CFR 870.3680 and 870.2050

Regulation Name: Accessory to cardiovascular permanent or temporary pacemaker
electrode; and biopotential amplifier and signal conditioner

Regulatory Class: Class II (two)

Product Code: LDF and DRR

Dated: October 30, 2003

Received: November 4, 2003

Dear Dr. Rothenberg:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050. This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (301) 594-4646. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>

Sincerely yours,



Bram D. Zuckerman, M.D.

Director

Division of Cardiovascular Devices

Office of Device Evaluation

Center for Devices and

Radiological Health

Enclosure

INDICATIONS FOR USE

This device is designed to connect an intravascular electrode to a monitor through a standard EKG patient lead for the purpose of displaying an intravascular signal in real time. Only the black pinjack is "active". The red pinjack is electrically blind and designed to isolate the proximal electrode from inadvertent stimulation.

Dina Secunde

(Division Sign-off)
Division of Cardiovascular Devices
510(k) Number K032613/

X - prescription device

K9-125 11

NOV 24 1997

**II. 510(k) SUMMARY of SAFETY and EFFECTIVENESS
in ACCORDANCE with SMDA'90**

B. Braun Medical, Inc 1997
824 Twelfth Avenue
Bethlehem, PA 18018
(610)691-5400

Contact: Mark S. Alsberge, Regulatory Affairs Director

Product Name: Epidural Catheter Connector

Trade Name: Conduction Anesthesia Kit

Classification Name:
Cardiovascular
Class II, 74 DQY, Percutaneous Catheter
21 CFR 870.1250

Substantial Equivalence¹ to:

510(k) number	Name	Applicant
K843263	Arrow-Johans ECG Adaptor	Arrow International, Inc.

Device Description:

In accordance with section 510(k) for the Federal Food, Drug, and Cosmetic Act, B. Braun Medical, Inc. intends to introduce into interstate commerce the Certodyn® RAECG Universal Adapter. The Adapter is designed to aid in the accurate placement of central venous catheters using the RAECG technique.

¹ The term "substantially equivalent" as use herein is intended to be a determination of substantial equivalence from an FDA -regulatory point of view under the Federal Food, Drug, and Cosmetic Act and relates to the fact that the product can be marketed without premarket approval or reclassification. These products may be considered distinct from a patent point of view. The term "substantially equivalent" is not applicable to and does not diminish any patent claims related to this product or the technology used to manufacture the product.

Materials:

The Certodyn® RAECG Universal Adapter is composed of materials that have been tested in accordance with Tripartite Guidance for Plastics and determined to be suitable for the intended use of this product.

Substantial Equivalence:

The Certodyn® RAECG Universal Adapter is equivalent in materials, form, and intended use to our the Arrow-Johans ECG Adaptor currently marketed under K843263 by Arrow International, Inc. There are no new issues of safety or effectiveness raised by the Certodyn® RAECG Universal Adapter.

Safety and Effectiveness:

All finished products are tested and must meet all required release specifications before distribution. The array of testing required for release include, but are not limited to; physical testing, visual examination (in process and finished product).

The physical testing is defined by Quality Control Test Procedure documents. These tests are established testing procedures and parameters which conform to the product design specifications.

The testing instruction records for each of the individually required procedures are approved, released, distributed and revised in accordance with document control GMP"s.



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20856

NOV 24 1997

Mr. Mark S. Alsberge
Director, Regulatory Affairs
B. Braun Medical, Inc.
824 12th Avenue
Bethlehem, PA 18018-0027

Re: K973371
Trade Name: Certodyn RAECG Universal Adapter
Regulatory Class: II
Product Code: DQY
Dated: September 3, 1997
Received: September 8, 1997

Dear Mr. Alsberge:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895.

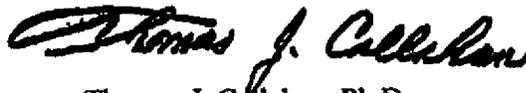
A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Page 2 - Mr. Mark S. Alsberge

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4648. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "dsmo@fdadr.cdrh.fda.gov".

Sincerely yours,



Thomas J. Callahan, Ph.D.
Director
Division of Cardiovascular, Respiratory,
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

[New Search](#)

[Back To Search Results](#)

510(k) Premarket Notification Database

Device Classification Name	<u>catheter, percutaneous</u>
510(k) Number	K843263
Device Name	ARROW-JOHANS ECG ADAPTOR
Applicant	ARROW INTL., INC.
Contact	
Regulation Number	<u>870.1250</u>
Classification Product Code	<u>DQY</u>
Date Received	08/20/1984
Decision Date	09/20/1984
Decision	substantially equivalent (SE)
Classification Advisory Committee	Cardiovascular
Review Advisory Committee	General & Plastic Surgery
Type	Traditional
Reviewed by Third Party	No
Expedited Review	

Database Updated 05/07/2009

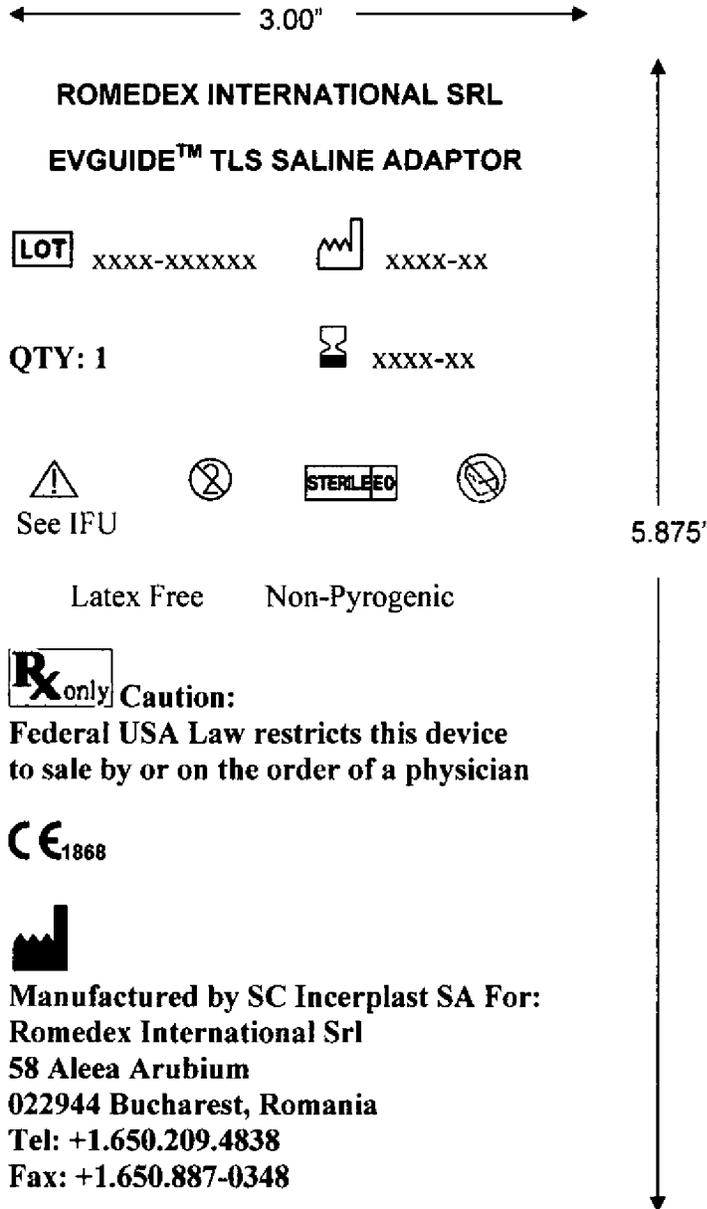


Appendix B: Labeling



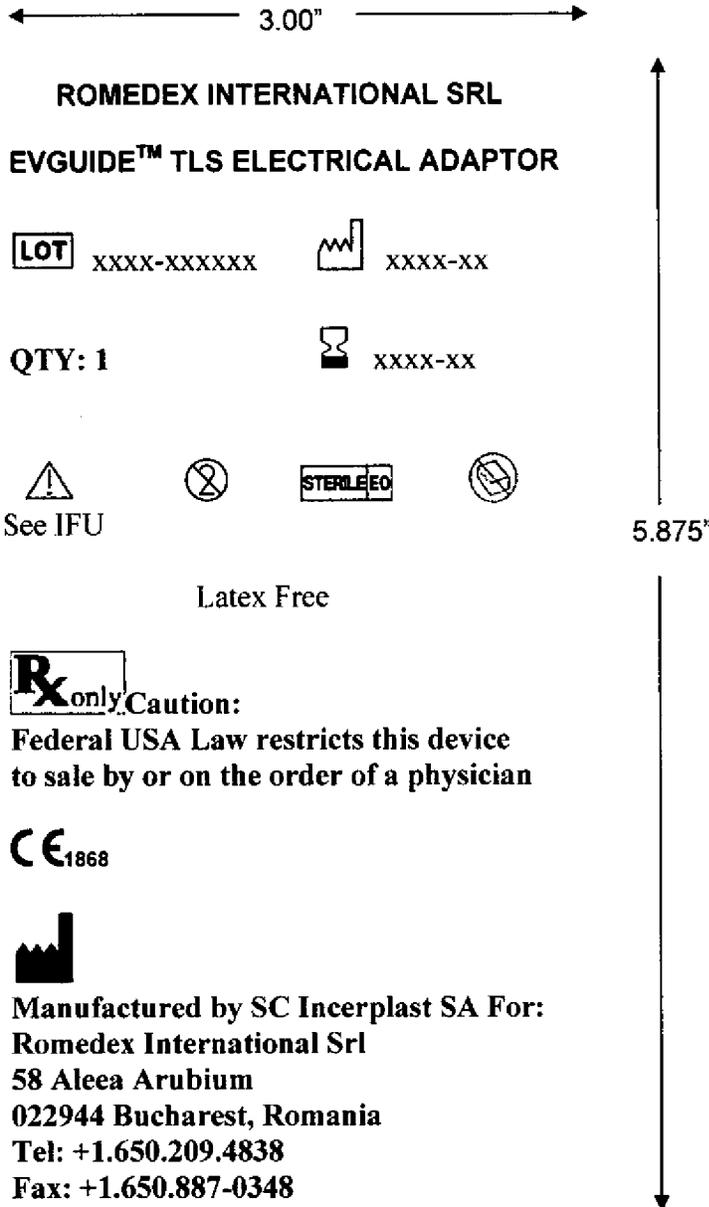
Notes:

1. Artwork on label must be clear and legible.
2. Print on label stock 3" X 5.875"
3. Manufacturing date: YYYY-MM
4. Lot Number: XXXX-XXXXXX (Variable information ####-MMDDYY)
5. Expiration Date: YYYY-MM (12 months from manufacturing date YYYY-MM)
6. Print in black only
7. Printing Instructions:



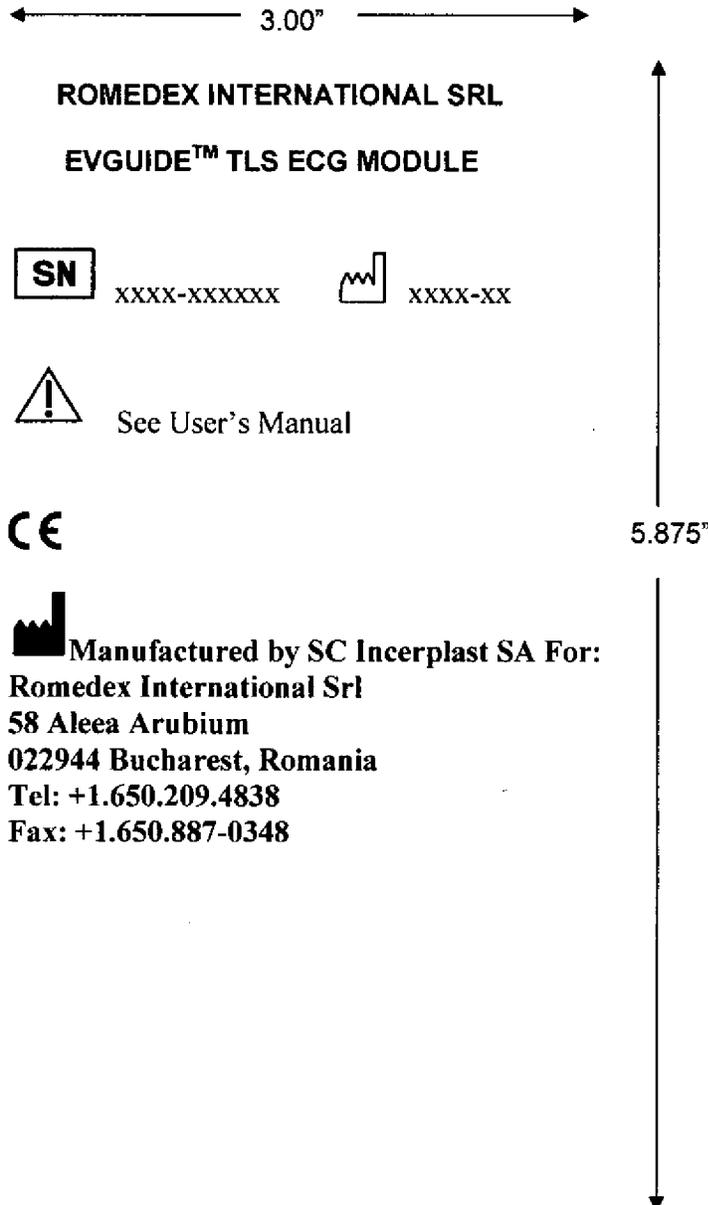
Notes:

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2. Print on label stock 3" X 5.875"
3. Manufacturing date: YYYY-MM
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6. Printing Instructions:



evGuide TLS™
USER'S MANUAL

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evGuide TLS™ USER'S MANUAL

Background

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health care institutions and as documented in many papers including the one attached in Appendix H: "The ECG method for positioning the tip of PICCs: results from two preliminary studies" by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008.

Figure I illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community (Appendix H).

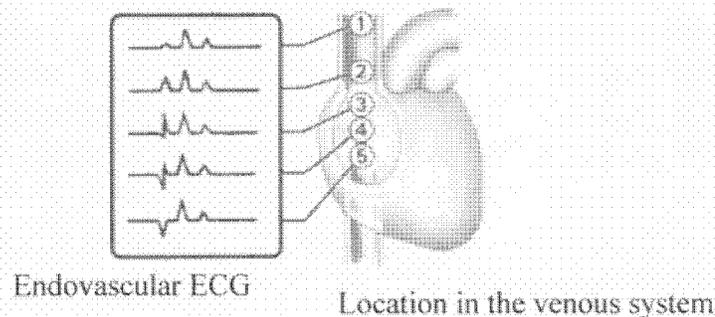


Figure I: Changes in the ECG waveform as function of location in the vasculature

The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the "red" or "right shoulder" electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A "giant" P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface ECG, the tip of the electrode is in the superior vena vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava). Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, which are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

evGuide™ TLS Overview

The evGuide TLS consists of the evGuide Saline Adaptor, the evGuide Electrical Adaptor, an ECG Module and an ECG cable, a laptop, and the evGuide TLS application software. The evGuide TLS components excluding the evGuide Adaptors are also referred to as the evGuide TLS System. An optional printer can be connected to the laptop for documentation purposes. The evGuide TLS Saline Adaptor can be connected to any commercially available central venous catheters and the evGuide TLS Electrical Adaptor to any commercially available stylets or guidewires used for the placement of central venous catheters. The evGuide system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, or intracavitary ECG) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and acquired in real time through the evGuide adaptors. Thus, the waveforms presented on the evGuide TLS graphical user interface can aid the placement of central venous catheters.

Indications for Use

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

Please also refer to the EvGuide TLS Adaptor **Instructions for Use**

Contraindications

- All contraindications of central venous catheters apply as specified by the central venous catheter manufacturer.
- There are no contraindications specific to the evGuide TLS System

WARNINGS

Monitor catheter tip placement during insertion procedure using your institution's guidelines.

This device is not to be used in the presence of combustible or flammable gases, anesthetics, or cleaners/disinfectants.

Electrical Shock Hazard: Do not remove system covers. To avoid electrical shock, use only the power cord supplied with the system and connect only to properly grounded wall outlets.

PRECAUTIONS

The evGuide TLS System should only be used by physicians and nurses trained in central lines placement procedures and in assessing the ECG information provided by the evGuide TLS System.

How Supplied

The evGuide TLS System is shipped in two subsystems: laptop running the evGuide TLS software and the evGuide TLS ECG module together with the corresponding cables.

Storage and Operating Conditions

Store the evGuide TLS System indoors at room temperature and condition.

Safety Information***General Safety Information***

Although the evGuide TLS System conforms to certain international safety and electromagnetic compatibility standards, the evGuide TLS System is intended for use by medical personnel who have received evGuide TLS System training. Only a trained User can determine if the evGuide TLS System use is appropriate. Awareness of the system's limitations is essential to making that determination and assuring safe operation for both User and patient.

CAUTION: Before using the evGuide TLS System for the first time, be sure to read and understand all of the information in this User's Manual.

Patient Safety

The evGuide TLS System is intended for use only by medical personnel trained in the operation of the evGuide TLS system and skilled in the clinical procedure to be used. To avoid any potential hazard to patients, follow the precautions outlined in this section.

WARNING

The system is not intended to diagnose or treat disease.

When using the evGuide TLS System with the evGuide TLS Adaptors, always follow the Instructions for Use provided with the evGuide TLS Adaptor.

Always use controls, make adjustments and perform procedures as specified in this Manual.

WARNING: Failure to follow the guidelines described in the User's Manual and in the Instructions for Use provided with the evGuide TLS Adaptor may result in injury to patients and damage to the evGuide TLS System.

The EvGuide TLS System is designed to meet the appropriate performance standards as established by the FDA guidance and CE Mark requirements.

User Safety

WARNING: The evGuide TLS system must be powered ONLY by the batteries provided with the evGuide TLS Laptop. Batteries may NOT be charged while using the evGuide TLS system in a medical procedure. The batteries can only be charged from the power outlet using the provided charger while the system is NOT in clinical use.

WARNING: All optional system components including the optional printer except the medical grade power supply itself MUST be powered by, and only by a medical grade power supply.

Electrical isolation separates the system components, and thus the patient, from dangerous leakage currents. If any of the system's components are directly connected to a wall outlet, the patient and the user are no longer safely isolated and may be exposed to dangerous electric currents.

WARNING: Failure to abide by the precautions detailed below causes the system and its use to be out of compliance with regulations and places the patient and the User at risk of injury or death.

Do NOT use additional cables, extension cords or outlets with the evGuide TLS System.

Do NOT remove system covers. Only qualified personnel should service the system.

Making Proper Electrical Connections

Carefully follow the safety guidelines described in this section when connecting the evGuide TLS System's battery charger power cord to the hospital or lab's AC outlet.

WARNING: Failure to abide by the electrical connection precautions detailed in this section causes the system and its use to be out of compliance with regulations and places the patient and the user at risk of injury or death and may damage the evGuide TLS System.

Connect the battery charger only to properly grounded hospital-grade AC outlets: The circuit must accommodate an additional load of up to 500 VA (4.2A @120V or 2.1 A @240VAC.) Make sure that any devices that connect to the network interface of the EvGuide TLS System comply with the appropriate IEC/national standard and are certified to IEC 60950 or equivalent for 240 VAC system operations. Use no electrical

peripherals within six feet of a patient unless the peripherals receive power from a medical grade power supply that meets medical safety standards.

NOTE If the system is used with peripherals that are powered from a separate wall outlet, then the combination is considered to be a medical system. It is the user's responsibility to comply with IEC 60601-1-1 and test the medical system according to the requirements.

evGuide TLS System Limitations

The EvGuide TLS System is intended for use by medical personnel who have received appropriate training. To determine if use is appropriate, the trained user must be aware of system limitations. Read carefully the User's Manual and also refer to the **Instructions for Use** included with each evGuide TLS Adaptor.

When using the electrical configuration of EVGUIDE TLS adaptor, a stylet or a guidewire typically provided with the kit of the vascular access device must be used in order to ensure an electrically conductive path between the proximal and the distal ends of the vascular access device.

When using the saline adaptor configuration of evGuide TLS, the user needs to ensure that the catheter lumen is constantly filled with saline and in contact with the evGuide TLS adaptor, such that electrical conductive trough the catheter lumen is ensured from the proximal to the distal end of the vascular access device.

When using the saline adaptor configuration of evGuide TLS, instability of the endovascular electrical signal baseline may occur if the user makes hand contact with the proximal end connection of the evGuide TLS adaptor.

The evGuide TLS system must be battery powered when used in a clinical case, i.e., as long as ECG electrodes are connected to the patient. The system battery lasts for approximately two hours. Recharging the battery must be done in between clinical cases.

The evGuide TLS system uses data processing algorithms to enhance the quality of the endovascular ECG signal. In situations when electrodes have been disconnected and reconnected again, e.g., when the red clip electrode is connected to the sterile adaptor, it may take several seconds for the system to transition from a no-signal to a stable signal state. Please wait while the system makes this transition and do not touch the electrical connections of the adaptor during this time.

The evGuide TLS system uses a serial communication protocol and a USB-Serial converter between the laptop and the ECG module. If the USB connector is not connected when the evGuide software application starts up or if the USB connector is disconnected before shutting down the evGuide software application, under certain circumstances the evGuide application must be restarted.

In order to prevent accidental installation of software on the evGuide laptop computer, the user does not have administrative rights to install software. Only Romedex personnel have the administrative rights to perform software installation on the evGuide laptop.

Directions for Use

System Components

Figure 2 shows the system components:

- ECG module (1)
- PC/Laptop running EvGuide TLS software (2)
- USB connection cable to the ECG box (3)
- Label printer (optional) (4)
- ECG cable (5)
- Sterile EvGuide TLS Adaptor connected to the stylet of a PICC catheter (6)
- A skin ECG electrode (7)

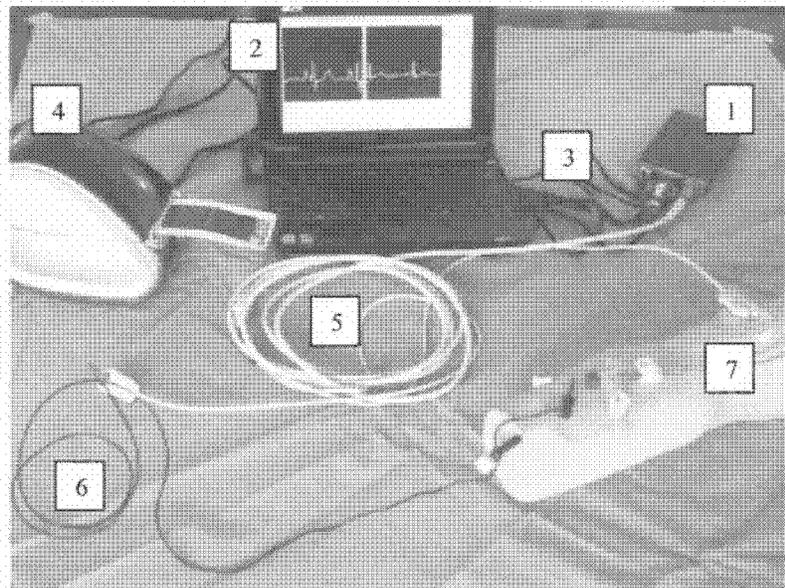


Figure 2: EvGuide TLS System Configuration

System Setup

Powering On and Shutting Down

Power on the system

Find an appropriate location for the system. Ensure the evGuide TLS System is placed no more than 4 feet away from the patient outside the sterile field.

Assure that all the individual power switches to the PC/Laptop, optional printer, and medical grade power supply, where appropriate, are turned OFF.

Make sure the power cord is connected to the system and is plugged into a grounded electrical outlet. For detailed information on electrical requirements, see section "Making Proper Electrical Connection" in this Manual.

The PC/laptop and the ECG module can run on the PC/laptop battery. In this case and if the optional printer is not used, then there is no need to connect the medical grade power supply to the power outlet. Fully charging the laptop battery should be accomplished before any procedure if the system runs on battery. A full battery charge lasts for approximately two hours.

Turn the system on by turning on the power switches on of the individual systems in the following order:

- a. PC/Laptop
- b. Optional printer

Power off the system

To power off the system:

- a. Close the evGuide application
- b. Power down the Windows operating system on the PC/Laptop
- c. Turn off the optional printer

Start the EvGuide TLS Software

Once PC/Laptop power up sequence is finished, the EvGuide TLS software will be launched automatically operation mode. The startup screen looks as shown in Figure 3.

The graphic elements on interface are:

- 1 - Toolbar containing controls for play / pause the data acquisition, load / save ECG files, printing to file / printer, settings and help. The following functions are available on the toolbar:
 - a) Pause/Play the ECG waveform in acquisition and playback modes.
 - b) Save the case to file. When clicking the "Save" icon, all the ECG waveforms (lead I, II, and III) are save in a file. The default name of the file the name of the patient to which the date and time are appended. The default directory is C:/Data created when installing the evGuide TLS application.
 - c) Print to file. Click on the button to select (highlight) it, click again to unselect it. When this button is selected, the printer output will be redirected to a file using a default name and location.
 - d) Print. By clicking this button, the print preview will be displayed. You need to freeze the desired information on the right hand side screen before you can

- print. The printer output will be redirected to the default printer. A default label printer is preinstalled on your system.
- e) Clicking on the Help button brings up the User's manual and information about the evGuide TLS software.
 - g) By dragging the question mark to a screen location, certain hints will be provided depending on the location.
 - h) Closes the evGuide TLS application before turning off the computer. If the user accidentally closes it and needs to reopen it again, double click on the evGuide TLS icon on the desktop.

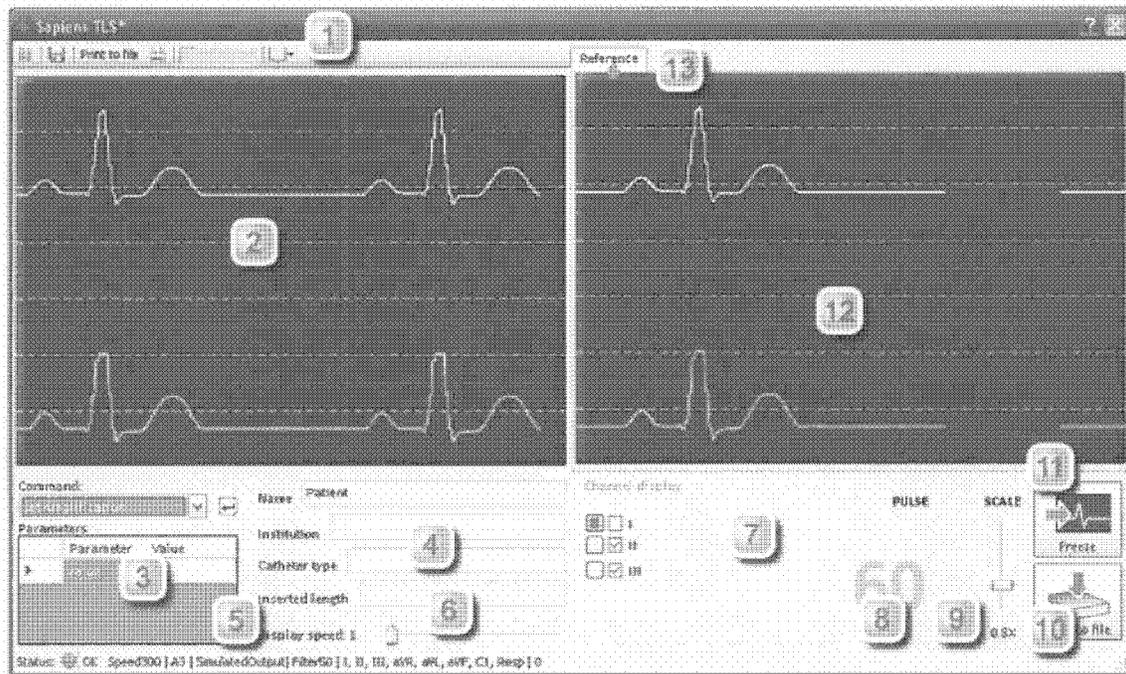


Figure 3: PC controls and start-up screen

- 2 - Main screen where the graphics are drawn.
- 3 - Available commands accepted by the device and respective parameters
- 4 - 'Patient name', 'institution', 'catheter type' and 'inserted length' information that will be shown on printed label.
- 5 - Status bar displaying various information about the ECG module status
- 6 - Scroll bar used for scaling the graphics.
- 7 - Color and visibility setting for channels.
- 8 - Frequency of R-Peaks measured in number of peaks / minute.
- 9 - Scale used to amplify the signals received from device.
- 10 - Pressing this button will save the current image shown in Main screen.
- 11 - Pressing this button will copy the current image shown in Main screen to Secondary screen.
- 12 - Secondary screen used for comparison.
- 13 - Tab container displays the 'Reference' page.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

WARNING: Do NOT install any software on the EvGuide TLS PC. This may result in patient and user harm and system damage.

Procedure Workflow

1. Connect the ECG Cable

Take the ECG cable supplied with the evGuide TLS System, Figure 2 and wipe the cable down according to hospital's guideline. If you are using a one-lead ECG cable, locate a new off-the-shelf electrode patch used for ECG measurement and place it on the patient's lower left abdomen per its instructions for use. Connect the green clip connector of the provided ECG cable to the electrode patch on the patient's arm near the insertion site.

If you are using a two-lead ECG cable, locate two new off-the-shelf electrode patches used for ECG measurement and place one the patient's lower left abdomen per its instructions for use and the second on the patient's left shoulder or arm per its instructions for use.

Connect the green clip connector of the provided ECG cable to the electrode patch on the patient's left lower abdomen.

Connect the yellow clip connector of the provided ECG cable to the electrode patch on the patient's left shoulder or arm.

If you are using a three-lead ECG cable, connect the low and the green clips as above and connect the black clip next to the green clip on the left lower abdomen.

2. Connect the EvGuide TLS Adaptor

WARNING: The evGuide TLS Adaptor is provided sterile in a sterile pouch. Handle the sterile evGuide TLS pouch and adaptor only with sterile gloves and pay attention not to compromise the sterile field.

Connect the red clip connector of the provided ECG cable to the plug end of the sterile evGuide TLS Adaptor.

When using an electrical adaptor, connect the alligator clip end of the evGuide TLS adaptor to the proximal end of the stylet or guidewire which is packaged with your venous access device or pre-inserted in one of the lumens of your venous access device.

When using a saline adaptor, please connect the adaptor between the proximal catheter hub and the syringe used for injection of saline solution. Make sure that the syringe is full with saline and no air is present in the syringe. Flush before connecting syringe. Inject saline until electrical conductivity is established between the distal and the proximal ends of the catheter.

Please also refer to the evGuide TLS Adaptor Instructions for Use.

3. Display ECG waveforms

As soon ECG signals are detected, they are displayed on the left hand side ECG window of the graphical user interface, Figure 3.

In the two lead configuration i.e., when the green and yellow electrodes are connected to the patient, a reference ECG signal is also displayed in addition to the waveform corresponding to the distal tip of the catheter. The waveforms on the top in Figure 3 on both left and right hand side display windows represent the skin ECG or reference ECG. The waveforms on the bottom in Figure 3 on both left and right hand side display windows represent the electrical signal detected at the tip of the central venous catheter.

The right hand side window is labeled "Reference". The reference window allows for saving the ECG waveforms at a desired location for further comparison.

Clicking on the "Freeze" button below the Reference window or using the left arrow key on the keyboard freezes the display, such that the frozen ECG waveform can be used as a reference.

The scroll speed of the ECG waveform can be selected by using the scroll bar "Display speed" (6 in Fig 3)

The amplitude scale for the ECG waveform can be manually selected by using the Scale scrollbar (9 in Fig 3) or the up/down arrow keys on the keyboard.

4. Document the Procedure

The ECG waveforms can be recorded real-time during the procedure by clicking on the "Record" button. The ECG waveforms are recorded in a file. The file name is automatically generated by the computer if a patient ID is not input. If a patient ID is input the file name is generated based on the patient ID. The file can be copied to a USB memory stick or memory card as a removable storage device.

Clicking the "Print/Save" button sends a screen shot to the printer if attached and save the screen shot in a file in JPG format. The file name is assigned automatically if no patient ID is input and a name is assigned based on the patient ID if a patient ID is input.

The following information can be input in the corresponding fields on the graphical user interface at any time:

5. Patient name
6. Institution name
7. Catheter type
8. Inserted length

This information is printed out in the corresponding fields of the print layout in Figure 4.

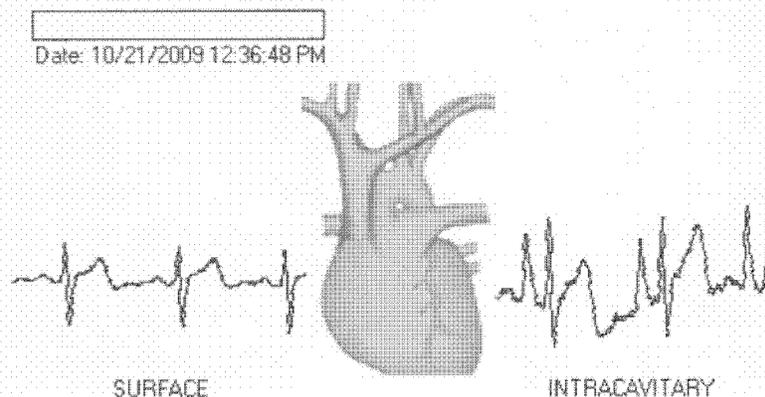


Figure 4: Print layout

To copy any file from the evGuide TLS laptop to a removable storage medium, exit the evGuide application and use the Windows XP operating system to copy the desired file to the desired location.

Note: The user does not have administrative rights on the evGuide computer and therefore cannot install any software on this computer.

Assessment of Catheter/Adaptor Location

1. Outside the thoracic cavity

Outside the thoracic cavity the ECG signals are similar to the ones at the skin level.

2. Target Tip Location

When the catheter and the stylet or guide adaptor in the catheter are advanced towards the heart, the ECG waveform changes. These changes are particularly visible when compared to the "Reference" skin ECG signal. As known from the published literature, the P-wave changes shape and amplitude

The right hand side window in Figure 5 illustrates a typical ECG waveform (bottom) at the caval-atrial junction with a maximum amplitude P-wave. This can be considered as a reference waveform.

The left hand side window in Figure 5 illustrates a typical ECG waveform characteristic of the desired target location of the tip of a central venous access device. The left hand side display window shows a typical ECG waveform (bottom) in the lower third of the superior vena cava. The amplitude of the P-wave is half of the amplitude of the P-wave at the caval-atrial junction on the right hand side display (reference).

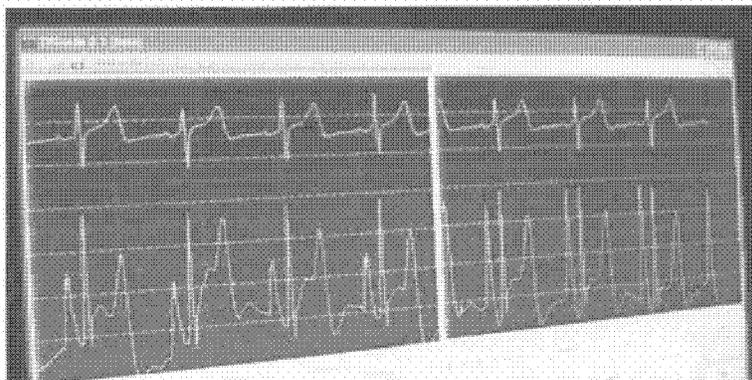


Figure 5: ECG signal at the target location

Figure 6 illustrates a biphasic P-wave characteristic of a deeper location inside the right atrium.

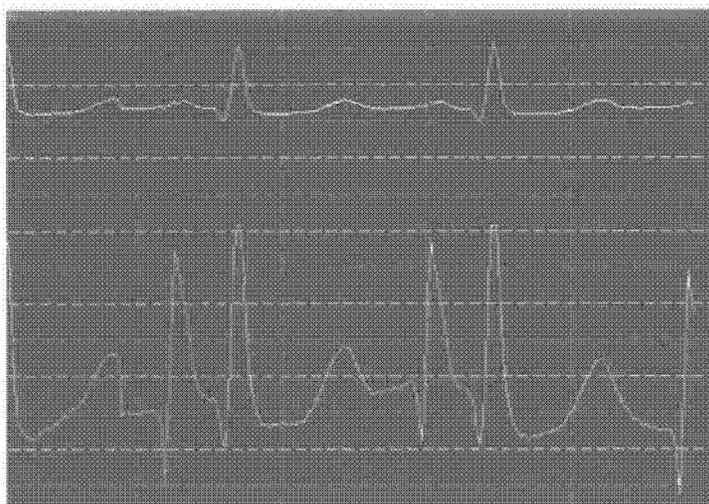


Figure 6: ECG signal too deep in the heart: biphasic P-wave

3. Label Printer Layout

Figure 4 illustrates the print layout. The print layout is displayed on clicking on the printer icon on the command toolbar at the top of the screen. The surface and the intracavitary ECG waveforms are displayed on the right hand side and respectively on the left hand side of the print. Between the two waveforms a heart symbol is printed in order to allow the user to mark with a pen on printed paper the location of tip where the corresponding ECG waveforms have been obtained.

The patient name, institution name, catheter type and length, are displayed as well as they were input in the corresponding fields of the graphical user interface.

Guidance and Manufacturer's Declaration

Warranty

The manufacturer, Romedex International Srl, warrants this product against defects in material and workmanship for a period of one year from the date of original purchase, and during such period agrees to repair, or at Romedex International's discretion, replace any defective unit free of charge. The warranty on the repaired or replaced unit continues from the purchase date of the original unit. This warranty does not cover damages resulting from misuse, abuse, modification, or alteration of the evGuide TLS.

Service and Repair

For servicing information or to return your evGuide TLS for repair, please contact Romedex International's technical support at service@romedex.com.

Please read this manual and follow its instructions carefully. The words WARNING, CAUTION and NOTE convey special meanings. When they are used throughout this manual, they should be carefully reviewed to ensure the safe and effective operation of this product.

Details of the evGuide TLS Adaptor use are covered in the Instructions for Use provided with the Adaptor and are not covered in this manual.

⚠ WARNING: A WARNING indicates that the personal safety of the patient or physician may be involved. Disregarding a WARNING could result in injury to the patient or physician.

⚠ CAUTION: A CAUTION indicates that particular service procedures or precautions must be followed to avoid possible damage to the product.



NOTE: A NOTE indicates special information to facilitate use of the product, or to clarify important information.

Contact Information

If you have any questions or comments regarding the use of this product contact:

*Romedex International Srl
58 Aleea Arubium Str
Bucharest, 022944 Romania
Tel: +40.743.490.892
Fax: +40.317.107.048
Email: info@romedex.com*

**evGuide TLS™
ADAPTOR**

INSTRUCTIONS FOR USE

DESCRIPTION:

- A family of sterile adaptors made of medical grade materials to facilitate placement of central venous access devices. evGuide Tip Location System (TLS) adaptors are packaged in sterile individual pouches. Alternatively, the evGuide TLS adaptors can be included in venous access device kits by the corresponding manufacturer of market available devices, e.g., PICC, CVC, hemodialysis catheters, implantable ports, and other central lines.
- The evGuide TLS adaptor must be used with the evGuide Tip Location System. The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide™ Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity. Please refer to the evGuide TLS system User's Manual.
- The evGuide TLS adaptor is provided in two configurations. In one configuration – Electrical Adaptor, the adaptor is a sterile 39" long isolated stainless steel wire with a plug connector at one end and an alligator clip at the other end. The alligator clip is used to attach the evGuide TLS adaptor to any commercially available stylet or guidewire used for central venous catheter placement. The plug connector is used to connect the adaptor to the ECG cable provided with the evGuide TLS system. In the second configuration

– Saline Adaptor, the adaptor consists of a universal catheter-syringe adaptor integrated with a 39" long sterile stainless steel wire with a plug connector at the end. The adaptor can connect to any commercially available catheter and syringe luer and allows for the injection of saline into the blood vessel. The plug connector is used to connect the adaptor to the ECG cable provided with the evGuide TLS system. When connected to the evGuide TLS system, the evGuide TLS adaptor can be used to detect cardiac electrical signals.

CONTRAINDICATIONS:

- All contraindications of central venous catheters apply as specified by the central venous catheter manufacturer.
- There are no contraindications specific to the evGuide TLS Adaptor

POSSIBLE COMPLICATIONS:

- All complications indicated by the manufacturer of the central venous catheter should be considered when using the evGuide TLS adaptor.
- There are no complications specific to the evGuide TLS Adaptor.

WARNINGS:

- Monitor catheter tip placement during insertion procedure per institutional policy.
- Release the central venous catheter after insertion according to your institution's guidelines
- Do not release the central venous catheter based on evGuide information if the signal on the screen is unstable or does not show the waveform according to the evGuide User's Manual. In such a case, use a different method for guiding the placement of your central line
- If the evGuide adaptor becomes damaged, remove the adaptor with caution as to not change the position of the catheter.
- The evGuide TLS adaptor is for Single Use Only.

- Do not re-sterilize the adaptor or accessories by any method.
 - The manufacturer shall not be liable for any damages caused by reuse or re-sterilization of this adaptor or accessories.
 - Contents are sterile in an unopened, undamaged package. **STERILIZED BY ETHYLENE OXIDE**
 - Do not use adaptor or accessories if package is opened or damaged.
 - Do not use adaptor or accessories if any sign of product damage is visible.
 - The evGuide TLS adaptor is not intended to diagnose or treat disease
2. Insert the central venous access device according to standard protocols and the device instructions for use.
 3. Place the evGuide TLS System on a table which is less than 4 feet away from the insertion site of the patient without compromising the intended sterile field.
 4. Take the ECG cable supplied with the evGuide TLS System, Figure 1 (2) and wipe the cable down according to hospital's guideline. If you are using a one-lead ECG cable, locate a new off-the-shelf electrode patch used for ECG measurement and place it on the patient's arm near the insertion site per its instructions for use. Connect the yellow clip connector of the provided ECG cable to the electrode patch on the patient's arm near the insertion site. If you are using a two-lead ECG cable, locate two new off-the-shelf electrode patches used for ECG measurement and place one the patient's arm near the insertion site per its instructions for use and the second on the patient's opposite shoulder or arm per its instructions for use. Connect the yellow clip connector of the provided ECG cable to the electrode patch on the patient's arm near the insertion site. Connect the black clip connector of the provided ECG cable to the electrode patch on the patient's opposite shoulder or arm.

ADAPTOR PRECAUTIONS:

- Do not use sharp instruments near the adaptor.
- Adaptor may be damaged if clamps other than what is provided are used.
- Examine adaptor before each insertion for damage.
- Read instructions carefully before using this device. The adaptor should be manipulated by a qualified, licensed physician or other qualified health care professional.
- The medical techniques and procedures described in these instructions for use do not represent all medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgment in treating any specific patient.
- Use standard hospital protocols when applicable.

Note: For detailed central venous catheter preparation and insertion information, follow the instructions stated in the catheter's Instruction for Use.

WORKFLOW

1. Prepare patient per standard sterile techniques.

5. Please refer to the evGuide TLS System User's Manual for details.
6. When using the evGuide TLS Electrical Adaptor, Figure 1, expose the stylet pre-inserted in the catheter at the distal end close to the touyh borst. Open the Adaptor package and take out the evGuide TLS Adaptor wire. Attach the mini-grabber connector to the exposed stylet close to the touyh borst. Follow the catheter manufacturer's instructions regarding the use of the stylet during procedure. Place the catheter onto the patient where sterile field is established. Clip the evGuide TLS Adaptor wire to the

sterile drape to ensure the catheter stays in the sterile field.

7. When using the evGuide TLS Saline Adaptor, remove the cap from the catheter luer connector. Flush the catheter with saline per manufacturer's instructions to ensure the catheter lumen is full of saline. Place the catheter onto the patient where sterile field is established. Open the Adaptor package and take out the evGuide TLS Adaptor. Connect the adaptor between the syringe and the catheter proximal end as illustrated in Figure 2. Clip the Adaptor wire to the sterile drape to ensure the catheter stays in the sterile field.
8. In either configuration, attach the plug connector of the evGuide TLS Adaptor wire to the red lead of the ECG cable provided with the evGuide TLS System according to User's Manual. Please refer to evGuide TLS User's Manual for further details.

CAUTION: Discard gloves and change to a new pair of sterile gloves after connecting the Adaptor to the evGuide TLS System and completing the setup of the evGuide TLS System per User's Manual.

CAUTION: Beware of the adaptor wire. Tripping over the adaptor might cause malfunction of the adaptor, detachment of the adaptor connectors from the system or injuries for the user.

9. Perform Veinuncture.

Note: If there is no blood return, verify catheter position before use.

10. Insert and advance the central catheter per catheter Instructions for Use provided by its manufacturer.
11. Complete catheter insertion.

Note: The central venous should be positioned with the catheter tip in the lower 1/3 of the superior vena cava

(SVC). Verify correct catheter tip position per standard hospital practice.

12. ECG patterns provided by the evGuide TLS Adaptor and System may be considered in assessing tip location. The distal tip should be positioned in the lower third of the SVC.

WARNING: Failure to verify catheter placement may result in serious trauma or fatal complications.

13. Aspirate, flush and secure the central venous catheter per instructions for use provided by the manufacturer.

REMOVAL:

14. When using the Electrical Adaptor, disconnect the alligator clip from the stylet or guidewire. Remove stylet according to the manufacturer's instructions. In case of Saline Adaptor, remove the Adaptor and attach touhy borst according to the manufacturer's instructions.
15. Stabilize the catheter position by applying light pressure to the vein distal to the insertion site.
16. Record catheter length, catheter lot number, adaptor's lot number and tip position on patient's chart.
17. Record patient name, catheter length on the evGuide TLS graphical user interface
18. Document tip location by printing using evGuide TLS.

Note: Refer to catheter's Instructions for Use for proper catheter maintenance, securement and wound dressing.

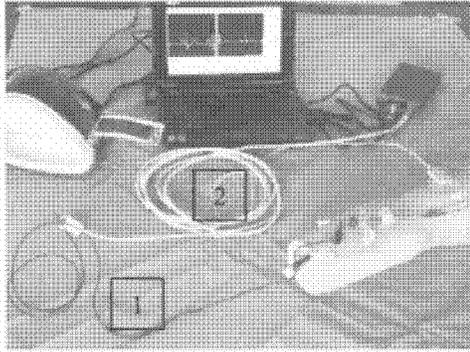


Figure 1:
EVGUIDE TLS System and Adaptor

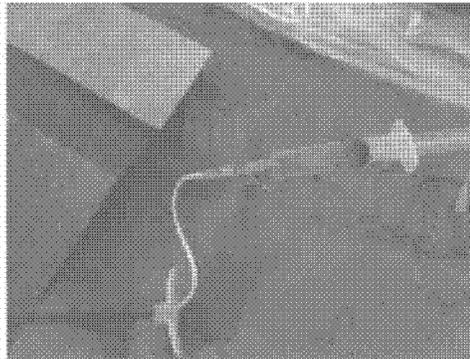


Figure 2:
EVGUIDE TLS Saline Adaptor –
Catheter-Syringe connection

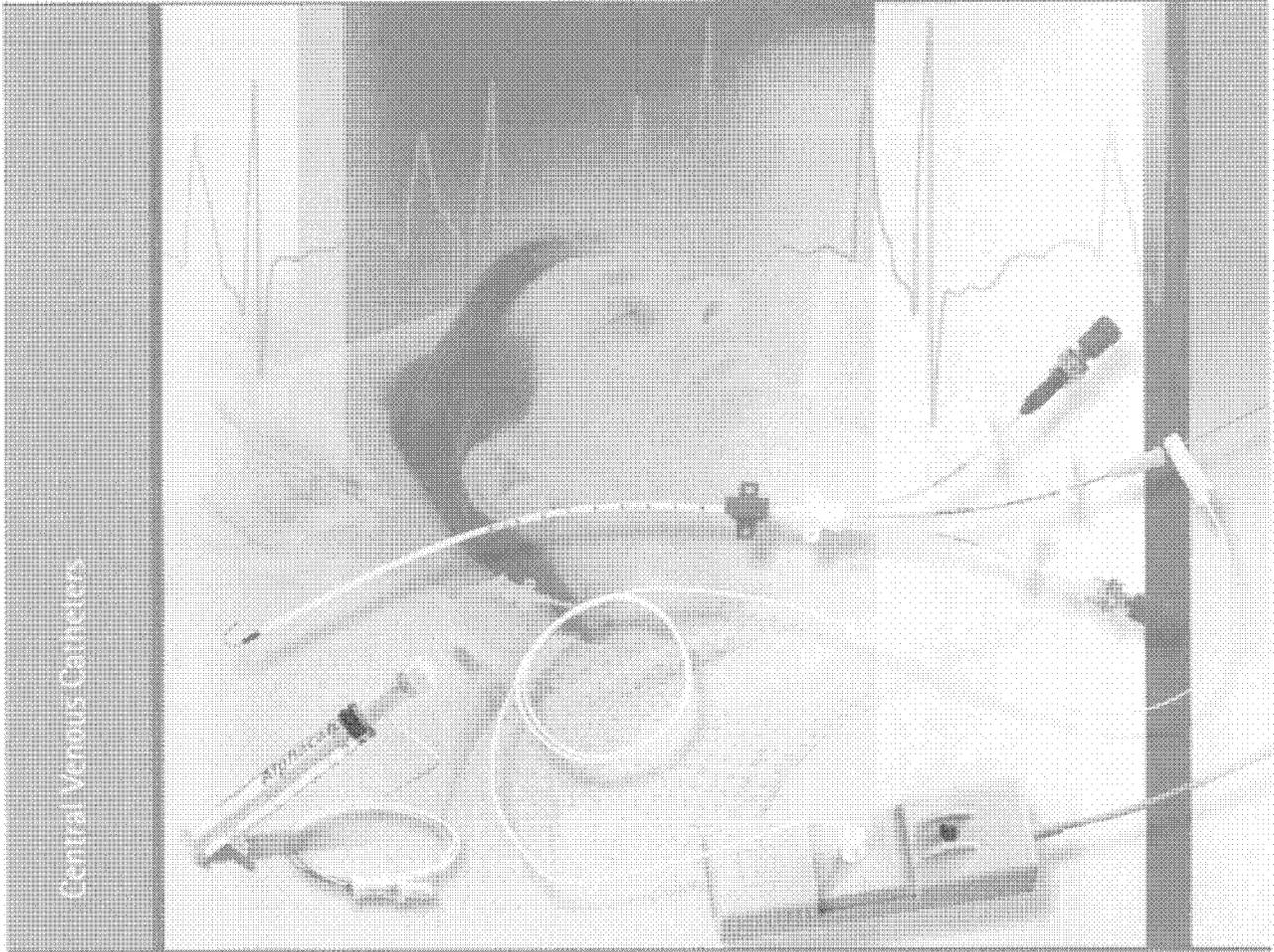
If you have any questions or comments
regarding this product, contact

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Fax: +40.317.107.048
Email: info@romedex.com*



Certofix®

ECG-lead – real-time CVC position verification
Every time: Simple, safe, reliable



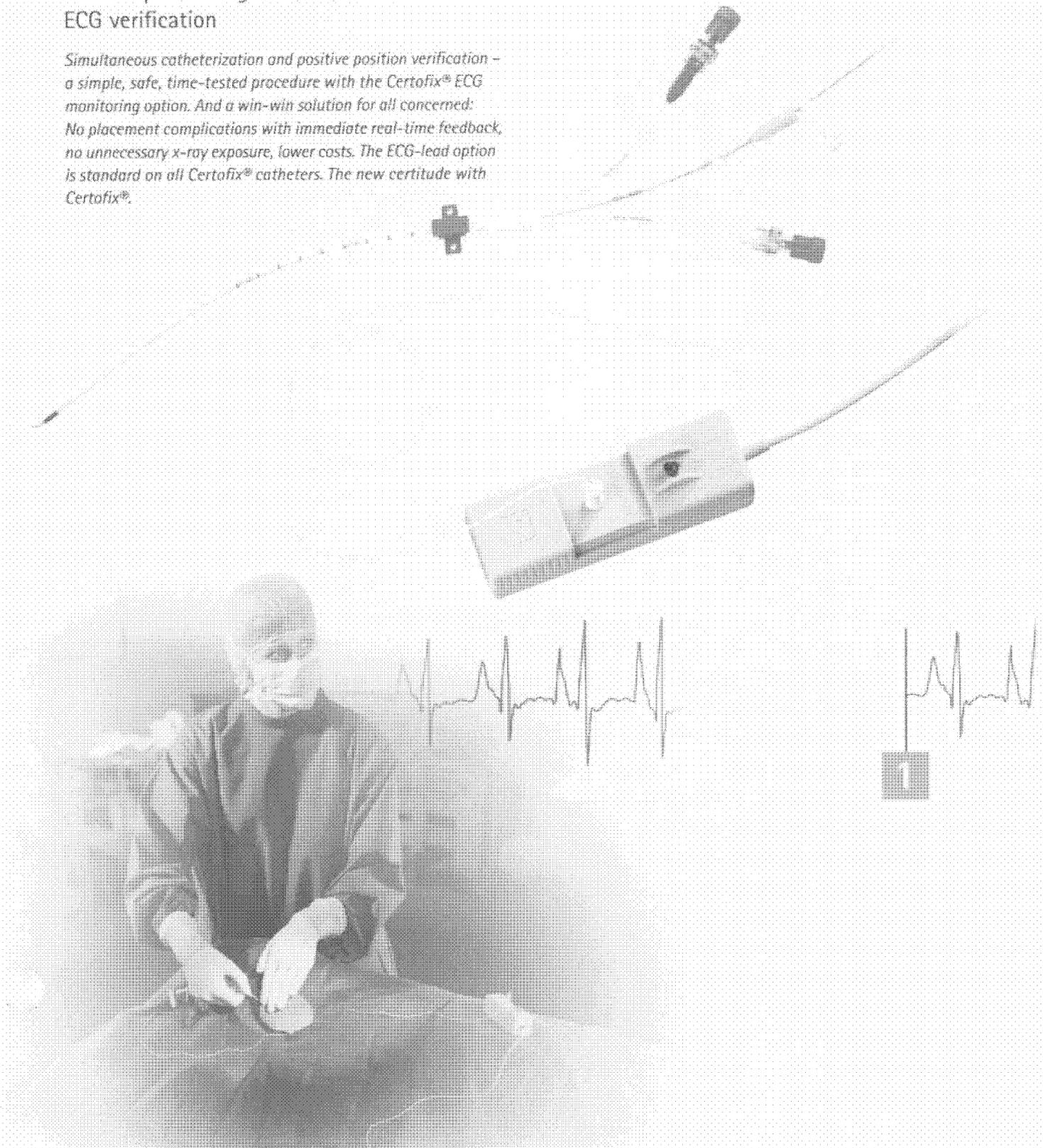
More certainty, more safety, more success

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ECG-lead – real-time position verification

Positive positioning with real-time ECG verification

Simultaneous catheterization and positive position verification – a simple, safe, time-tested procedure with the Certofix® ECG monitoring option. And a win-win solution for all concerned: No placement complications with immediate real-time feedback, no unnecessary x-ray exposure, lower costs. The ECG-lead option is standard on all Certofix® catheters. The new certitude with Certofix®.

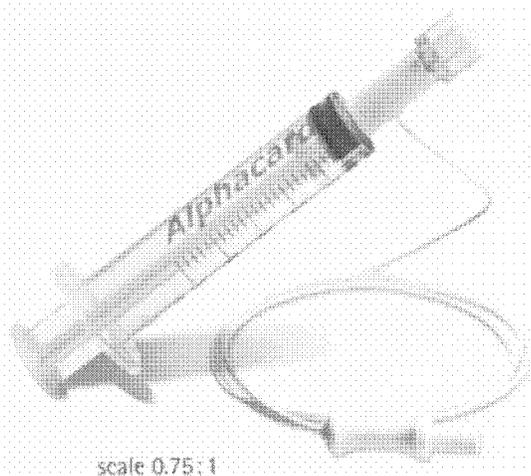




Alphacard®

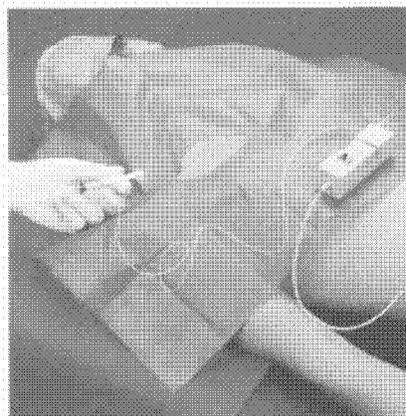
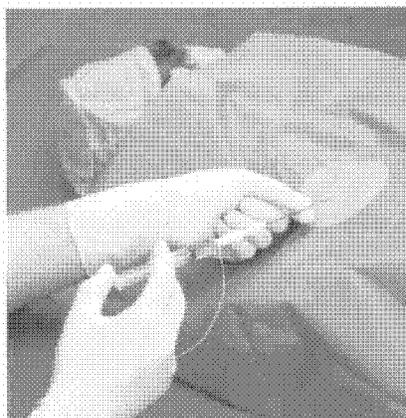
Alphacard® ...

The CVC has been successfully placed and now, after a couple of days, there is a need to verify that it still is correctly positioned. With the Alphacard® single-use syringe and ECG monitoring, the verification procedure is simple, safe and reliable.



- A quick look at the ECG monitor shows:
The P wave is clearly elevated indicating that the catheter tip is directly before the right atrium.
- The catheter tip has been withdrawn 2 to 3 cm in the superior vena cava and the P wave has normalized. Now the catheter has reached its final verified position.

Real-time information:
simple and sure



B. Braun Alphacard® and
Universal Adapter –
perfect compatibility for quick
and reliable readings



The new certainty

Central Venous Catheters

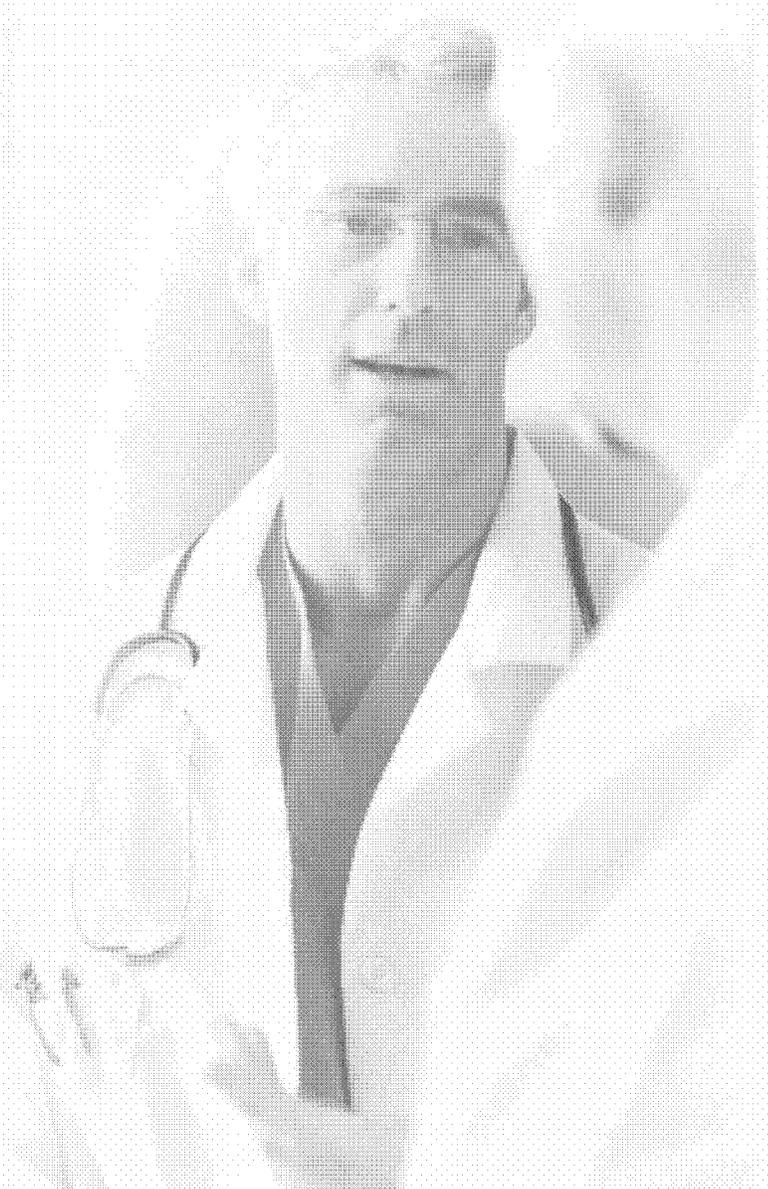
Presentations

PRESENTATION	DESCRIPTION
Alphacard®	U1800401
Universal adaptor	4150228
Universal adaptor for pediatrics	4150724

User benefits

- Well-established procedure in routine clinical practice
- High reliability through easy handling
- No chance of unrecognized catheter misplacement
- Economical time-saving technique
- No x-ray exposure for positioning control

For further information please visit our website
www.cvc-partner.com



Certofix®: safety by design



Central Venous Catheters

The Certodyn® universal adapter – for a no-fuss, no-worry ECG connection

The Certodyn® universal adapter allows easy connection with nearly all patient cables. And switches simply from extracorporeal to intra-atrial ECG.

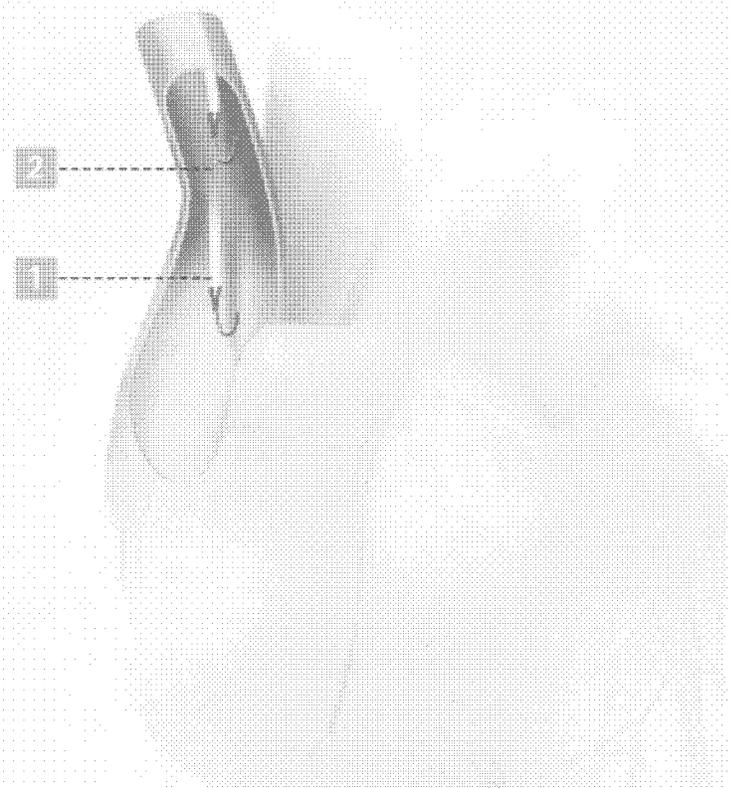
Guide wire tip- alignment marking

The specially provided marking on the guide wire indicates when the catheter tip and the end of the guide wire are in proper alignment for further advancement.



User benefits

- ECG-lead position monitoring
 - Real-time placement verification
 - On-the-spot certainty without the delays and expense of x-ray exposure
- Easy handling for every time reliability
- Always at hand with all Certofix® catheters



- A quick look at the ECG monitor shows: The P wave is clearly elevated indicating that the catheter tip is directly before the right atrium.
- The catheter tip has been withdrawn 2 to 3 cm into the superior vena cava and the P wave has normalized. Now the catheter has reached its final verified position.

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Catheter positioning

Anatomy

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Appendix C: Software Documentation

Romedex International

ECO #: DATE RECEIVED: INITIALS:

RISK ANALYSIS - EVGUIDE SOFTWARE
 REFERENCE SOP-1010

Product Manufacturer's Number(s):	
Date of Risk Analysis:	15-Oct-09
Attendees:	

Originator: _____ Date: / /

1. APPROVALS (CEO; R & D; Regulatory/Clinical; Quality; Marketing; Manufacturing; Other)

Department	Name	Signature	Date
CEO			
R&D			
Regulatory/Clinical			
Quality			
Marketing			
Manufacturing			
Other			

PRODUCT SPECIFICATION

TITLE: Software Requirement Specification (SRS)

REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
Sorin Grunwald	17	A	10/15/09	New document

PRODUCT SPECIFICATION

1. Introduction**1.1. Purpose**

The purpose of this document is to define the Software Requirements Specification (SRS) for evGuide TLS Software in order to meet the product requirements detailed in evGuide Marketing and Product Specifications. The intended users for this SRS are qualified personnel including the Product Development Team and the Software Development Team, and others who are familiar with the product / system specification. From this SRS, software engineer (s) shall be able to produce a detailed software design and eventually implementation in code.

1.2. Scope

The document defines specifications for the evGuide TLS Software as related to the evGuide TLS Marketing and Product Specifications. The evGuide TLS Software is intended to be used in conjunction with the evGuide TLS System.

1.3. Definitions, Acronyms, and Abbreviations

The term "Off-the-shelf software" refers to a generally available software component, used by a medical device manufacturer.

The term "shall" means that compliance with a requirement is mandatory for compliance to this specification. This is marked as "R" in this document.

The term "should" means that compliance with a requirement is recommended but is not mandatory for compliance with this specification. This is marked as "D" in this document.

The term "may" is used to describe a permissible way to achieve compliance with a requirement.

The terms "as applicable" and "as appropriate" indicate that a requirement must be fulfilled only if the conditions for the requirement have been met.

Software level of concern: An estimate of the severity of injury that a system could permit or inflict (directly or indirectly) on a patient or operator as a result of latent failures, design flaws, or use of the medical device software.

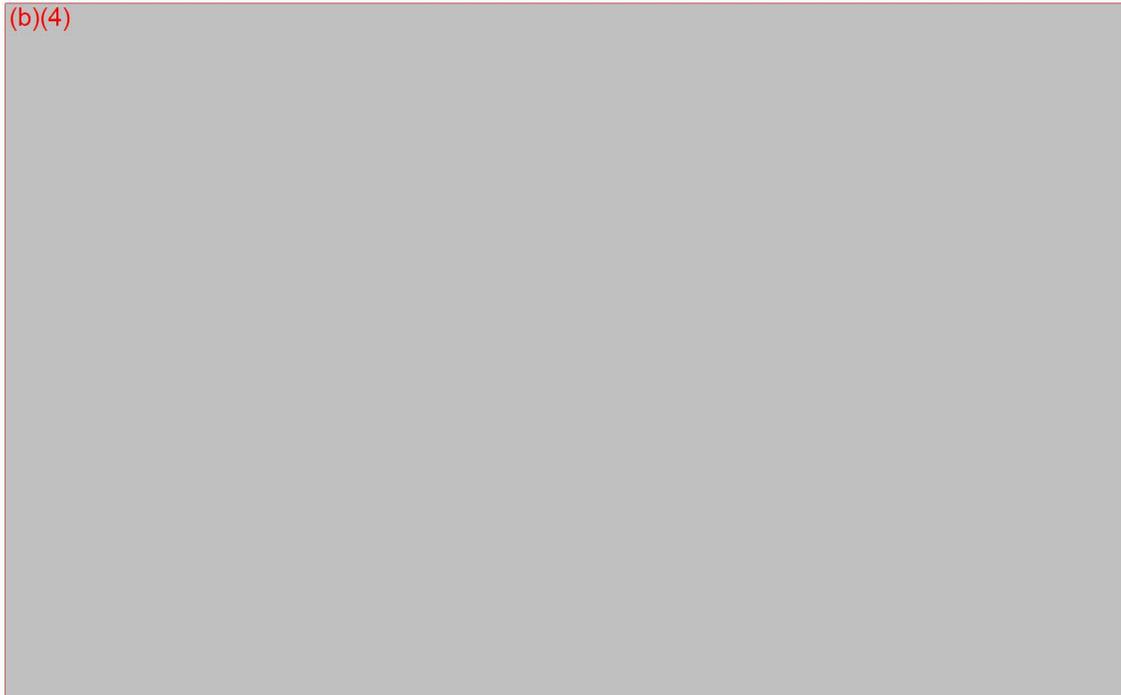
PRODUCT SPECIFICATION

Traceability – A quality attribute of product development that describes the correspondence between originating requirements, their resulting system features, and the tests that proved the system features correctly implemented the original requirements.

Traceability matrix: A matrix that records the relationship between two or more products of the development process, for example, a matrix that records the relationship between the requirements and the design of a given software component.

API	Application Programming Interface
GUI	Graphical user interface
LA	Left arm
N/A	Not applicable
OS	Operating System
PICC	Peripherally inserted central catheter
RA	Right atrium
SVC	Superior Vena Cava
UI	User interface
UICU	User interface and control unit

1.4. References [M13]



PRODUCT SPECIFICATION

(b)(4)

2. Overall Description

2.1. Product Perspective

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and re-verification of placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity. The evGuide TLS system consists of the evGuide Saline Adaptor, the evGuide Electrical Adaptor, an ECG Electronic Module and an ECG cable, a laptop, and the evGuide TLS application software. An optional printer can be connected to the laptop for documentation purposes. The evGuide TLS Saline Adapter can be connected to any commercially available central venous catheters and the evGuide TLS Electrical Adapter to any commercially available stylets or guidewires used for the placement of central venous catheters. The evGuide system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, intracavitary ECG, and intravascular ECG or endovascular electrograms) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and acquired in real time through the evGuide adapters. The endovascular ECG technique currently in use worldwide shows that the endovascular ECG waveform has distinctive shapes in accordance with the location in the patient's vasculature. Thus, the waveforms presented on the evGuide TLS system graphical user interface can aid the placement of central venous catheters.

The evGuide TLS consists of the following elements seen in the Figure 11.1:

1. ECG module
2. PC/Laptop running evGuide TLS software
3. USB connection cable to the ECG module
4. Label printer (optional)
5. ECG cable
6. Sterile evGuide TLS Electrical Adapter connected to a venous catheter (6)
7. A skin ECG electrode (7)

PRODUCT SPECIFICATION

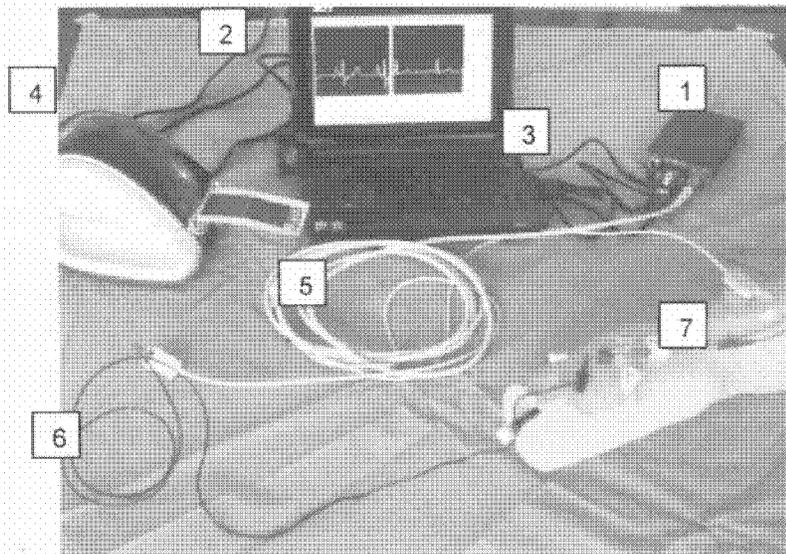


Figure 11.1 evGuide TLS system configuration

During the catheter placement procedure, one or several electrodes (7) are connected to the patient's skin using non-sterile off-the-shelf electrodes the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the patient's central veins per the institution's guidelines, an evGuide TLS adapter either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. The sterile evGuide TLS adapter transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (figure below) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated below, the user can estimate the location of the catheter tip. For example, in the Figure 11.2 the yellow waveform on the right hand side of the screen is representative of a location very close to the sino-atrial node (the pacemaker of the heart) and the yellow waveform on the left hand side of the screen shows a waveform representative of the lower third of the superior vena cava. The white waveforms on both screens shows the skin ECG signal used for comparison.



PRODUCT SPECIFICATION

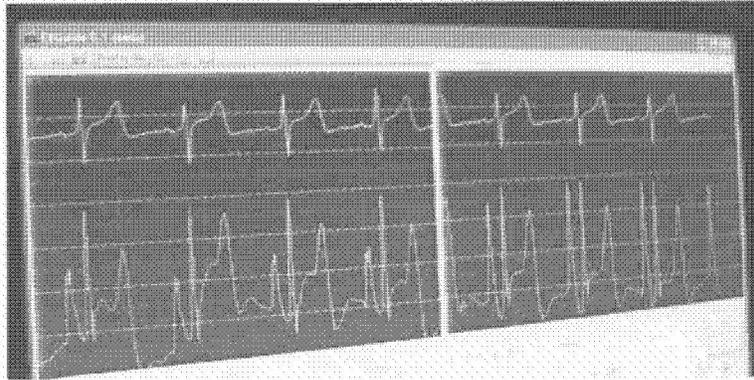
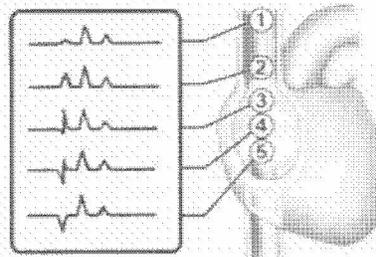


Figure 11.2: evGuide TLS reference screen and waveform

The relationship between the ECG waveform and the location around the sino-atrial node of the heart has been extensively documented in the literature and is in use in many clinical institutions world-wide. The paper “The ECG method for positioning the tip of PICCs: results from two preliminary studies” by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008 is attached in Appendix H of this submission. Figure 11.3 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community (Appendix H).



Endovascular ECG Location in the venous system

Figure 11.3 Changes of the signal waveform as a function of location in the vasculature (from Dr. M. Pittiruti, Appendix H)

2.2. Product Functions

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PRODUCT SPECIFICATION

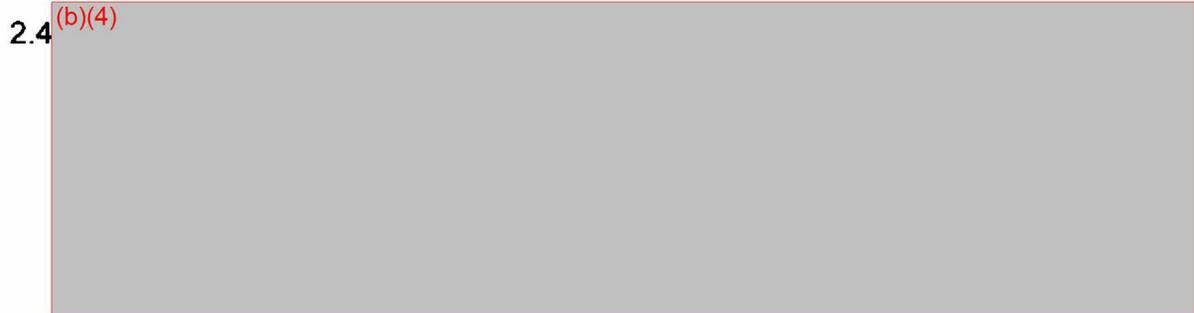
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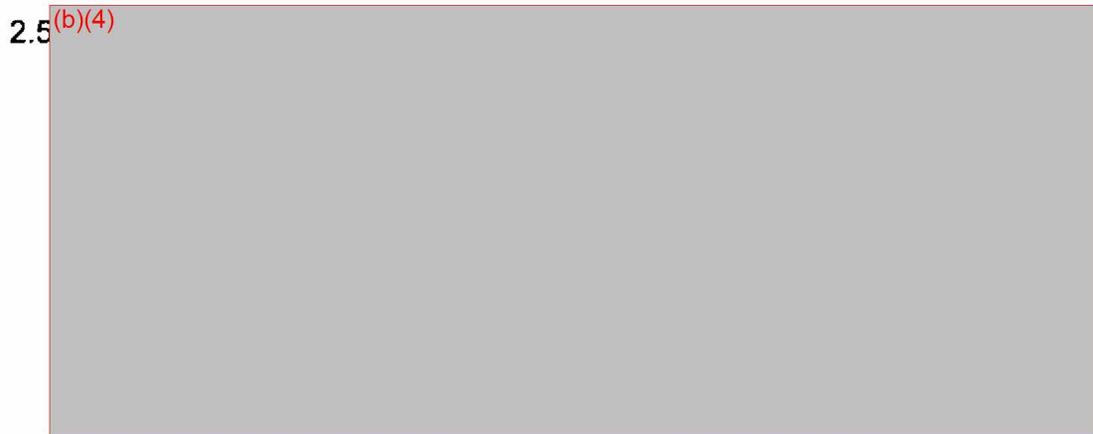
2.3. User Characteristics

The evGuide TLS Software will be developed with and used by accredited PICC nurses, interventional radiologists, and other physicians trained in the placement of central venous catheters.

2.4 (b)(4)



2.5 (b)(4)





PRODUCT SPECIFICATION

2.5.3. User interface equipment

- An input tracking device, such as a PC mouse
- Alpha-numeric input device, such as a PC keyboard and a touch screen
- 2 x USB port interface

2.5.4. Display requirements

- LCD monitor with resolution of minimum 1024 x 600 pixels

2.5.5. Communication between system components

- ECG Data Acquisition Module
- Optional printer

2.6. Assumptions and Dependencies

2.6.1. evGuide TLS Operating System (OS)

The OS for evGuide TLS should be Windows XP or Embedded CE.

2.6.2. ECG Module Support Software

The evGuide TLS Software should communicate with the ECG Module Software/Firmware supplied by the ECG Module manufacturer (OTS).

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3. Software Level Of Concern

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PRODUCT SPECIFICATION

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PRODUCT SPECIFICATION

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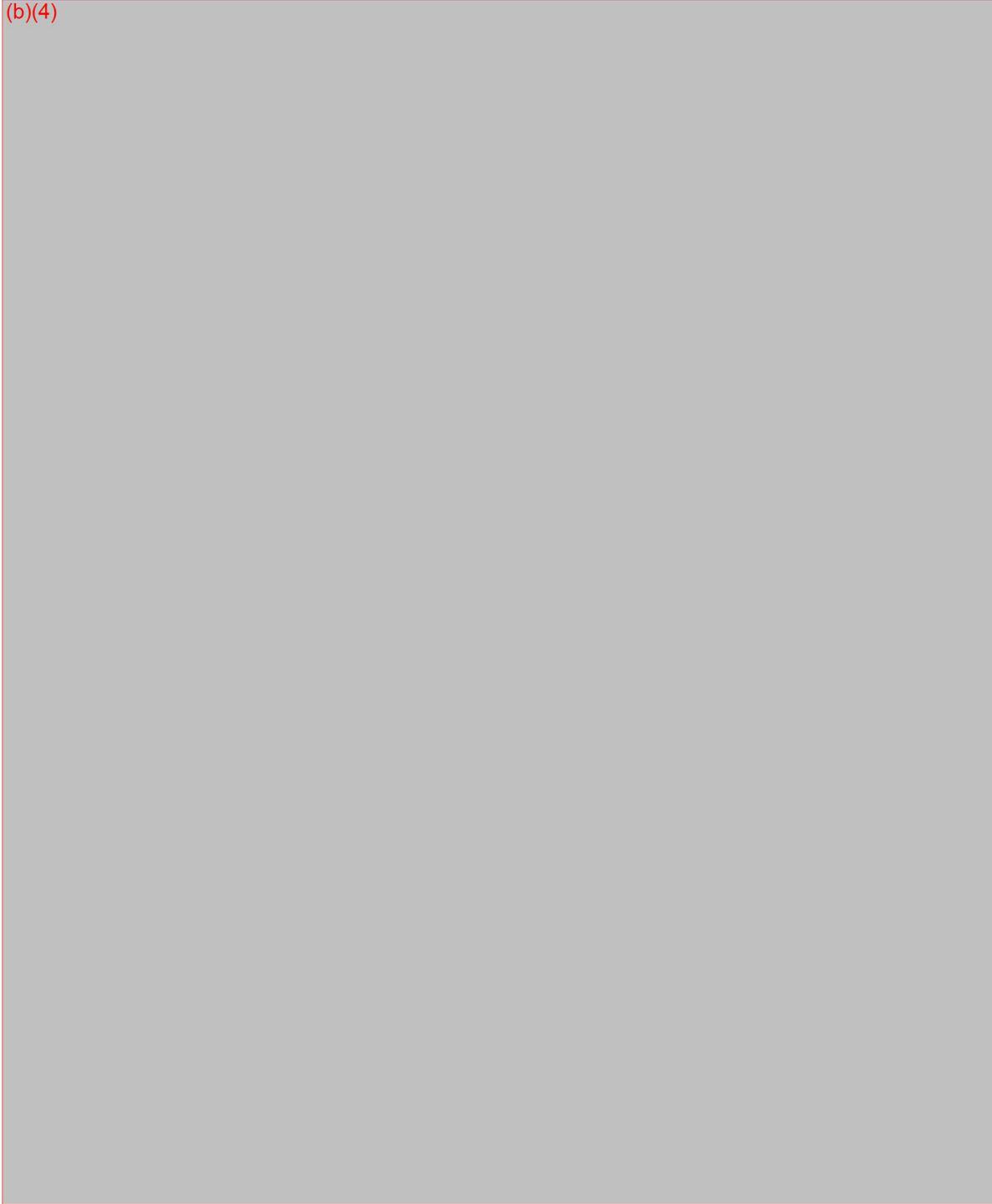
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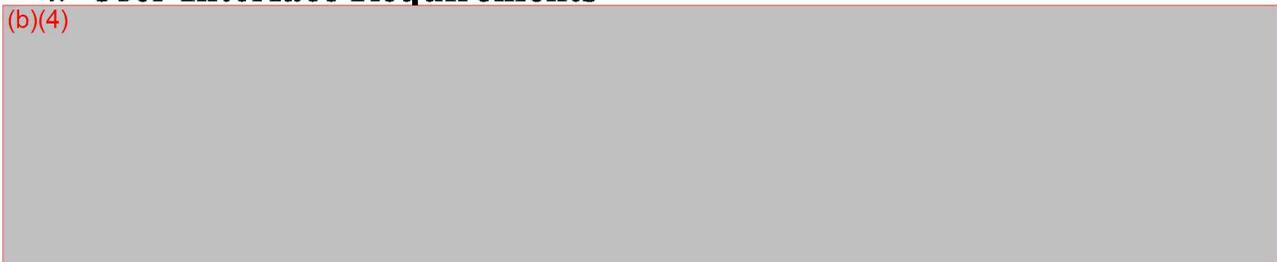
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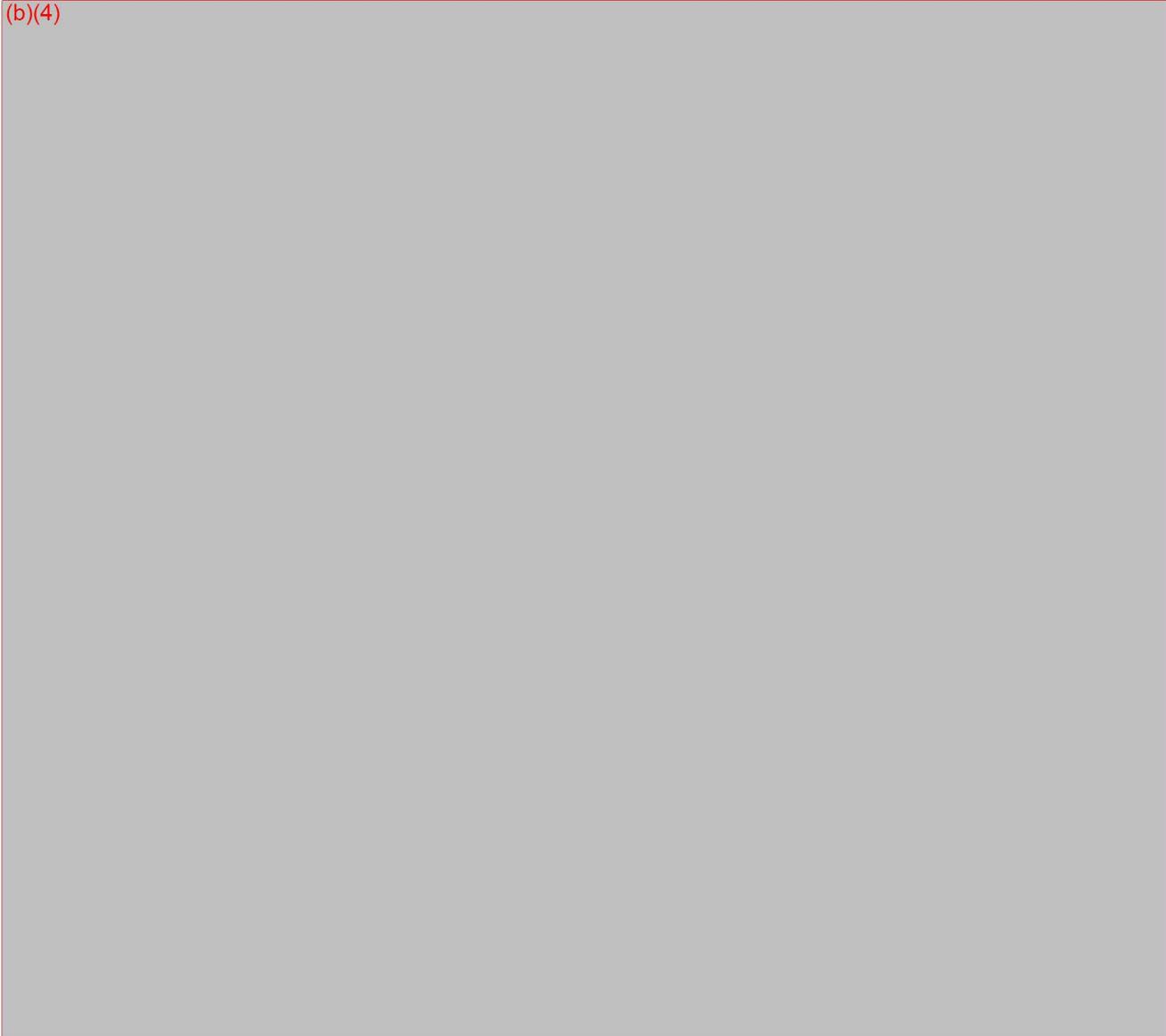
4. User Interface Requirements

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PRODUCT SPECIFICATION

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5. Intravascular ECG Requirements

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PRODUCT SPECIFICATION

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6. Information Processing Requirements

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7. Data Storage, Retrieval, and Documentation Requirements

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PRODUCT SPECIFICATION

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8. Performance Requirements

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9. Labeling Requirements

(b)(4)



10. Safety Requirements

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SOFTWARE DESIGN DESCRIPTION

EVGuide

Software Design Description

STANDARD OPERATING PROCEDURE

TITLE: SOFTWARE DESIGN CONTROL

REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
Sorin Grunwald		A		New procedure



STANDARD OPERATING PROCEDURE

TITLE: SOFTWARE CONTROL

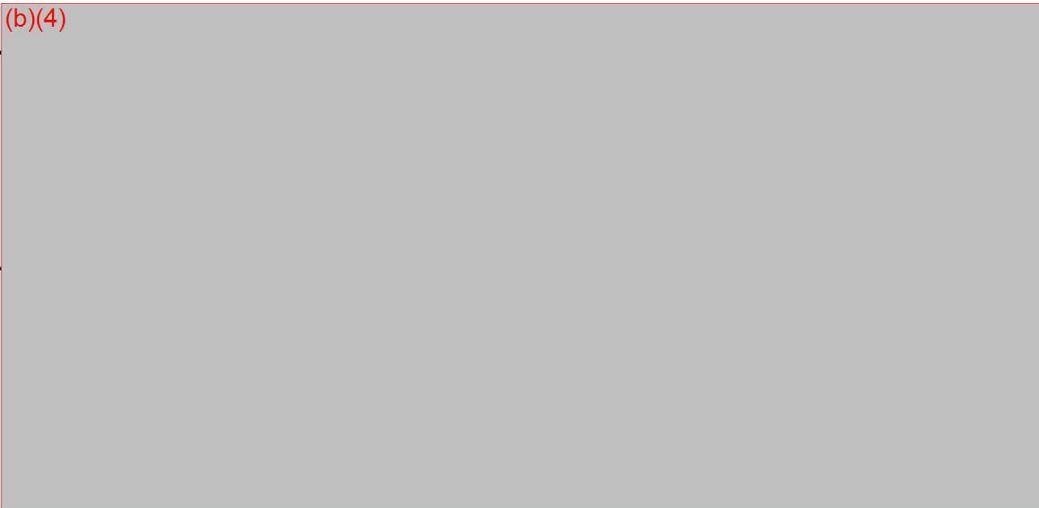
1. PURPOSE

This procedure provides an overall view of the activities of the software development life-cycle and the processes associated with them. These software activities and processes support the development of software within the company framework. If a subcontractor participates in the development process or is outsourced, the subcontractor shall work according to this software development life-cycle procedure or according to an equivalent process. This document maps the various software development and support processes onto the software development life cycle.

2. SCOPE

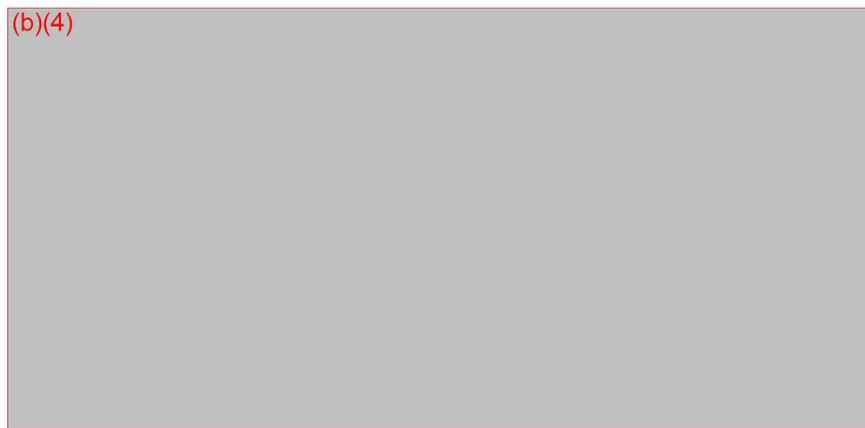
2.1. (b)(4)

2.2.



3. REFERENCES

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STANDARD OPERATING PROCEDURE

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STANDARD OPERATING PROCEDURE

4. DEFINITIONS

- 6.1 Level of concern (LOC) refers to an estimate of the severity of injury that a device could permit or inflict either directly or indirectly on a patient or operator as a result of device failures, design flaws, or simply by virtue of employing the device for its intended use. Defined as major, moderate or minor for the operator or patient when:
 - A failure or latent flaw could directly result in death or serious injury or indirectly through incorrect or delayed information or through the action of a care provider then the LOC is major.
 - A failure or latent flaw could directly result in minor injury or indirectly result in minor injury through incorrect or delayed information or through the action of a care provider then the LOC is moderate.
 - A failure or latent flaw or unlikely to cause any injury to the patient or operator then the LOC is minor.
- 6.1 Serious injury is one that is life threatening, results in permanent impairment of a body function or permanent damage to a body structure or necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
- 6.1 Verification means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.
- 6.1 Software validation means establishing by objective evidence that device specifications conform to the user needs and intended use.

5. RESPONSIBILITIES

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STANDARD OPERATING PROCEDURE

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6. PROCEDURE

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STANDARD OPERATING PROCEDURE

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STANDARD OPERATING PROCEDURE

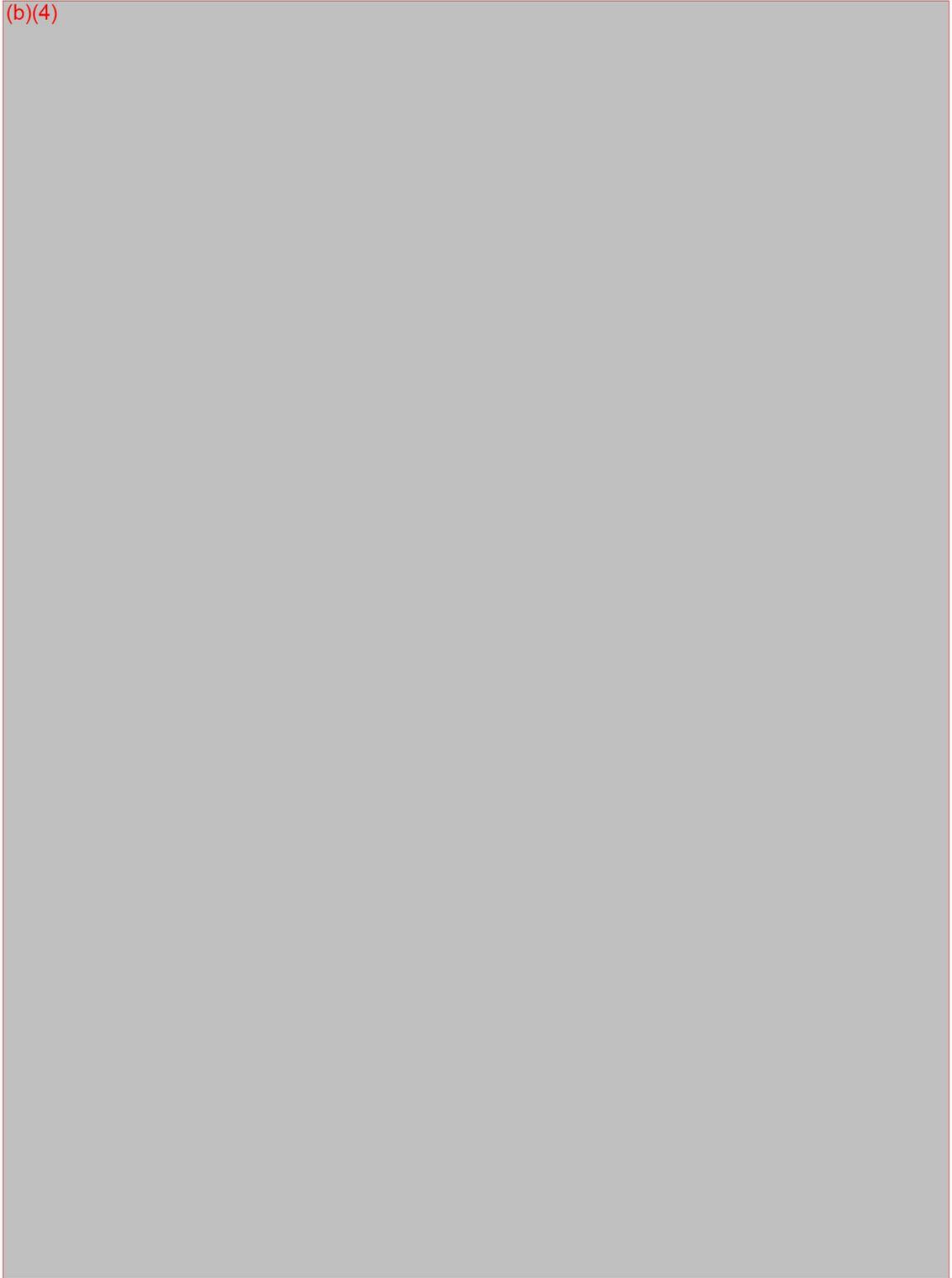
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STANDARD OPERATING PROCEDURE

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STANDARD OPERATING PROCEDURE

TITLE: OFF THE SHELF (OTS) SOFTWARE VALIDATION

REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
S. Grunwald	14	A		New procedure

Appendix D: EMC and Electrical Safety Testing



Appendix E: Product Specifications

MARKETING SPECIFICATION

TITLE: evGuide™ Tip Location System (TLS)

REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
S. Grunwald		A	9/1/2009	Initial document

MARKETING SPECIFICATION

1.0 PURPOSE

This document specifies the marketing specifications for the Romedex International evGuide Tip Location System (TLS).

2.0 SCOPE

This document applies to all products of the Romedex International evGuide TLS family.

3.0 CUSTOMER REQUIREMENTS

3.1 General

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health care institutions and as documented in many papers including "The ECG method for positioning the tip of PICCs: results from two preliminary studies" by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008.

Figure 1 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community.

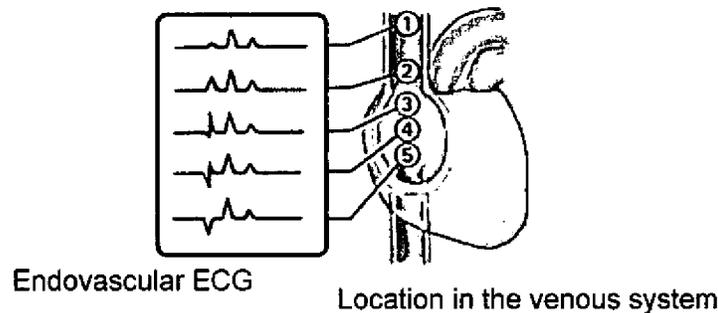


Figure 1: Changes in the ECG waveform as function of location in the vasculature

The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the "red" or "right shoulder" electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A "giant" P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the



MARKETING SPECIFICATION

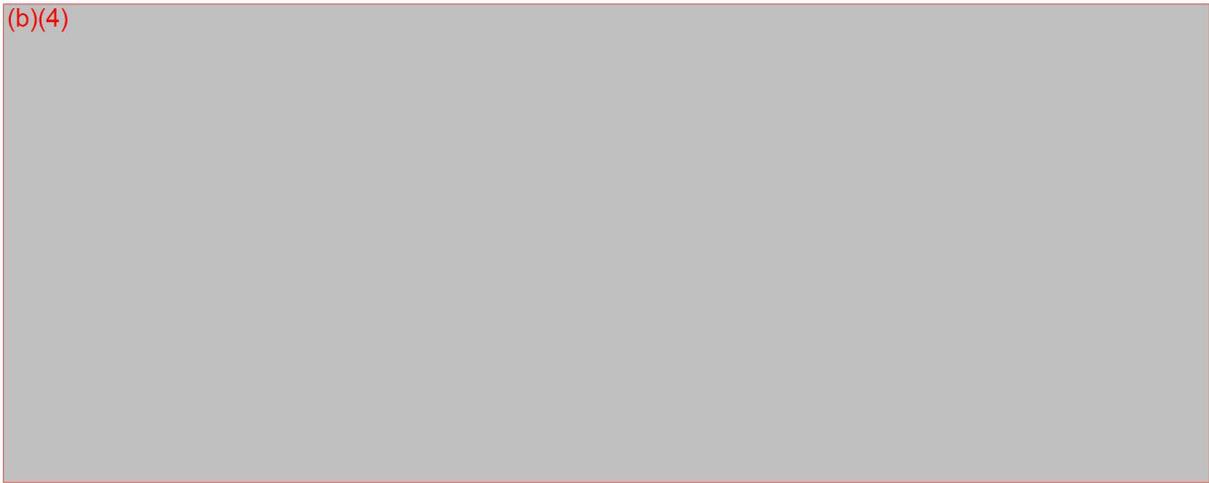
surface ECG, the tip of the electrode is in the superior cava vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava). Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, which are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

3.2 Indications to Be Addressed

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

3.3 Market Considerations

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4.0 REFERENCE DOCUMENTS

N/A

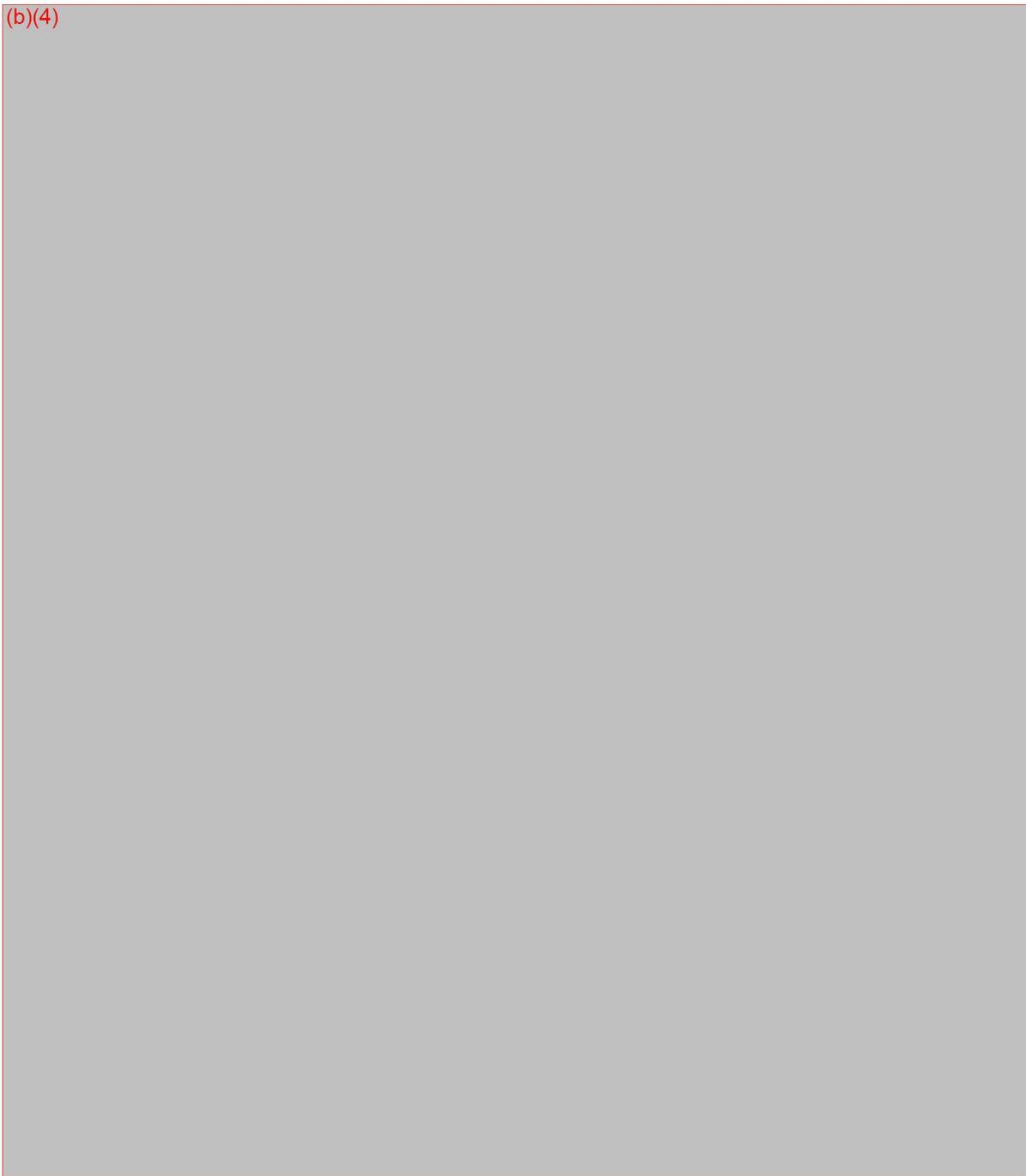


MARKETING SPECIFICATION

5.0 FEATURES

5.1 Performance

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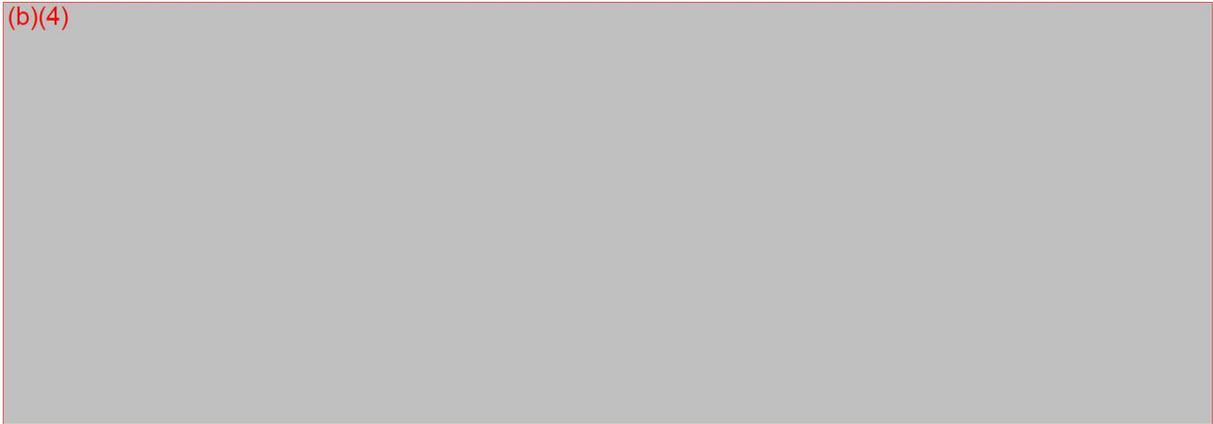
MARKETING SPECIFICATION

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5.2 Safety

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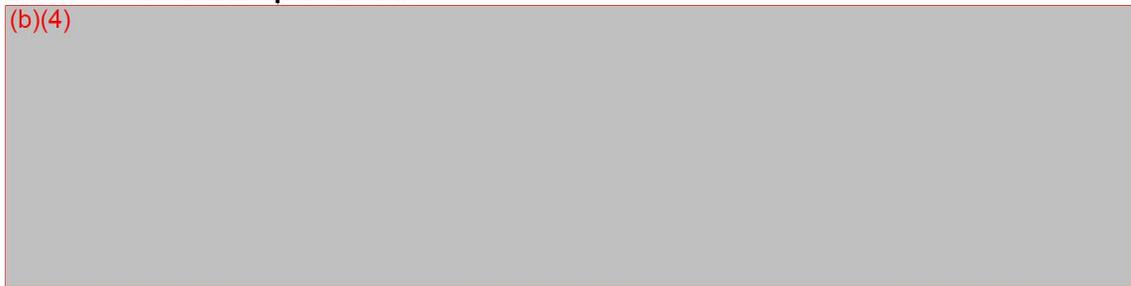
5.3 Mechanical Requirements

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5.4 Electrical Requirements

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5.5 Clinical Performance

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MARKETING SPECIFICATION

5.6 Packaging And Shelf-Life

- 5.6.1 [M29]. It shall be possible to transport and store the system under the relevant standard transport conditions.
- 5.6.2 [M30]. The Adaptor, if sold separately, shall be packaged in a sealed and sterile package suitable for sterilization. The package shall meet the requirements of package integrity testing (peel strength, cosmetic etc). The sterile product should have at least a shelf-life of one (1).

5.7 Sterilization

- 5.7.1 [M31]. The EvGuide system will be supplied non-sterile but shall be easy to clean and meet hospital guidelines for equipment wipe-down.
- 5.7.2 [M32]. The EvGuide Adaptor shall be capable of being sterilized and must maintain its functionality and integrity after being sterilized. A recognized expert laboratory may be utilized to develop the sterilization process and test/validation methods.

5.8 Labeling

- 5.8.1 [M33]. Product labeling shall include labels and instructions for use that comply with all applicable U.S. and international standards.



PRODUCT SPECIFICATION

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6.6 ECG Requirements..... 8

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PRODUCT SPECIFICATION

1 Purpose

The purpose of this document is to specify the requirements that the evGuide Tip Location System (TLS) must meet. The document is intended to translate the marketing specifications into quantitative input to be used for generating:

- DFMECA
- Design documents
- Tests plans and protocols
- Operator's manual

2 Scope

This document specifies the requirements for Version 1.0 of evGuide TLS

Target users for evGuide are trained individuals in placing central venous catheters and in the use of the evGuide TLS.

Each specification is prioritized separately as follows:

- "R" Required Mandatory requirement to fulfill.
- "D" Desired Not mandatory for this product version. Should be considered for inclusion for the full product launch.

3 References

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PRODUCT SPECIFICATION

4 Abbreviations

ECG	Electrocardiogram (electrical activity of the heart)
GUI	Graphical user interface
CVC	Central venous catheter
PICC	Peripherally inserted central catheter
RA	Right atrium
SVC	Superior Vena Cava

5 System Description

5.1 Overview

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health care institutions and as documented in many papers, e.g., "The ECG method for positioning the tip of PICCs: results from two preliminary studies" by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008.

Figure 1 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community.

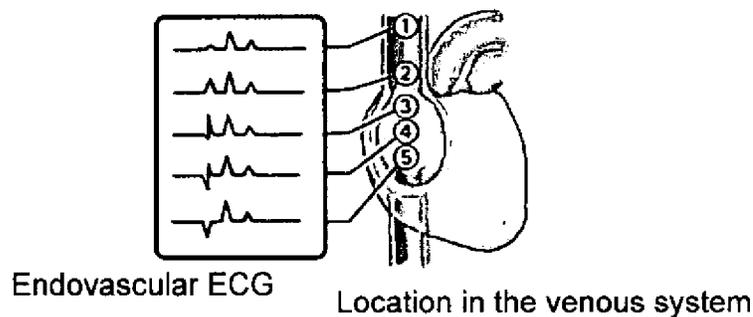


Figure 1: Changes in the ECG waveform as function of location in the vasculature

PRODUCT SPECIFICATION

The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the "red" or "right shoulder" electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A "giant" P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface ECG, the tip of the electrode is in the superior cava vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava). Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, which are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

evGuide™ TLS Overview

The evGuide TLS consists of the evGuide Saline Adaptor, the evGuide Electrical Adaptor, an ECG Module and an ECG cable, a laptop, and the evGuide TLS application software. The evGuide TLS components excluding the evGuide Adaptors are also referred to as the evGuide TLS System. An optional printer can be connected to the laptop for documentation purposes. The evGuide TLS Saline Adaptor can be connected to any commercially available central venous catheters and the evGuide TLS Electrical Adaptor to any commercially available stylets or guidewires used for the placement of central venous catheters. The evGuide system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, or intracavitary ECG) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and acquired in real time through the evGuide adaptors. Thus, the waveforms presented on the evGuide TLS graphical user interface can aid the placement of central venous catheters.



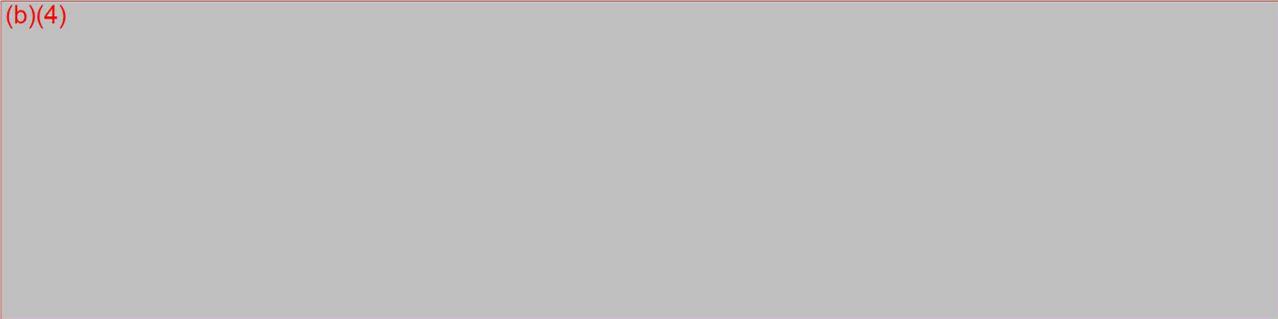
PRODUCT SPECIFICATION

5.2 Indications for Use

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

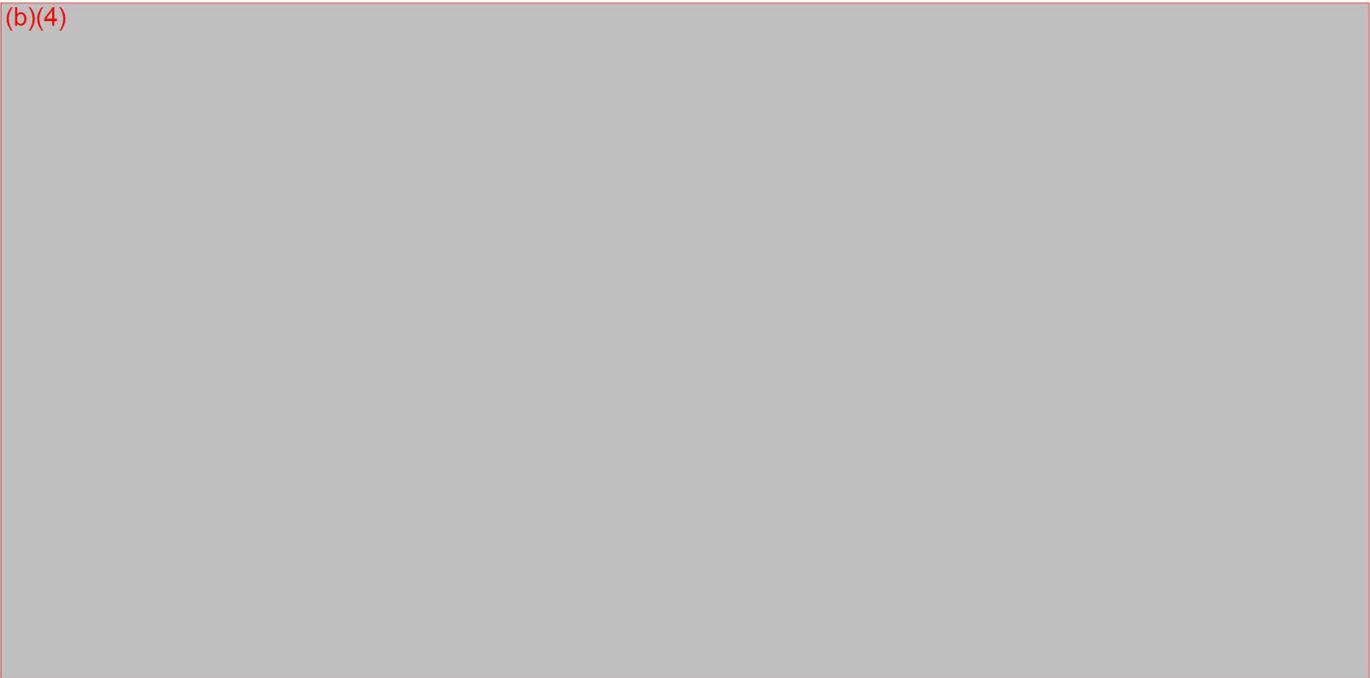
5.3 Contraindications

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6 General System Specifications

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PRODUCT SPECIFICATION

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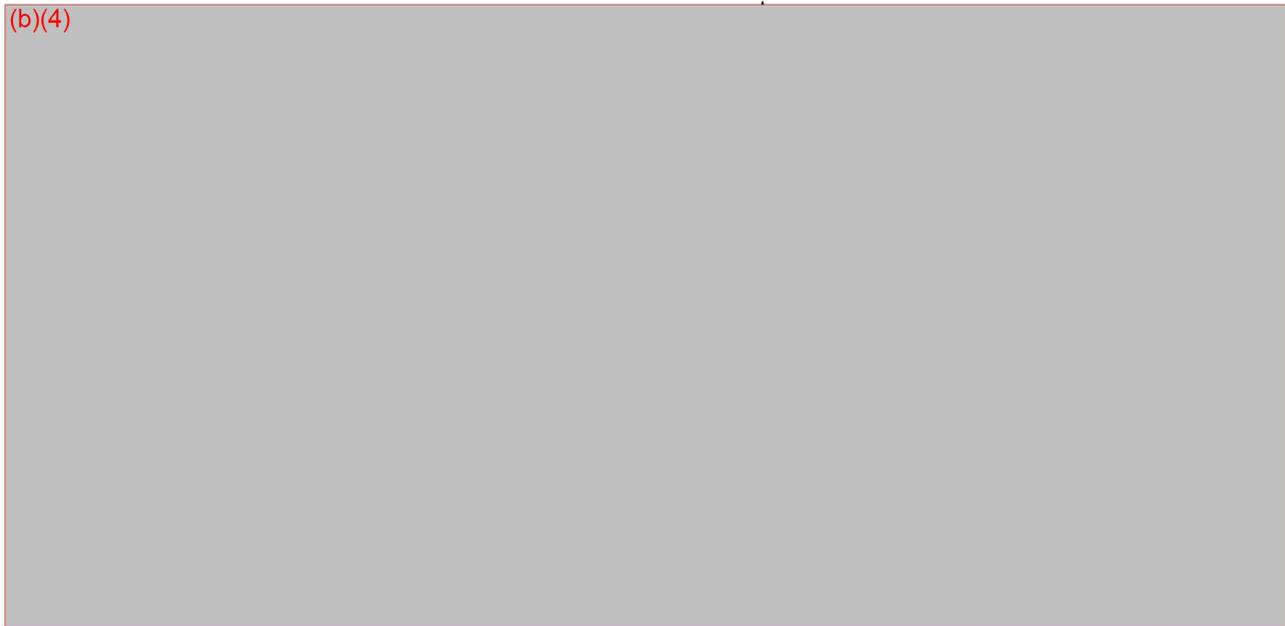
6.3 Documentation and Labeling Requirements

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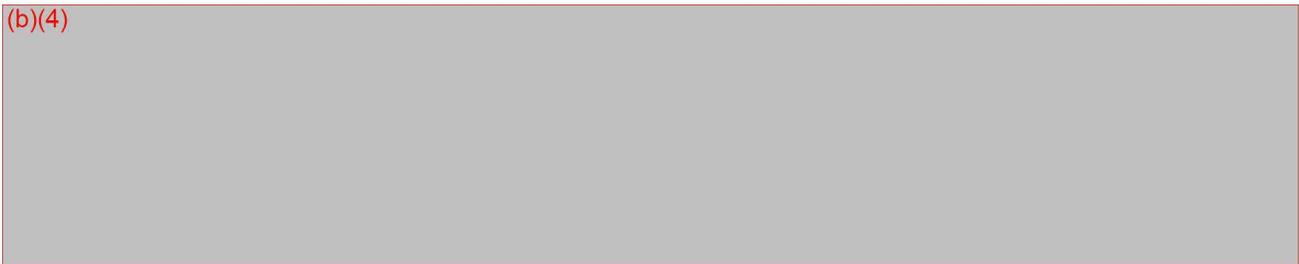
6.4 User Interface Requirements

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6.5 ECG Requirements

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PRODUCT SPECIFICATION

6.6 Data Storage, Retrieval, and Documentation Requirements

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Figura 1 - (b)(4)

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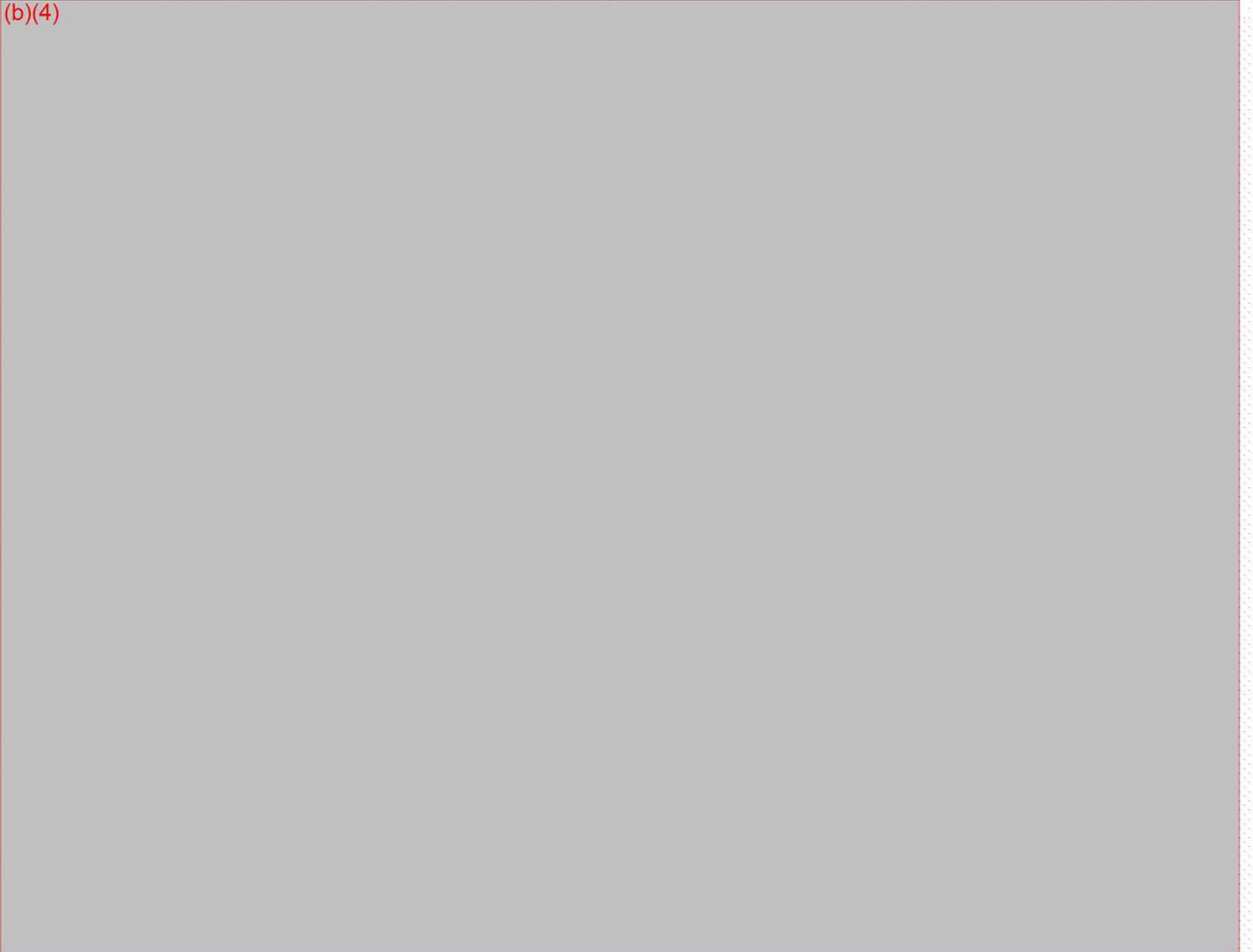


Figura 2 - (b)(4)

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Figura 3 - (b)(4)

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Figura 4 -

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Figura 5 - (b)(4)

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Figura 1 - (b)(4)

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Figura 2 - (b)(4)

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Figura 3 - (b)(4)

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Figura 4 - (b)(4)

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Figura 5 - (b)(4)

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Appendix F: Risk Management

Appendix G: System Performance Testing

Romedex International	PN :	PRT	Revision:	01		
	Document Title:	evGuide system Traceability Analysis				

eVGuide TLS Traceability Analysis

REVISION HISTORY

Section	Description	Author	Date
ALL	Initial Release	Sorin Grunwald	10/1/09

Romedex International	PN :	PRT	Revision:	01	
	Document Title:	System Validation Protocol – evGuide system			

System Validation Protocol evGuide System

REVISION HISTORY

Section	Description	Author	Date
ALL	Initial Release	Sorin Grunwald	3/1/09

Romedex International	PN :	PRT	Revision:	01		
	Document Title:	System Validation Protocol – evGuide system				

1. Introduction

The evGuide system has been subject to extensive verification testing. A pre-clinical animal study on March 24, 2009 confirms safety and effectiveness. (b)(4)

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2. Purpose and Objectives of this study

Evaluate the ability of the evGuide system to help in the placement of central venous catheters by detecting and displaying electrical signals of the heart during the catheter placement procedure.

The main areas of interests to be examined are:

1. Superior Vena Cava (SVC) (important for catheter guidance in the right direction)
2. Superior Vena Cava (SVC) and Right Atrium (RA) junction or caval-atrial junction (CAJ) (important for correct catheter tip placement).
3. Right atrium (RA) (important for determining that the catheter has passed the CAJ)

3. Study date and duration

The study will be conducted on or about March 24th, 2009 on at least one animal.

4. Device Setup description

The evGuide TLS system consists of the following elements seen in the Figure 4.1:

1. ECG module
2. PC/Laptop running evGuide TLS software
3. USB connection cable to the ECG module
4. Label printer (optional)
5. ECG cable
6. Sterile evGuide TLS Saline and / or Electrical Adapter connected to a venous catheter (6)
7. One or more skin ECG electrodes (7)

Romedex International	PN :	PRT	Revision:	01	
	Document Title:	System Validation Protocol – evGuide system			

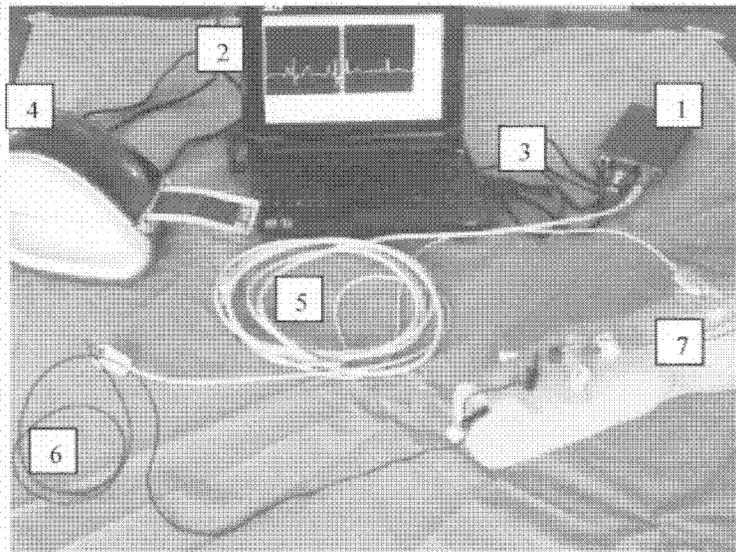


Figure 4.1: evGuide TLS – system configuration

During the catheter placement procedure, one or several electrodes (7) are connected to the subject's skin using non-sterile off-the-shelf electrodes the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the central veins per the institution's guidelines, an evGuide TLS adapter either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. The sterile evGuide TLS adapter transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (figure below) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes the user can estimate the location of the catheter tip.

The relationship between the ECG waveform and the location around the sino-atrial node of the heart has been extensively documented in the literature and is in use in many clinical institutions world-wide. The paper "The ECG method for positioning the tip of PICCs: results from two preliminary studies" by Dr. Mauro Pittiruti et al published in the Journal of the Association for Vascular Access in 2008 is attached in Appendix H of this submission. The Figure 4.3 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community (Appendix H).

Romedex International	PN :	PRT	Revision:	01	
	Document Title:	System Validation Protocol – evGuide system			

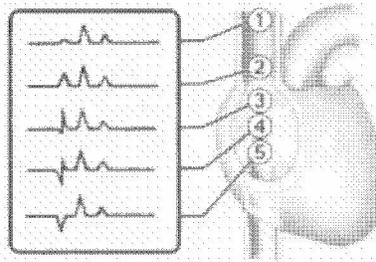


Figure 4.3: Changes in the ECG waveform as function of location in the vasculature (from Dr. M. Pittiruti, Appendix H)

a. evGuide Equipment and Material Required

1. ECG module
2. PC/Laptop running evGuide TLS software
3. USB connection cable to the ECG module
4. Label printer
5. ECG cable
6. Sterile evGuide TLS Saline and / or Electrical Adapter connected to a venous catheter
7. One or more skin ECG electrodes

b. Additional Equipment and Material Required

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5. Recording of Data

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TEST PROTOCOL COVER SHEET

evGuide Software Verification Test Protocol

Sorin Grunwald

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1. Purpose & Scope

The purpose of this console software verification is to demonstrate that the evGuide TLS Software meets its intended use as described in evGuide Software Requirements Specification PS-1011(A)

The evGuide Software has been tested in the following environments:

- Bench
- Animals
- Clinical studies

2. Commercial Off the Shelf (COTS) Software Validation

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3. Recording of Data

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4. Acceptance Criteria

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5. Equipment, Material & Setup

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6. References

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7. Test Protocols and Test Results

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7.1. User interface requirement:

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5.0 Acceptance Criteria

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Romedex International	PN :	RPT	Revision:	01		
	Document Title:	Verification Report – evGuide Software				

VERIFICATION REPORT COVER SHEET

evGuide Software Verification Test Report

Romedex International	PN :	RPT	Revision:	01		
	Document Title:	Verification Report – evGuide Software				

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1. Purpose

The purpose of this report is to summarize the results of the execution of Software Verification on evGuide software. The report covers the execution of Software Verification Protocol on evGuide application version 1.0.8, unless otherwise specified.

2. Abstract

Software Verification was performed on evGuide system #4 loaded with evGuide software version 1.0.8 per Software Verification Protocol v1.108. All tests defined within the protocol passed.

3. Scope

The scope of this verification report is to discuss the results, analysis and deviations found during the execution of the software verification protocol.

4. Equipment, Material & Setup

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5. References

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6. Test Results Analysis

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Appendix H: Published Paper in JAVA



The EKG method for positioning the tip of PICCs: results from two preliminary studies

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Abstract

Two preliminary studies were conducted to determine feasibility of using the electrocardiography (EKG) method to determine terminal tip location when inserting a peripherally inserted central catheter (PICC). This method uses the guide-wire inside the catheter (or a column of saline contained in the catheter) as an intracavitary electrode. The EKG monitor is then connected to the intracavitary electrode. The reading on the EKG monitor reflects the closeness of the intracavitary electrode (the catheter tip) to the superior vena cava (SVC). The studies revealed that the EKG method was extremely precise; all tips placed using the EKG method and confirmed using x-ray were located in the superior vena cava. In conclusion, the EKG method has clear advantages in terms of accuracy, cost-effectiveness, and feasibility in conditions where x-ray control may be difficult or expensive to obtain. The method is quite simple, easy to learn and to teach, non-invasive, easy to reproduce, safe, and apt to minimize malpositions due to failure of entering the SVC.

Background

The importance of the position of the tip of any central venous access device (VAD) was stressed in 1998 by the Position Statement of the National Association of Vascular Access Network (NAVAN, now AVA). This position states the optimal position of the tip of a central VAD (excluding the VADs designed for hemodialysis) is the lower third of the superior vena cava (NAVAN, 1998; Scott, 1988; Scott, 1995). Though guidelines from other USA and European associations (Royal College of Nurses, Infusion Nursing Society, Society of Interventional Radiology, American Society of Parenteral and Enteral Nutrition, European Society of Parenteral and Enteral Nutrition, etc.) have offered different definitions of the optimal tip position, there is wide agreement that no central VAD should have its tip above the middle third of the superior cava vein or below the mid-portion of the right atrium (McGee and Gould, 2003; Taylor and Palagiri, 2007). In fact, positioning of the tip of a central line in an inappropriate site of the venous system is associated with a significant increase in the risk of malfunction, fibrin sleeve formation and venous thrombosis.

A 'short' catheter - i.e. a catheter whose tip is located in the upper or middle third of the superior vena cava (SVC) or in the innominate veins - has a 10 to 50 percent increased risk of central venous thrombosis (Caers et al., 2005) (Table I). Also, a high position of the tip of the VAD is associated with intimal damage due to mechanic irritation of the endothelium, with erosion and even perforation to the walls of the vein. Formation of a fibrin sleeve around the catheter occurs more frequently with a short catheter; this is typically associated with VAD malfunction (persistent withdrawal occlusion, or ball valve obstruction). In addition to these complications, the presence of a sudden or sustained increase of central venous pressure such as coughing, vomiting, etc. has been known to cause the 'short' catheter to dislocate, also known as 'tip migration' (Puel et al., 1993).

Conversely, a 'long' catheter, a catheter whose tip is in the lower portion of the right atrium or in the right ventricle or beyond, may carry the risk of arrhythmias, tricuspid valve dysfunction, erosion, or atrial thrombosis (Korones et al., 1996).

Finally, the tip of the catheter may be inadvertently positioned in the subclavian vein, in the internal jugular vein, or in other thoracic veins (internal mammary vein, azygos, etc.). This type of malposition is almost constantly associated with pain on infusion, early VAD malfunction and subsequent venous thrombosis.

While correct positioning of the tip of the catheter is of great importance during any central venous cannulation, it plays a crucial role in mid-term and long term VADs such as peripher-

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ally inserted central catheters (PICC), tunneled catheters and ports, which are frequently inserted in patients requiring chemotherapy with vesicant drugs or hyper-osmolar nutritional solutions. Standard of Care for central venous catheters (CVC) dictates in the United States that the position of the tip must be confirmed by x-ray prior to use (INS 2006; NAVAN 1998). When the tip location cannot be confirmed in the superior vena cava, the catheter must be repositioned. Tip verification techniques have focused primarily on the x-ray. Other forms of tip verification have been used throughout Europe, with or without x-ray, incorporating electrocardiogram interpretation.

Methods for Preventing Malpositions

At present, the 'gold standard' for preventing malpositions and verifying the tip of the catheter is through radiology, either as intra-procedural fluoroscopy or as a post-procedural chest x-ray. On the fluoroscopic monitor or on the radiological film, the tip must be seen in the area correspondent to the lower third of the superior vena cava, i.e. no more than 2 cm below the image of the main right bronchus.

While confirmation of tip placement in the superior vena cava is mandatory, the radiological assessment of the tip position does have a few limitations and disadvantages:

- any type of radiological assessment is associated with x-ray exposure for the patient and/or for the health operator; such exposure can be relevant for intra-operative fluoroscopy or with repeated chest x-rays;
- the radiological landmarks used to determine catheter tip location may be unclear or significantly affected by physiological or pathological anatomic variations, false perspectives, or errors of interpretation (this is particularly true for intra-procedural fluoroscopy). In the case of post-procedural control, greater accuracy can be achieved by studying the chest in both the anterior-posterior view and in the lateral view. The use of dual views, while it increases accuracy, requires longer x-ray exposure and higher costs.
- In most cases, the radiological assessment requires the availability of an expensive and logistically cumbersome machine plus a radiology technician and/or a radiologist all adding to the procedural cost. This gives us an inappropriate cost-effectiveness ratio. Radiological assessment a problem with a PICC insertion which, in the United States, is most frequently performed by nurses at bedside. In this situation, the intra-procedural fluoroscopy may be difficult or impossible to adopt while the post-procedural chest x-ray carries a significant burden in terms of costs, organization and time delay. Also, in most cases the nurse who has inserted the PICC must rely on the intervention of the radiologist to interpret tip location.*

**This aspect might be overcome in some countries such as UK or USA, where there is a growing tendency to authorize nurses, if specifically trained, to interpret the x-ray. In April 2008, the Association for Vascular Access (AVA) published a Position statement on this subject. (AVA, 2008).*

Tip confirmation by chest x-ray is less expensive, safer and more commonly used than fluoroscopy, though, in some cases the catheter has to be repositioned. Catheter tip repositioning

Table 1: Incidence of catheter-related thrombosis and catheter dysfunction, depending on tip position (modified from Caers et al., 2005)

Tip position	# cases	Thrombosis	Dysfunction
Brachiocephalic vein	31	45.2%	6.5%
Cranial 1/3 SVC	42	19%	16.7%
Middle 1/3 SVC	142	4.2%	1.4%
Caudal 1/3 SVC	66	1.5%	0%
RA or IVC	18	5.6%	5.6%

requires a new procedure, a second radiological assessment, major discomfort for the patient and for the nurse or physician who has implanted the device, a significant time delay, repeated x-ray exposure, and increased costs.

Some non-radiological methods which can be useful in reducing the risk of malposition of the tip of the catheter include establishing the proper choice for venous access, using ultrasound for guidance, establishing baseline anthropometric estimates from landmarks, and using electromagnetic tools to detect direction of insertion.

1) Proper choice of the venous approach

In centrally inserted VADs, the supraclavicular approach to the right internal jugular vein, to the right subclavian vein or to the right innominate vein (by ultrasound guidance) is characterized by a lower incidence of malposition since the catheter almost invariably enters the superior vena cava vein. Nonetheless, the risk of malpositioning with a 'short' or 'long' catheter still persists.

2) Ultrasound Guidance

The use of ultrasound for needle guidance with CVC placement is known to increase success and reduce complications. Soon after PICC insertion, while the stylet is still inside the PICC, ultrasound examination of the internal jugular veins is a simple and reliable method to rule out a gross malposition, though it cannot give information about the correct length of the catheter. Post-procedural ultrasound control of tip position can be done by surface or trans-esophageal echocardiography, but the cost is high and requires specially trained operators.

3) Anthropometric estimates and surface landmarks.

There are several landmark methods for estimating the desired length of a central venous catheter or a PICC; usually, they are based on the assumption that the atrio-caval junction is located at the level of the third intercostal space, on the right parasternal border. The anthropometric methods utilized for central venous catheters apply formulas which are derived from large population studies. These measurements estimate the desired length of the catheter knowing the site of venipuncture and the height of the patient (Peres, 1990). Both anthropometry and surface landmark methods are quite precise in estimat-

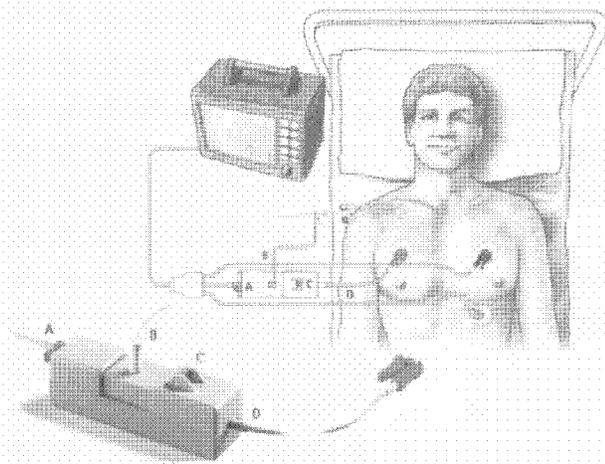


Fig. 1 – Diagram showing how the intracavitary electrode replaces the 'red' or 'right shoulder' electrode of the standard surface EKG (Figure reproduced by courtesy of BBraun. A = electrode connected with EKG monitor; B = cable connecting to intracavitary electrode; C = switch to shift from surface electrode to intracavitary electrode; D = surface electrode to the right shoulder of the patient)

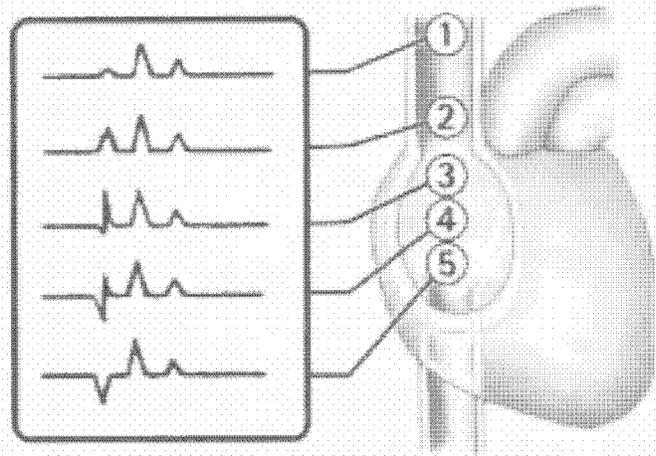


Fig. 2 – Changes of the P wave as a function of the tip of the intracavitary electrode (Figure reproduced by courtesy of BBraun)

ing the length of the catheter in the adult patients, but not in children. Measurements provide a possible length for catheter placement in the SVC without adjustment for anatomical variations, directional or functional malpositioning.

4) Electromagnetic tracking methods.

These usually consist of an electromagnetic signal from a wire installed in the catheter by means of a surface apparatus connected to a monitor (Navigator, manufactured by Viasys; Sherlock, manufactured by Bard; Cath-Finder, manufactured by Pharmacia Deltec). They are primarily used with PICCs and need a specific technological design of the catheter and/or of its stylet. Some authors have demonstrated a significant reduction in the incidence of malposition, from 13.4% down to 2.5%, using such devices (Naylor, 2007). Their main limitation is that, while they do ascertain that the PICC is in the right direction, they do not give information about the correct location of the catheter (Royer and Earhart, 2007).

The Electro-cardiographic Method for Positioning the tip of Central Lines

The "ideal" method for checking the position of the tip should have the following features:

1. It should provide a way to check the position of the tip both during the procedure (to avoid repositioning manoeuvres) as well as after the procedure (to confirm tip position of the VAD);
2. The method should be easily and autonomously performed by the inserter of the VAD, either a nurse or a physician;
3. The method should be accurate enough to ascertain that the catheter has gone in the *right direction* (straight along the axis internal jugular vein – innominate vein – SVC) and to

the *right depth* (not too long, not too short, but exactly at the atrio-caval junction);

4. It should be inexpensive, non-invasive, and easy to repeat with reproducible results;
5. It should be easy to learn and easy to teach;
6. It should provide a way to print and record the results to allow for documentation in the patient's records.

Correct determination of catheter terminal location, in addition to identification and correction of malpositioning are all necessary components of PICC or CVC placement. Finding a method to perform these processes with ease during the insertion procedure will reduce time, speed usage, and save the patient from additional exposure and cost. We suggest the method that most closely meets all of these requirements is the location of terminal tip by use of the electrocardiographic (EKG) method. This method interprets the location of the catheter tip by using EKG with an intracavitary electrode (Corsten et al., 1994; Francis et al., 1992; Cavatorta et al., 1999; Gebhard et al., 2007; Antonaglia et al., 2008; David et al., 2005; Schummer et al. 2005; Cavatorta et al., 2001; Dionisio et al., 2001).

The basic principle of the EKG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an intracavitary electrode which replaces the 'red' or 'right shoulder' electrode of the standard surface EKG (Figure 1). When the EKG monitor is connected to the intracavitary electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the intracavitary electrode (i.e. the tip) to the sino-atrial nodus. A 'giant' P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface EKG, the

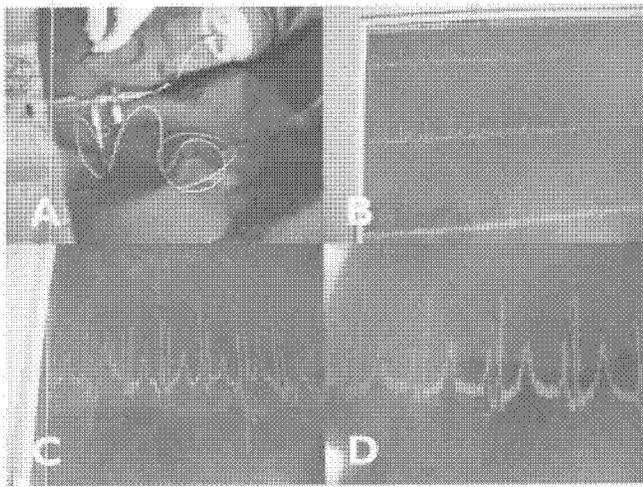


Fig. 3 – EKG method for positioning the tip of an open-ended PICC:
 a – the PICC is inserted for the estimated length (previous anthropometric measurement), filled with normal saline and connected to the EKG monitor through the VygoCard, so to work as intracavitary electrode

- b – standard EKG reading
- c – tip in right atrium (giant P wave)
- d – tip at atrio-caval junction (P wave half of QRS)

tip of the electrode is in the superior vena vein or above; a P wave whose height is half of the QRS is considered indicative of the atrio-caval junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava) (Figure 2). Thus, simply by monitoring the height of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium.

Limiting factors for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. The EKG method was first introduced in 1949 (Von Hellerstein et al., 1949) and has been successfully used for central venous catheter placement in Europe (especially Germany) since the '90s (Schummer et al., 2004).

During the last two decades, many clinical papers have demonstrated – with a few exceptions (Schummer et al., 2003; Schummer et al., 2004) – the accuracy of the EKG method, compared to the standard radiological assessment. Quite recently, other Authors (Gebhard et al., 2007) provided substantial research that has proven the EKG method is more specific and more precise when compared to conventional methods (i.e.: methods based on anthropometric measurements or standard formulas for estimating depth of catheter insertion, as available in the literature). In this clinical randomized study, all tips checked with the EKG method were in the superior vena cava or above, in contrast with other methods which showed 16% of those tips in the right atrium or in the right ventricle; also, only 3% of the tips checked by the EKG method were located above the superior vena cava (axillary, subclavian, internal jugular vein, innominate vein) versus

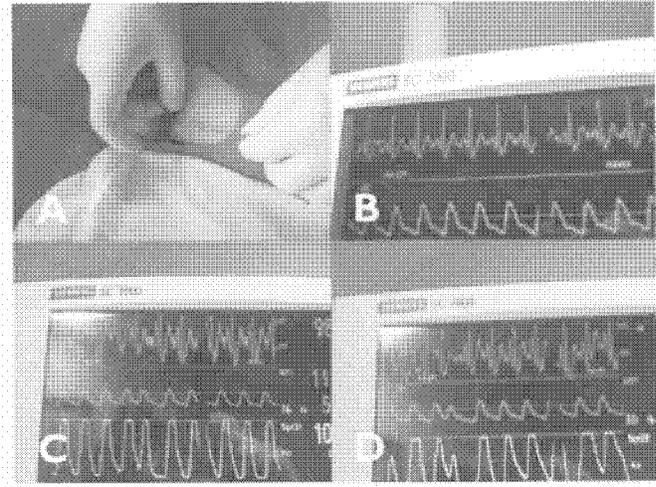


Fig. 4 – EKG method for positioning the tip of a closed-ended PICC:
 a – the PICC is inserted for the estimated length, filled with normal saline and connected to the EKG monitor through the VygoCard; to make the catheter work as intracavitary electrode, it must be flushed continuously with saline so keep the valve open

- b – standard EKG reading
- c – tip in right atrium (giant P wave)
- d – tip at atrio-caval junction (P wave half of QRS)

15% of the tips positioned with other methods.

This same clinical trial has shown that the EKG method did not significantly increase the length of time required to perform the procedure, and actually saved time by avoiding the need to reposition the catheter and get a second chest x-ray.

Many clinical trials have shown that the EKG method has clear advantages in terms of accuracy, cost-effectiveness and feasibility in conditions where X-ray control can be difficult or expensive to obtain (Corsten et al., 1994; Francis et al., 1992; Gebhard et al., 2007; Antonaglia et al., 2008; David et al., 2005). The method is quite simple, easy to learn and to teach, non-invasive, easy to reproduce, safe, and apt to minimize both malpositions due to failure of entering the superior vena cava (tip in internal jugular or subclavian or innominate vein) as well as malpositions due to error in the length of the catheter (catheter too short or too long). Though a thorough computation of the actual costs may differ, depending on the choice of technique and clinical setting, overall costs of the EKG method are consistently lower if compared to the standard check of the tip position by post-procedural X-ray. In fact, (a) the technique is inexpensive (the additional materials needed for the manoeuvre cost less than twenty dollars), (b) it can be performed at bedside, (c) the costs related to performing and interpreting chest X-ray are avoided, and (d) intra-procedural check of the tip position protects from expensive and timely repositioning manoeuvres sometimes needed after chest x-ray.

The trials concerning testing EKG have taken into consideration short term and long term central venous access devices inserted by puncture of the subclavian or the internal jugular vein (Chu et al., 2004; Cheng et al., 2002); in a few cases, the method

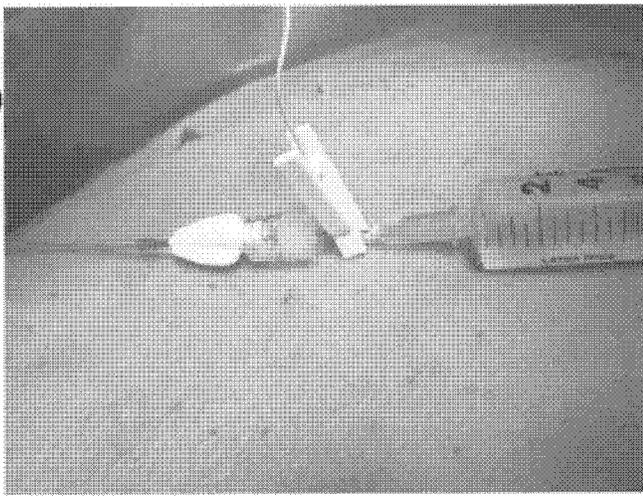


Fig. 5 – Alternative method for using the PICC as intracavitary electrode: electrode with alligator clip attached to a needle inserted in an injectable cap.

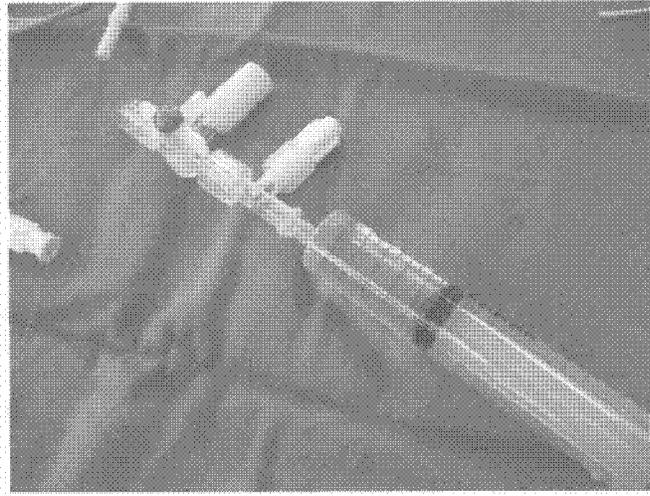


Fig. 6 – Vygocard (manufactured by Vygon)

has also been tested in neonates (Biban et al., 2000; Tierney et al., 2000), with umbilical catheters and epicutaneo-caval catheters.

Considering demonstration of safety and cost-effectiveness of the EKG trial results carried out with central venous catheters within the past few years, we decided to apply this method, which appears so safe and cost-effective, to PICC placement.

The EKG Method for Positioning PICCs

In our 1200 bed University Hospital, PICCs are inserted by members of a dedicated team. The team consists of four physicians (two surgeons, two infectious disease practitioners) and ten nurses. Our team inserts approximately 1000 PICCs and 700 long term central venous access devices per year, and is committed to several clinical tasks, including monitoring VAD related complications, counselling in VAD indications and maintenance, education and training of nurses in our institution, and, most importantly, teaching on a national level. We provided more than 40 courses in 19 different Italian hospitals training clinicians to use ultrasound guided placement of PICCs.

Our experience with the EKG method for standard short term and long term central venous access devices began many years ago. In our hands, the method has proven to be safe and cost-effective, and it has dramatically reduced the number of chest x-rays necessary to check the position of the tip.

Recently, we began a project for verifying the feasibility of applying this method to PICC. Until 2006, our standard protocol for PICC positioning consisted (Pittiruti et al., 2005) of (a) anthropometric estimate of the desired length of the PICC by anatomical landmarks (from the site of puncture to the third intercostal space on the right sternal border); (b) ruling out the presence of the catheter in the internal jugular vein by direct ultrasound examination during the procedure; and (c) postoperative, chest x-ray.

After a few preliminary clinical experiments carried out in 2007, whose goal was to define the technical aspects of the meth-

od, in the first months of 2008 we performed two pilot studies, one on open ended PICCs and one on closed ended (Groshong) PICCs. The details of these studies are listed below.

First study: Open Ended PICCs*

The aim of the first study was to verify the feasibility of the EKG method to open-ended PICCs. After approval of the Ethical Committee of our University, twelve consecutive patients requiring PICC lines were enrolled in this study. Exclusion criteria were: atrial fibrillation or other supra-ventricular arrhythmias; presence of a pace-maker. Desired catheter length was pre-operatively estimated by means of anthropometric parameters. We used the Vygocard device (Vygon) as the electrical transducer between the catheter (filled with standard 0.9% saline solution) and the EKG cable. The Vygocard transducer is part of a 3-way stopcock connected with the catheter and with a cable going to lead III of a standard EKG monitor. The catheter acts as an intracavitary electrode which replaces the traditional 'red' electrode on the right shoulder. The PICCs were inserted in the basilic (first choice) or brachial (second choice) vein at mid-arm under direct ultrasound guidance. Then, the catheter was slowly advanced in the venous system while observing the morphological intracavitary EKG changes until the P wave reached the desired shape and amplitude (one-half of the QRS complex), corresponding to the atrio-caval junction (Fig. 3). The catheter was then secured to the skin by means of a sutureless device. All patients underwent a post-operative chest x-ray (postero-anterior and lateral views). X-ray films were evaluated by an independent radiologist not involved in the insertion procedure; the atrio-caval junction was radiologically identified as 2 cm below the carina.

In this study, all twelve PICCs were successfully inserted. The "atrio-caval junction p-wave" was observed in all cases, in one patient after withdrawing and re-introducing the catheter. Final position at the atrio-caval junction was confirmed by postoperative intracavitary EKG control and chest x-ray in all

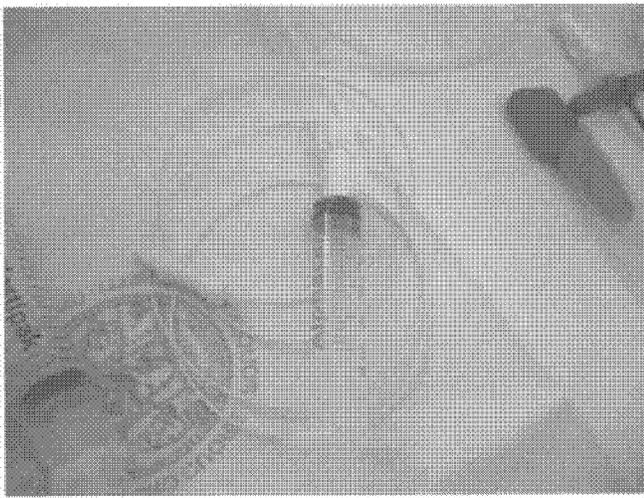


Fig. 7 – AlphaCard (manufactured by BBraun)

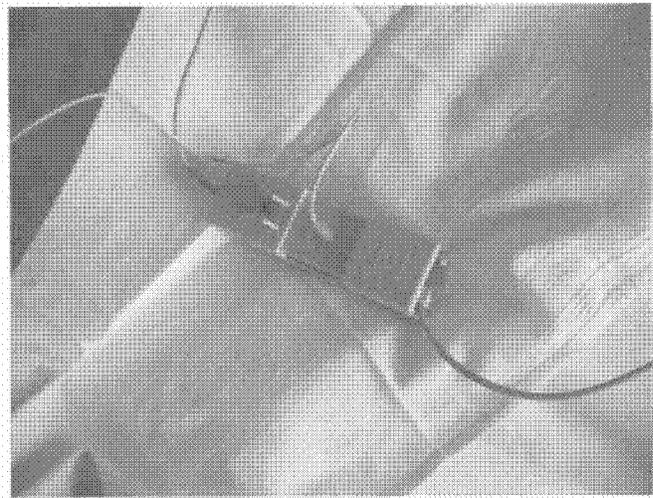


Fig. 8 – Certodyn (manufactured by BBraun)

patients. Consistently, no primary malpositions were observed on chest X-ray and all catheter tips appeared to be at the atrio-caval junction on X-ray films. In 3 cases the catheter length, as preoperatively estimated by anthropometric measurement, was significantly different (> 2 cm) from the length measured by the atrio-caval junction P wave; though, the final tip position was chosen according to the EKG measurement, and chest X-ray films were consistent with the EKG data.

***This study has been presented at the 2008 Meeting of the Infusion Nursing Society (Pittiruti, LaGreca, Scoppettuolo et al., 2008).*

Second study: Groshong PICCs**

In the second pilot study, six consecutive ICU patients requiring PICC lines were studied. The aim of this study was to verify the feasibility of the EKG method during the insertion of closed ended PICCs. Exclusion criteria were atrial fibrillation or other supra-ventricular arrhythmias, and/or the presence of a pace-maker. We used the Vygonard device (Vygon) as the electrical transducer between the catheter (filled with standard 0.9% saline solution) and the EKG cable. After ultrasound guided insertion in the basilic (first choice) or brachial (second choice) vein at mid-arm, each catheter was connected to an infusion line and a continuous saline infusion was started to keep the distal valve open. Baseline EKG rhythm was visualized. Then the catheter was slowly advanced in the venous system while observing the morphological changes of the P wave until the P wave reached the desired amplitude (one-half of the QRS complex), corresponding to the atrio-caval junction (Fig. 4). All patients underwent a post-operative chest x-ray (posterior-anterior and lateral views): the atrio-caval junction was radiologically identified as 2 cm below the carina. All x-rays confirmed EKG results of atrio-caval placement.

In this study, all six Groshong PICCs were successfully inserted. The "atrio-caval junction P wave" was observed in 5 patients.

In one case, the baseline cardiac signal was disturbed by electrical artefacts and the patient was excluded from the protocol. No primary malpositions were observed on chest x-ray and all catheter tips appeared to be at the atrio-caval junction on x-ray films.

**This study has been presented at the 2008 Meeting of the European Society of Intensive Care Medicine (Pittiruti, LaGreca, Brutti et al., 2008)*

Discussion

At present, the most common technique utilized for checking the position of the tip of CVCs by the EKG method employs the use of a guidewire inserted in the catheter as an intracavitary electrode, with the tip of the guidewire free in the bloodstream.

To adapt the EKG method to PICC insertion, we chose the alternative technique (already described for dialysis catheters and umbilical catheters), where the intracavitary electrode is the column of saline contained in the catheter itself (Pawlik et al., 2004; Madias, 2003; Madias, 2004). This is made possible by two different options: (a) With the first option, the PICC is closed proximally with a needle-injectable cap; a blunt needle or blunt ended connector is partially inserted in the cap, and an extension cable is connected to the access (Fig. 5); (b) The second option is more simply done with the proximal end of the PICC connected to a special device consisting of a 3-way stopcock with a transducer (VygoCard, Vygon, Fig. 6) or in a transducer directly attached to a syringe (AlphaCard, BBraun, Fig. 7); the transducer has an extension cable which connects to the EKG monitor.

The manoeuvre is further simplified by utilizing a specific commutator (Certodyn, BBraun, Fig. 8) connected to both the standard 'red' surface electrode on the right shoulder of the patient and to the intracavitary electrode. Changing the position of the switch, it is possible to read the EKG either as standard surface EKG or as intracavitary EKG. The changing morphology of the P wave is best appreciated reading D II.

Before reading the P wave change but after removal of the internal stylet, the PICC is filled with normal saline. If the PICC has a closed end, in order to maintain a column of fluid which may act as continuous intracavitary electrode, it is necessary to have a continuous infusion of saline through the system. Open ended PICCs have not additional requirements other than connection and saline flushing.

The best way to precisely locate the atrio-caval junction is to advance the PICC inside the venous system downward to the superior vena cava and beyond, until the typical 'giant' P wave (as high as the QRS) appears. This full sized P wave indicates that the right atrium has been reached. Once the P wave reaches full height, the PICC is slowly drawn backward until the P wave progressively reduces its height to ½ of the QRS: this corresponds to the atrio-caval junction. The PICC can then be secured to the skin in this position with the knowledge that the terminal end is at the caval-atrial junction.

Disadvantages of this method for checking the position of the tip of PICCs are:

- The method assumes the presence of a P wave on the standard EKG; in situations where the P wave is not present or not readable (atrial fibrillation, atrial flutter, marked tachycardia, pacemaker-driven rhythm), the method cannot be used;
- In some cases of closed ended PICCs, the Groshong valve may not open easily or continuously; intermittent flow across the valve may be consistent with a good infusion, but it causes intermittent EKG reading because the column of saline is interrupted.

Advantages of the EKG method:

- The method is accurate, safe, simple, non-invasive, easy to perform, easy to learn and easy to teach;
- It is inexpensive since it only requires an EKG monitor and a disposable sterile transducer (either Vygocard or Alphacard) with the extension cable;
- The manoeuvre can be performed at bedside, like most PICC insertions, and can easily be carried out by a nurse after minimal training;
- The method gives definitive information about the position of the tip directly during the procedure, thus saving time and resources;
- The costs as well the x-ray exposure associated with the radiological assessment are avoided in most cases;
- The correct position of the tip can be documented in the medical chart by appropriate printing of the EKG track.

Conclusion

The EKG method for determining caval-atrial junction terminal tip location is well documented in Europe and, through this study, has demonstrated accurate and safe use with PICCs. Though more studies are needed to standardize the procedure and to evaluate the accuracy of the method in different clinical situations and for different types of PICCs, we think these two pilot studies are very promising. This research suggests that the EKG method may strongly improve both the cost-effectiveness and the safety of the procedure for terminal tip interpretation on insertion and potentially, any time evaluation is desired.

Acknowledgments

We wish to thank Nancy Moreau for her friendly support and suggestions during the preparation of this paper and for her revision of our manuscript.

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Appendix I: Clinical Experience

EKG method with a new dedicated system:
Sapiens TLS

Mauro Pittiruti, Università Cattolica, Roma

I

EKG method: several advantages

- ▷ Safe
- ▷ Accurate
- ▷ Easy
- ▷ Inexpensive
- ▷ Suitable for every central venous access
- ▷ Allow to verify tip location during the procedure

EKG Method

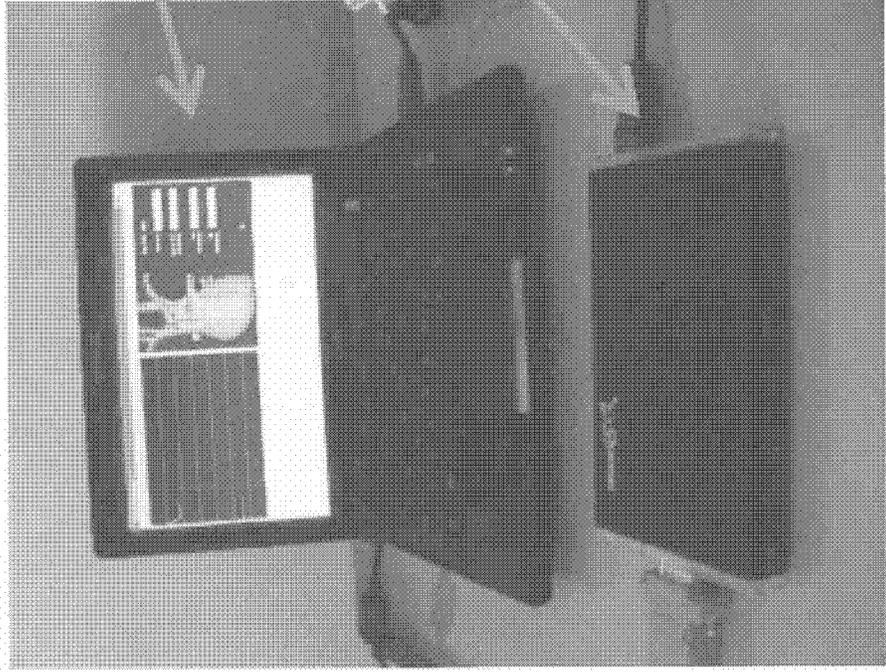
- ▷ Saline column is preferred vs. Guidewire
 - ▷ Suitable for every device
 - ▷ No risk of arrhythmias at all
 - ▷ Allow to re-verify tip location some time after the implant procedure, too



One step forward

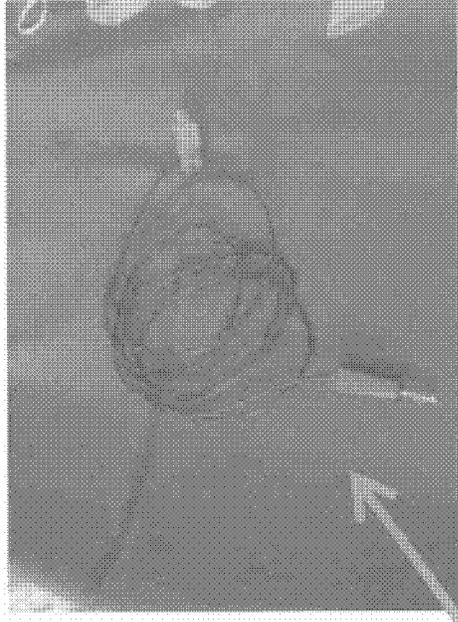
- ▷ The use of EKG method with saline column by applying a new technique for standardization and ease of use:
- ▷ **Sapiens TLS**
 - ▷ EKG Module + USB cable + cables with EKG leads
 - ▷ Sterile cable for catheter/EKG connection
 - ▷ Software

Sapiens TLS



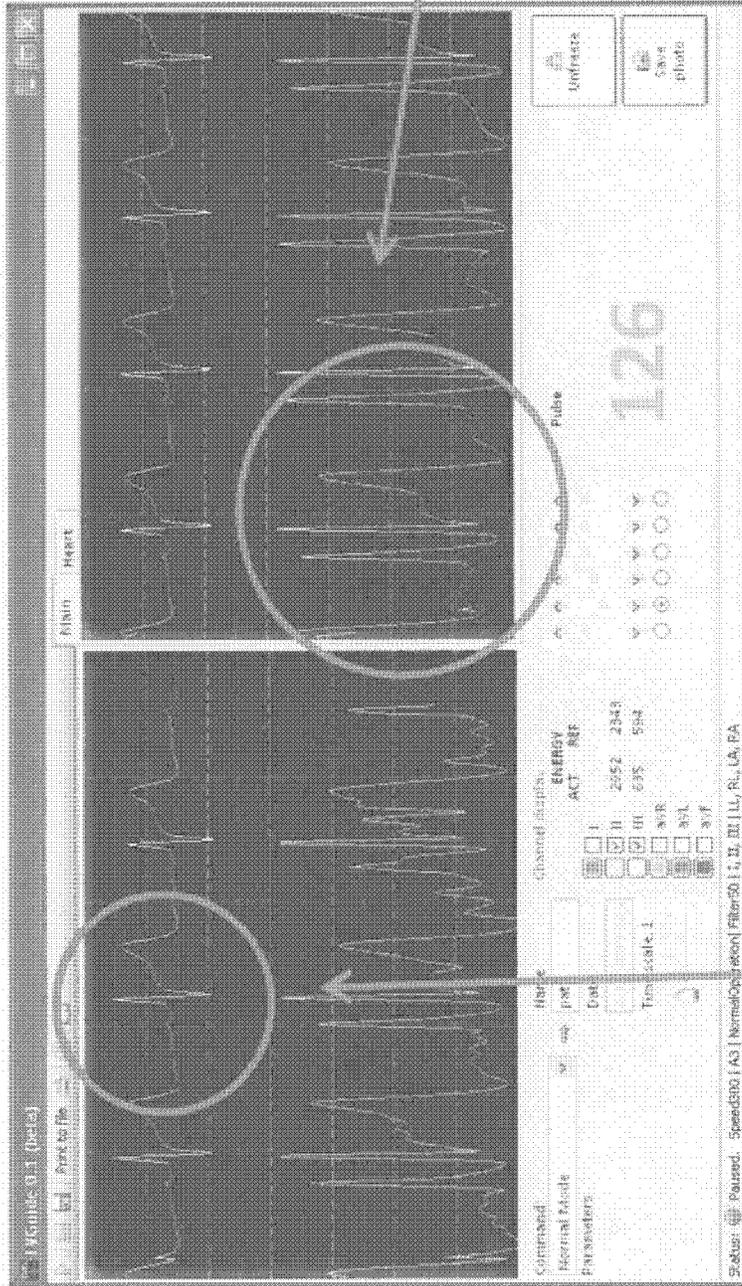
software

EKG Module (USB cable + EKG leads)



Sterile cable

Sapiens TLS

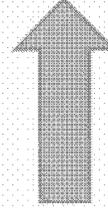
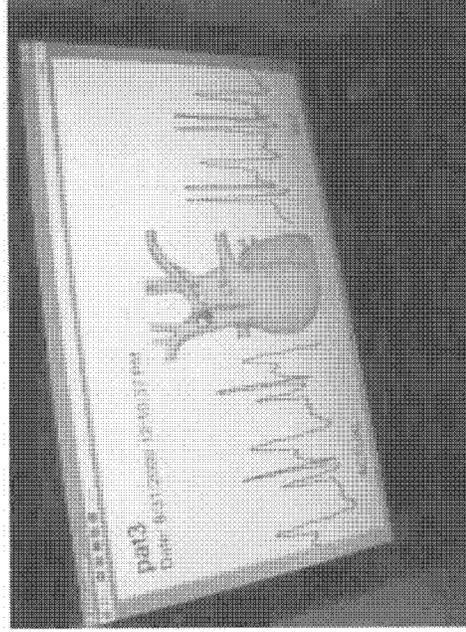
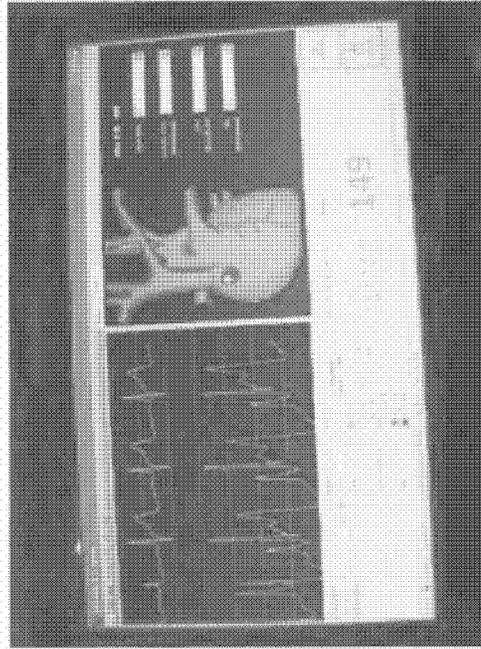


Intracavitary EKG
(atrial P wave)

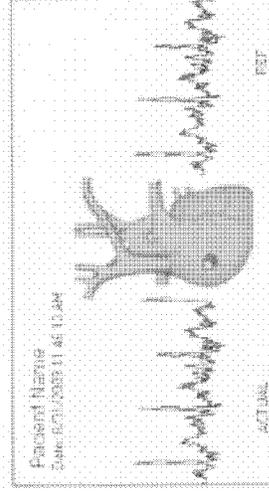
Surface EKG



Sapiens TLS



Print out for the clinical file



Sapiens TLS advantages

- ▷ The current EKG monitor replacement with a dedicate, portable screen
- ▷ EKG waveform lead standardization for an easier interpretation
- ▷ The mechanical switch of the current method is not needed anymore since surface and intracavitary EKG are displayed simultaneously
- ▷ It allows the printing out for the clinical file documentation

Experience with Sapiens TLS Oncology Day Hospital UCSC

- ▷ October - November 2009
 - ▷ 53 patients from both Medical Oncology (35) and Gynecological Oncology (18)
 - ▷ US guided venipuncture + EKG technique with Sapiens TLS
 - ▷ 32 ports (open tip catheter)
 - ▷ 25 in right hand side veins (innominate, internal jugular, axillary, subclavian)
 - ▷ 7 in left hand side veins (innominate)
 - ▷ 21 PICC (both open and closed tips)
 - ▷ 19 on the right arm (basilic, brachial)
 - ▷ 2 on the left arm (basilic)

Method

- ▷ Goal: tip location at caval-atrial junction
- ▷ **Intra-procedural comparison:**
 - ▷ Assessment based on antropometric finding
 - ▷ Central Access:
 - From the exit site to the third intercostal space on the right parasternal line
 - ▷ Peripheral access:
 - From the exit site to 1/2 clavicle + from 1/2 clavicle to 3° right intercostal space
 - From the exit site to the omolateral sternum-clavicular articulation + 10 cm (right side) or 15 cm (left side)
 - ▷ Measurement (and final positioning) according with EKG method
 - ▷ Saline column method + **Sapiens TLS** use
- ▷ **Post procedural Rx check**
 - ▷ Rx standard criteria
 - ▷ 2 cm behind right main bronchus

Results

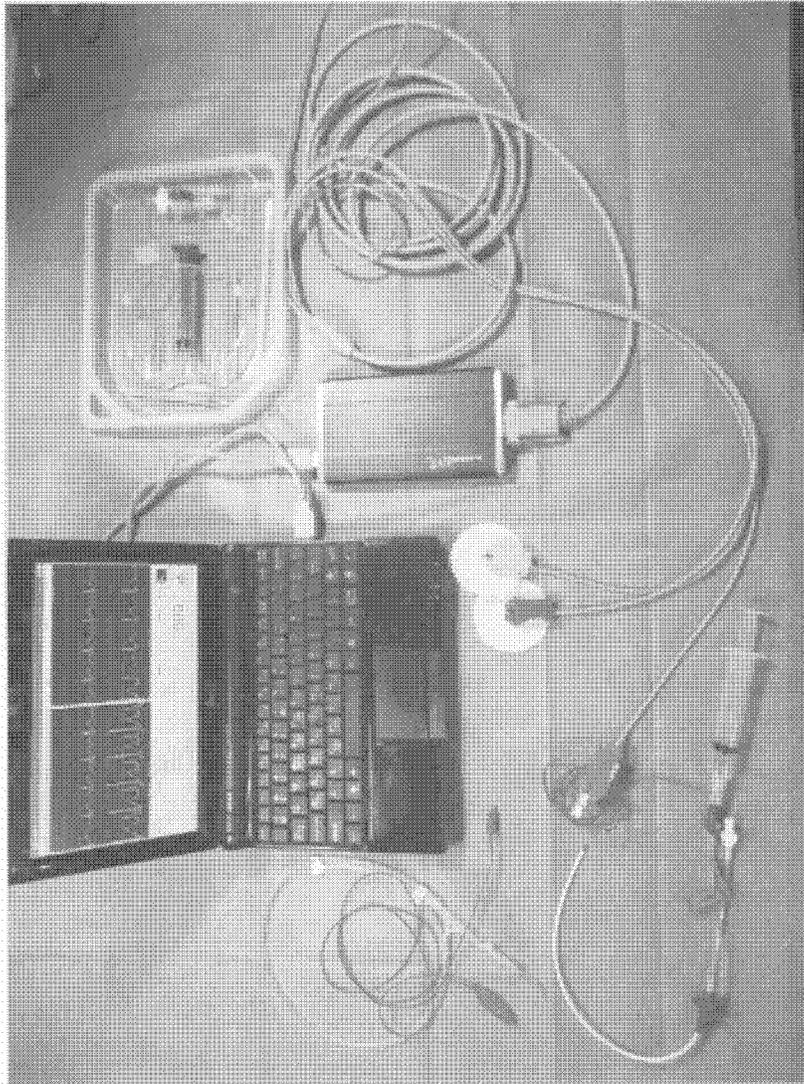
- ▷ All catheters were in proximity of the atrial-caval junction (+/- 1 cm) according to radiological confirmation
- ▷ The comparison between antropometric assessment and EKG method:
 - ▷ Port
 - ▷ In the 30% of the cases, antropometric assessment oversized catheter's length of 1cm
 - ▷ PICC
 - ▷ In the 20% of the cases, antropometric assessment catheter's length < 2cm; in 15% of the cases ≤ 2 cm

Anecdotal observation

- ▶ Two patients apparently not eligible for EKG method (**atrial fibrillation**), both undergoing port placement
- ▶ Despite the lack of P wave, specific variations of the waveform (increase of both amplitude and frequency of waves not belonging to the QRS complex) allowed to identify the moment in which the catheter “entered in the right atrium”

Results

- ▷ No complications
- ▷ No documented malpositions
- ▷ The EKG intra-procedural method executed with Sapiens TLS has been as accurate as the Rx-check post-procedural and more accurate than antropometric assesement (it tends to oversize the lenght needed to reach the atrial-caval junction)
- ▷ Sapiens TLS made the procedure easier, by standardizing EKG waveforms as well as by simplifying its interpretation



✓ Saline Adaptor

✓ Electrical Adaptor

✓ EKG Module

✓ EKG Cable

✓ Laptop

✓ Software

✓ Printer

WoCoVA

WoCoVA

With the world of vascular access devices (VADs) is expanding, and new solutions techniques and devices are becoming available, a group of the top VAD manufacturers in Europe, Asia and USA have decided to collaborate in organizing the 1st World Congress on Vascular Access.

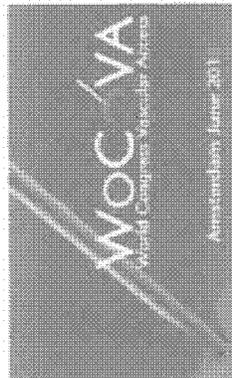
This multi-national and multi-ethnic event is named WoCoVA, and covers all aspects of vascular access.

Participants to the show in the device, materials, techniques and by professionals of all VAD-related companies: production, distribution, installation, etc.

Discussion will focus on the issues of safety, cost, efficiency and efficiency in the field of vascular access, as well as on the need for water-treated dialysis for the optimal therapy.

All health care professionals involved in the field of vascular access, including those who are directly involved in the training, scientific and educational sessions, invited by the most important international experts will offer an exceptional occasion for spreading knowledge in this field, share experiences and learn the latest trends in the area of VADs.

The most relevant companies active in the field of vascular access will participate in the commercial exhibition and will present their latest innovative products.



The 1st World Congress on Vascular Access is organized by the WoCoVA Foundation
 P.O. Box 678, 1220 AD Amsterdam
 The Netherlands
 Tel: +31 20 857 857 737
 Email: info@wocova.com
www.wocova.com

The Congress will be held at the Stedelijk Conference Center in the heart of Amsterdam on June 16th - 18th, 2010.

There is a wide variety of exhibition zones in the conference center and the locations adjacent to the city center. Amsterdam has a rich international history of trading, famous markets and typical Dutch streets and their atmosphere. There is the perfect time to extend your stay in the Netherlands and visit the flower gardens, museums and many beautiful...

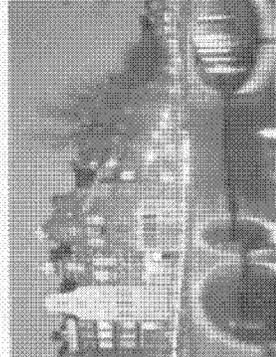
Visit our website for further information on the program, registration and housing at www.wocova.com

<p>Jacobs Christoffel, Chairman and Treasurer van Oosterhout, Dutch Society Intensive Technology The van Oosterhout Group</p>	<p>Australia: Martin Bower Brisbane, Melbourne, Perth Canada: Steve Kettle China: Henry Huang Czech Republic: Milan Slovacek Denmark: Peter Jensen France: Eric Deschamps Germany: Ulf Fockens Italy: Massimo Cirio Japan: Takao Kobayashi Korea: Mirak Park Romania: Sorinel Sorocob Spain: Maria Carrero Carrero Sweden: Mats Stromberg Switzerland: Brian Burt The Netherlands: Ton van Bode United Kingdom: Janet Gabriel USA: Paul Blackburn</p>
<p>Amsterdam, June 16-18, 2010</p>	<p>Amsterdam, June 16-18, 2010</p>

WoCoVA Foundation
 Amsterdam, NL

WoCoVA 1st World Congress on Vascular Access

Amsterdam
 June 16-17-18, 2010



Amsterdam RAI
 European Bld. NL 1078 GC
 Amsterdam, The Netherlands

www.wocova.com



Thank you!



Appendix J: Certifications of Main Suppliers



STANDARD OPERATING PROCEDURE

TITLE: SUPPLIER APPROVAL

REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
Sorin Grunwald	11	A		New procedure



STANDARD OPERATING PROCEDURE

TITLE: SUPPLIER APPROVAL PROCEDURE

1. PURPOSE

To define the general requirements for the selection, qualification, and ongoing evaluation of suppliers of production materials, services, and supplies at Romedex International Srl (Romedex).

2. SCOPE

2.1. This procedure applies to any supplier who provides components, manufacturing materials, or services (including Manufacturing and Labeling) that may have the potential to impact the quality of products at Romedex.

2.2. This procedure is documented using the Supplier Update Request Form (SURF).

3. REFERENCES

(b)(4)

4. RESPONSIBILITIES

(b)(4)



Appendix K: Sterilization and Biocompatibility



Appendix L: FDA Forms 3654

Department of Health and Human Services
 Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ANSI/AAMI/ISO 13485 - Medical devices - quality management systems - requirements for regulatory purposes, 2003

Please answer the following questions

Yes No

Is this standard recognized by FDA ²? Yes No

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)? Yes No

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)? Yes No
 If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device? Yes No

Does this standard include acceptance criteria? Yes No
 If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests? Yes No
 If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard? Yes No
 If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵? Yes No

Were deviations or adaptations made beyond what is specified in the FDA SIS? Yes No
 If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard? Yes No
 If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard? Yes No
 If yes, was the guidance document followed in preparation of this 510k? Yes No

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE
ANSI/AAMI/ISO 13485 - Medical devices - quality management systems - requirements for regulatory purposes, 2003

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced only for guidance

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

* Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to:

Center for Devices and Radiological Health
1350 Piccard Drive
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

ANSI/AAMI/ISO 14971 Medical Devices - application of risk management to medical devices, 2007

Please answer the following questions

Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # 5-40

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS)⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
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Is there an FDA guidance⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

ANSI/AAMI/ISO 14971 Medical Devices - application of risk management to medical devices, 2007

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
All		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

- * For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.
- ♦ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

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Rockville, MD 20850

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Department of Health and Human Services
Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

ISO 11135-1 Sterilization of Health Care Products - Ethylene Oxide - Part 1 2007

Please answer the following questions

Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # 14-228

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS)⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
If yes, report these exclusions in the summary report table.

Is there an FDA guidance⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE
ISO 11135-1 Sterilization of Health Care Products - Ethylene Oxide - Part 1 2007

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced only for guidance

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

ISO10993-4 Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood 2002

Please answer the following questions

Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

ISO10993-4 Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood 2002

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

Haemocompatibility, Partial Thromboplastin Time (PTT)

JUSTIFICATION

Referenced only for guidance

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

Haemocompatibility, Platelet and Leucocytes Count

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

Hemolysis Test

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

ISO10993-5 Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity 1999

Please answer the following questions

Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # 2-64

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?
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Title of guidance: _____

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² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE
ISO10993-5 Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity 1999

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION
Test for Cytotoxicity, in vitro method

JUSTIFICATION
Referenced only for guidance

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

- * For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.
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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ISO10993-6 Biological evaluation of medical devices — Part 6: Tests for local effects after implantation 1994

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # 2-120

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
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Is there an FDA guidance ⁶ that is associated with this standard?
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Title of guidance: _____

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

ISO10993-6 Biological evaluation of medical devices — Part 6: Tests for local effects after implantation 1994

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

Implantation test in rabbit

JUSTIFICATION

Referenced only for guidance

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A
----------------	---------------	--

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

ISO 10993-7 Biological evaluation of medical devices, Part 7: Ethylene oxide sterilization residuals 2008

Please answer the following questions

Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # 14-279

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?
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Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

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Title of guidance: _____

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

ISO 10993-7 Biological evaluation of medical devices, Part 7: Ethylene oxide sterilization residuals 2008

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION
Residual of Ethylene Oxide - Sterilization batch release

JUSTIFICATION
Referenced only for guidance

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

ISO10993-10 Biological evaluation of medical devices — Part 10: Tests for irritation and delayed-type hypersensitivity 2002

Please answer the following questions Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # 2-87

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

ISO10993-10 Biological evaluation of medical devices — Part 10: Tests for irritation and delayed-type hypersensitivity 2002

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION
Intracutaneous injection test in rabbit

JUSTIFICATION
Referenced only for guidance

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

 Traditional Special Abbreviated
STANDARD TITLE¹

IEC/EN 60601-1-1 Medical electrical equipment-Part1: General Requirements for Safety, 2000/2001

Please answer the following questions

Yes No

Is this standard recognized by FDA²? FDA Recognition number³ # 5-27Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)? Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?
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If no, include the results of testing in the 510(k).Does this standard include more than one option or selection of tests?
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If yes, were deviations in accordance with the FDA supplemental information sheet (SIS)⁵? Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.Were there any exclusions from the standard?
If yes, report these exclusions in the summary report table.Is there an FDA guidance⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

IEC/EN 60601-1-1 Medical electrical equipment-Part 1: General Requirements for Safety, 2000/2001

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
19	Leakage current	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
20.2	Hi-pot	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

IEC/EN 60601-1-2 Medical electrical equipment-Part1: General Requirements for Safety, 2003/2006

Please answer the following questions

Yes No

Is this standard recognized by FDA²? FDA Recognition number³ # 5-27Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)? Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?

If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device? Does this standard include acceptance criteria?

If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?

If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard? If yes, were deviations in accordance with the FDA supplemental information sheet (SIS)⁵? Were deviations or adaptations made beyond what is specified in the FDA SIS?

If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?

If yes, report these exclusions in the summary report table.

Is there an FDA guidance⁶ that is associated with this standard? If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

IEC/EN 60601-1-2 Medical electrical equipment-Part1: General Requirements for Safety, 2003/2006

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
EN 61000-4-2	Electrical discharge	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
EN 61000-4-3	Radiated RF immunity	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

ISO 594-2 Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical devices-Part 2:Lock fittings 1998

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # 6-129

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

ISO 594-2 Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical devices-Part 2:Lock fittings 1998

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION
Used for the design and test as applicable to the device under consideration

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

BS EN 1041 Information supplied by the manufacturer of medical devices, 2008

Please answer the following questions

Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?
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Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

BS EN 1041 Information supplied by the manufacturer of medical devices, 2008

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced for labeling considerations

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

EN 980 Graphical symbols for use in labeling of medical devices 2003 & 2008

Please answer the following questions

Yes No

Is this standard recognized by FDA²?

FDA Recognition number³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?

If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE
EN 980 Graphical symbols for use in labeling of medical devices 2003 & 2008

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	--

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced for labeling considerations

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

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JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EN 55011 Industrial, scientific and medical RF equipment - radio disturbances characteristics - limits and methods, 2007

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

EN 55011 Industrial, scientific and medical RF equipment - radio disturbances characteristics - limits and methods, 2007

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
5.2	Radiated emissions	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

IEEE 730 Software Quality Assurance, 1998

Please answer the following questions

Yes No

Is this standard recognized by FDA ²? Yes No

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)? Yes No

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)? Yes No
If no, complete a summary report table.

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Does this standard include acceptance criteria? Yes No
If no, include the results of testing in the 510(k).

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Were deviations or adaptations made beyond what is specified in the FDA SIS? Yes No
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Were there any exclusions from the standard? Yes No
If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard? Yes No
If yes, was the guidance document followed in preparation of this 510k? Yes No

Title of guidance: _____

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⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE
IEEE 730 Software Quality Assurance, 1998

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced only for guidance in software testing

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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- * Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

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1350 Piccard Drive
Rockville, MD 20850

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Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

IEEE 829 Software test documentation, 1998

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

IEEE 829 Software test documentation, 1998

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced only for guidance in software testing

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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Food and Drug Administration
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(To be filled in by applicant)

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

IEEE 830 Recommended practices for software requirements specification, 1993

Please answer the following questions

Yes No

Is this standard recognized by FDA ²? Yes No

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)? Yes No

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)? Yes No
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device? Yes No

Does this standard include acceptance criteria? Yes No
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests? Yes No
If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard? Yes No
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵? Yes No

Were deviations or adaptations made beyond what is specified in the FDA SIS? Yes No
If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard? Yes No
If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard? Yes No
If yes, was the guidance document followed in preparation of this 510k? Yes No

Title of guidance: _____

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² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

IEEE 830 Recommended practices for software requirements specification, 1993

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced only for guidance in the development of software requirements specification

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

IEEE 1058 Software project management, 1998

Please answer the following questions

Yes No

Is this standard recognized by FDA ²? Yes No

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)? Yes No

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)? Yes No
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device? Yes No

Does this standard include acceptance criteria? Yes No
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If yes, was the guidance document followed in preparation of this 510k? Yes No

Title of guidance: _____

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

IEEE 1058 Software project management, 1998

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION
Referenced only for guidance in software project management

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
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JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

IEEE 1074 Developing software life cycle, 1997

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # _____

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE
IEEE 1074 Developing software life cycle, 1997

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	--

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced only for guidance in software development and life cycle management

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE¹

IEEE J-STD-06 Software Development Plan, 1995

Please answer the following questions

Yes No

Is this standard recognized by FDA²? FDA Recognition number³ # _____Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)? Is a summary report⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device? Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).Does this standard include more than one option or selection of tests?
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Title of guidance: _____

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**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

IEEE J-STD-06 Software Development Plan, 1995

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	--

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

Referenced only for guidance in software development activities

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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COVER SHEET MEMORANDUM

From: Reviewer Name NIKHIL THAKUR
Subject: 510(k) Number 1093775/81
To: The Record

- Please list CTS decision code SE
- Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%20202%2007.doc)
 - Hold (Additional Information or Telephone Hold).
 - Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	Attach IFU	X	
510(k) Summary /510(k) Statement	Attach Summary	X	
Truthful and Accurate Statement.	Must be present for a Final Decision	X	
Is the device Class III?			X
If yes, does firm include Class III Summary?	Must be present for a Final Decision		X
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)		X	
Is this a combination product? (Please specify category _____ see http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC)			X
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			X
Is this device intended for pediatric use only?			X
Is this a prescription device? (If both prescription & OTC, check both boxes.)		X	
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?			X
Is clinical data necessary to support the review of this 510(k)?			X
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If not, then applicant must be contacted to obtain completed form.)			X
Does this device include an Animal Tissue Source?			X
All Pediatric Patients age <=21			X
Neonate/Newborn (Birth to 28 days)			X
Infant (29 days -< 2 years old)			X
Child (2 years -< 12 years old)			X
Adolescent (12 years -< 18 years old)			X
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age >= 21 (different device design or testing, different protocol procedures, etc.)			X

Transitional Adolescent B (18 <= 21; No special considerations compared to adults => 21 years old)	x
Nanotechnology	
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.htm)	Contact OC. x

Regulation Number	Class*	Product Code
21 CFR 880.5970	II	LJS
(*If unclassified, see 510(k) Staff)		

Additional Product Codes: _____

Review: Richard C. Chagnon 7/15/10
 (Branch Chief) (Branch Code) (Date)

Final Review: [Signature] 7/15/10
 (Division Director) (Date)



	Yes	No	N/A
Indications for Use page (Prescription Use Only): Section 4	*		
Truthful and Accuracy Statement: Section 6	*		
510(k) Summary: Section 5	*		
Standards Form: Appendix L	*		

III. **Device Description (Section 11)**

	Yes	No	N/A
Is the device life-supporting or life sustaining?		*	
Is the device an implant (implanted longer than 30 days)?		*	
Does the device design use software?	*		
Is the device sterile? (Only some components are marked as sterile)	*		
Is the device reusable (not reprocessed single use)?	*		
Are "cleaning" instructions included for the end user?	*		

General Description

The evGuide Tip Location System (TLS) consists of a sterile electrical adaptor, a sterile saline adaptor (connection assemblies), an ECG module and data acquisition and display software running on a laptop. Optionally, a printer can be attached to evGuide TLS. The system is designed to aid in central venous catheter tip positioning through ECG signal information. The evGuide TLS detects and displays a cardiac electrical signal from three ECG electrodes, including the evGuide electrical or saline adaptor and two body electrodes, which provide catheter tip positioning information.

System Components

The evGuide TLS consists of the following elements (See Figure 1 below):

1. evGuide TLS ECG module
2. PC/Laptop running evGuide TLS software
3. USB connection cable to the cardiac electrical signal (ECG) module
4. Label printer (optional)
5. ECG cable
6. Sterile evGuide TLS Saline Adaptor & Sterile evGuide TLS Electrical Adaptor
7. Skin ECG electrodes (supplied by user)

Operational Description

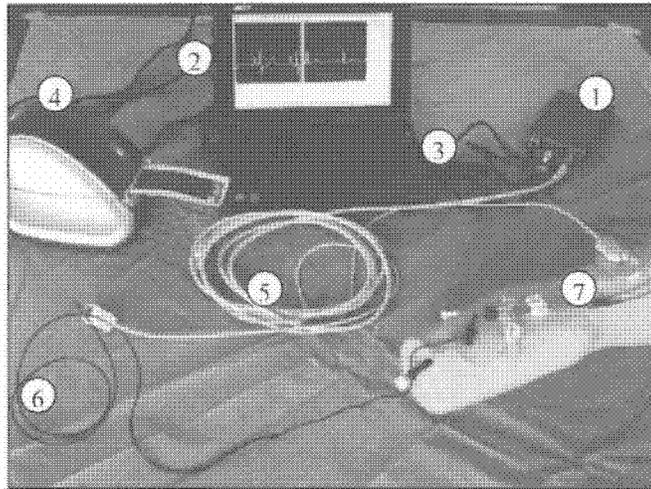


Figure 1 – evGuide Tip Location System

During the catheter placement procedure, one or several electrodes (7) are connected to the patient's skin using non-sterile off-the-shelf electrodes and the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the patient's central veins per the institution's guidelines, an evGuide TLS adaptor either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. (See Figure 3 for the Electrical Adaptor and Figure 4 for the Saline Adaptor) The sterile evGuide TLS adaptor transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (Figure 11.4) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated below, the user can estimate the location of the catheter tip. For example, in the Figure 2 below the yellow waveform on the right hand side of the screen is representative of a location very close to the sino-atrial node (the pacemaker of the heart) and the yellow waveform on the left hand side of the screen shows a waveform representative of the lower third of the superior vena cava. The white waveforms on both screens shows the skin ECG signal used for comparison.

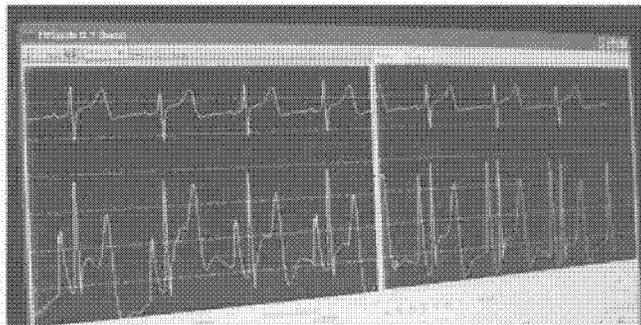


Figure 2 – evGuide TLS Graphical User Interface

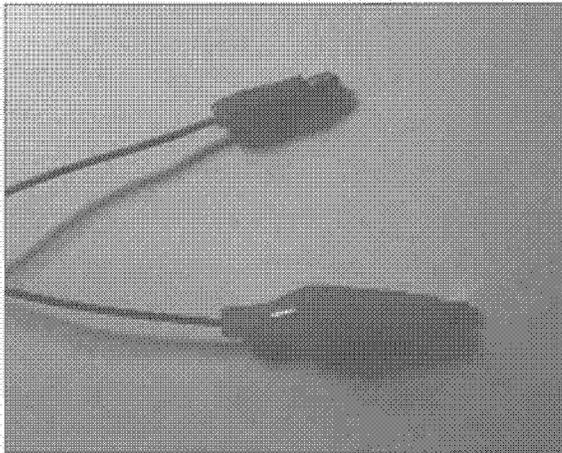


Figure 3 – evGuide TLS Electrical Adaptor

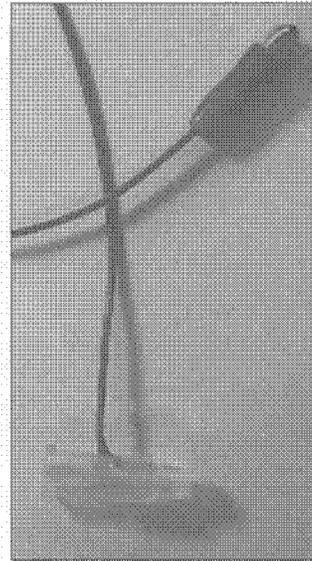


Figure 4 – evGuide TLS Saline Adaptor

IV. Indications for Use (Section 4)

Subject Device K093775

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide™ Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

Predicate Devices K091324 (Bard Access Systems, Sherlock 3CG TPS)

The Sherlock 3CG™ Tip Positioning System (TPS) is indicated for central venous catheter guidance and positioning during catheter placement. The Sherlock 3CG™ TPS provides real time catheter tip location information through the use of passive magnet and cardiac electrical signal detection.

Predicate Devices K032613 (Peter Rothenberg, Transvenous Pacemaker Placement Assist Device)

This device is designed to connect an intravascular electrode to a monitor through a standard EKG patient lead for the purpose of displaying an intravascular signal in real time. Only the black pinjack is "active". The red pinjack is electrically blind, and designed to isolate the proximal electrode from inadvertent stimulation.

Predicate Devices K973371 (B. Braun Medical, Conduction Anesthesia Kit – Certodyn)

To aid in the accurate placement of central venous catheters using the RAECG technique.

Predicate Devices K843263 (Teleflex/Arrow International, Arrow-Johans ECG Adaptor)

The adaptor is to be used in the placement of central venous catheters and more accurately diagnosing atrial dysrhythmias.

Discussion: The Subject Device appears to have the same indications for use that were previously cleared for the stated Predicates.

V. Predicate Device Comparison (Section 12 and Appendix A)

Device Name → Manufacturer → 510(k) →	Subject Device: K093775 Romodex International Srl The evGuide™ Tip Location System (TLS)	Predicate Device: K091324 Bard Access Systems Sherlock 3CG TPS	Predicate Device: K032613 Peter Rothenberg Transvenous Pacemaker Placement Assist Device	Predicate Device: K973371 B Braun Medical Conduction Anesthesia Kit – Certodyn)	Predicate Device: KB43263 Teleflex/Arrow International Arrow-Johans ECG Adaptor
Characteristic ↓					
How does the device locate the tip?	Uses cardiac electrical signal through a guide wire OR a catheter filled with a saline column to determine tip location	Uses cardiac electrical signal and passive magnets to determine the tip location.	Uses cardiac electrical signal through a guide wire to determine the tip location.	Uses cardiac electrical signal through a guide wire to determine the tip location.	Uses cardiac electrical signals through a catheter containing a saline column to determine tip location.
evGuide TLS Electrical Adaptor					
Wire Length	39 in.	32 in.	39 in.	24 in.	No Electrical Lead Wire
Electrical Resistance	10 ohm	N/A	10 ohm	10 ohm	N/A
Materials of Construction (MOC)	• (b)(4) • • • •	• (b)(4) • • •	• (b)(4) • • •	• (b)(4) • • •	(b)(4)
evGuide TLS Saline Adaptor					
Description	Adaptor with a female Luer Lock fitting at one end and a cone fitting at the other end	N/A	N/A	N/A	Adaptor with a female Luer Lock fitting at one end and a male Luer Lock fitting at the other end
Wire Length	39 in.	N/A	N/A	N/A	No wire involved. This is a compact device.
Electrical resistance	< 10 ohm	N/A	N/A	N/A	< 10 ohm
MOC	<ul style="list-style-type: none"> Medical grade PVC PVC isolated stainless steel threaded wire PVC adhesive, polyvinyl-chloride Stainless steel ECG cable connector 				<ul style="list-style-type: none"> Medical grade polyethylene or polycarbonate Gold plated stainless steel piece Adhesive (unknown) Gold plated stainless steel ECG cable connector
evGuide TLS System					
Description of Electronic System and User Interface	<ul style="list-style-type: none"> User interface running on laptop. ECG data acquisition 	<ul style="list-style-type: none"> User interface and ECG data acquisition module 	This system does not have an integrated user interface or electronic	This system does not have an integrated user interface or electronic	This system does not have an integrated user interface or electronic

Device Name→ Manufacturer→ 510(k) →	Subject Device: K093775 Romodex International Srl The evGuide™ Tip Location System (TLS)	Predicate Device: K091324 Bard Access Systems Sherlock 3CG TPS	Predicate Device: K032613 Peter Rothenberg Transvenous Pacemaker Placement Assist Device	Predicate Device: K973371 B. Braun Medical Conduction Anesthesia Kit – Certodyn)	Predicate Device: K843263 Teleflex/Arrow International Arrow-Johans ECG Adaptor
Characteristic↓	<p>module is a separate component</p> <ul style="list-style-type: none"> • Standard ECG Cable (non-sterile) • Sterile evGuide electrical or Saline Adaptor connecting ECG cable with CVC in sterile field. • Sterile insertion of CVC to which the evGuide adaptor (electrical or saline) is connected. 	<p>integrated into one module.</p> <ul style="list-style-type: none"> • Also has ultrasound imaging and magnetic tip locator device. • Standard ECG Cable (non-sterile) • Sterile electrical wire connecting detection sensor beneath a sterile drape with CVC in sterile field. • Sterile insertion of CVC to which the sterile electrical wire under a sterile drape. 	<p>data acquisition module. The device is connected to a standard ECG device.</p>	<p>data acquisition module. The device is connected to a standard ECG device.</p>	<p>data acquisition module. The device is connected to a standard ECG device.</p>
Hardware Platform	PC-Based	PC-Based	N/A	N/A	N/A
Printing capability	Yes if printer is connected	Yes if printer is connected	N/A	N/A	N/A

Discussion:

(b)(4)

(b)(4)



VI. 510(k) Summary / 510(k) Statement (Section 5)

The sponsor has provided its 510(k) Summary in Section 5 of the Submission:

		YES	NO	N/A
Required Elements for 510(k) Summary (21 CFR 807.92)				
	Clearly labeled "510(k) Summary"	✗		
	Submitter's name, address, phone #, a contact person	✗		
	Date the summary was prepared	✗		
	The name of the device/trade name/common name/classification name	✗		
	An identification of the legally marketed Predicate	✗		
	Description of the subject device	✗		
	Statement of intended use(identical to indications for use)	✗		
Technological characteristics	if same, a summary of comparison of technological characters			✗
	If different, a summary of how do they compare to the Predicate		✗	
Performance Data	Brief discussion of non-clinical data submitted, referenced, or relied on		✗	
	Brief discussion of clinical data submitted, referenced, or relied on, including: <ul style="list-style-type: none"> ▪ Description upon whom the device was tested, ▪ Data obtained from the tests and especially: ▪ Adverse events and complications ▪ Other information for SE determination 		✗	
	Conclusion that data demonstrate SE	✗		
Required Elements for 510(k) Statement (21 CFR 807.93)				

	YES	NO	N/A
Signed verbatim statement			*

Discussion:

(b)(4)



VII. Labeling (Section 13 and Appendix B)

Infusion Pump Guidance Labeling Recommendations	Yes	No
Does the submission contain proposed labels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for use?	*	
Does the labeling describe the intended uses?	*	
Does the labeling include adequate directions for use?	*	
Does the labeling include a prescription statement (21 CFR 801.109)?	*	
Labeling should include a list of device specifications including: reservoir volume, accuracy, residual volume, and the operational conditions (e.g., temperature and pressure) under which these are valid.	*	

Are route(s) of administration described as indicated in the statement of intended use?	*	
Are the fluid(s) to be administered by the device described as indicated in the statement of intended use?	*	
Does the labeling include comprehensive directions for preparation and use for all possible functions of the device?	*	
Does the labeling include a description of all warning and alarm features, and what actions to take for each alarm condition?	*	
MR/CT/X-ray warnings?		*

Discussion:

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Vitro Diagnostic Devices Intended for Professional Use” (November 30, 2004) is only recognized by CDRH’s Office of In Vitro Diagnostics, and does not apply to your device.

3. *Regarding electromagnetic compatibility, the evGuide TLS User Manual states that “Although the evGuide TLS System conforms to certain international safety and electromagnetic compatibility standards, the evGuide TLS System is intended for use by medical personnel who have received evGuide TLS System training.”. FDA’s review of electromagnetic compatibility and electrical safety testing for the Subject Device shows that the evGuide TLS was only partially tested for electrical safety. Please modify the labeling to specifically identify precautions that the end user should take when operating your device in the presence of electromagnetic radiation (i.e. MRI, CT Scan, X-rays).*

VIII. Sterilization/Shelf Life/Reuse (Section 14 and Appendix K)

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Discussion:

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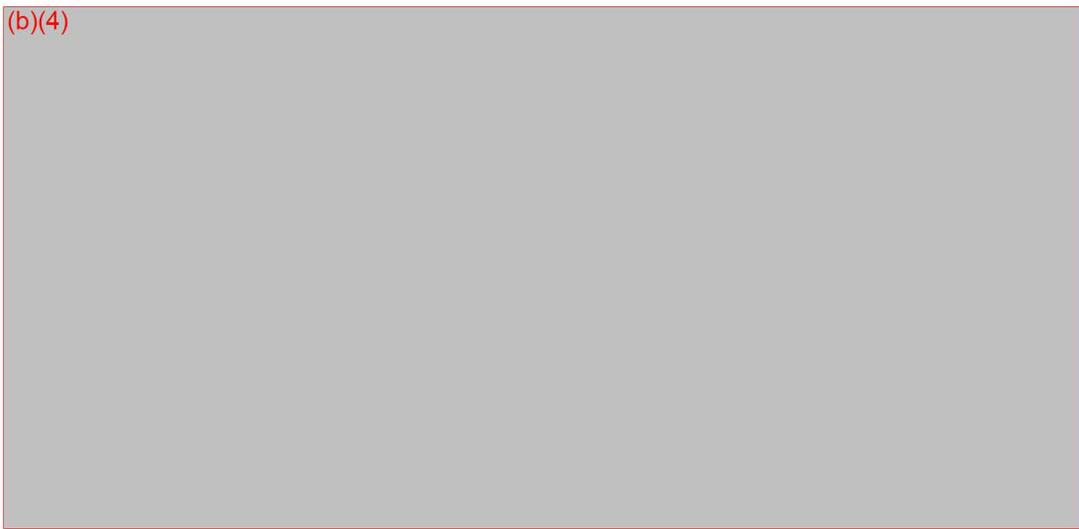
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IX. Biocompatibility (Section 15)

Discussion:

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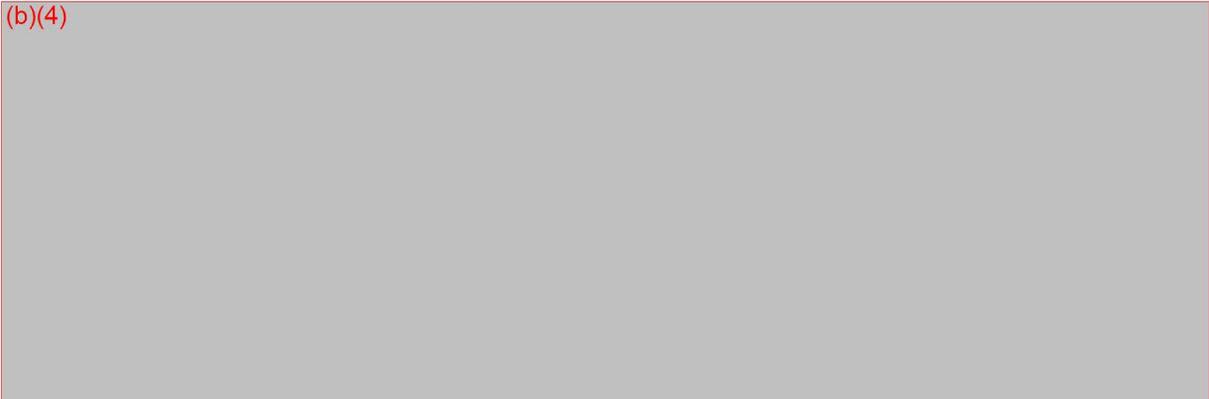


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X. Software (Section 14 and Appendices C & G)

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Design Specifications: Appendix C	✘	
Traceability Analysis/Matrix: Appendix G	✘	
Development: Appendix C	✘	
Verification & Validation Testing: Appendix G	✘	
Revision level history: Section 16.3	✘	
Unresolved anomalies: Sponsor states that there are No unresolved anomalies (Section 16.10)	✘	

Discussion:

I consulted Mr. Lenning Shen, Software Engineer on December 30, 2009. Mr. Shen's, March 2, 2010, response to this consult identified concerns regarding the software testing performed on the device. A copy of this consult has been included at the end of this memorandum. Based on the consult, there were no software deficiencies identified.

XI. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety (Section 17 and Appendix D)

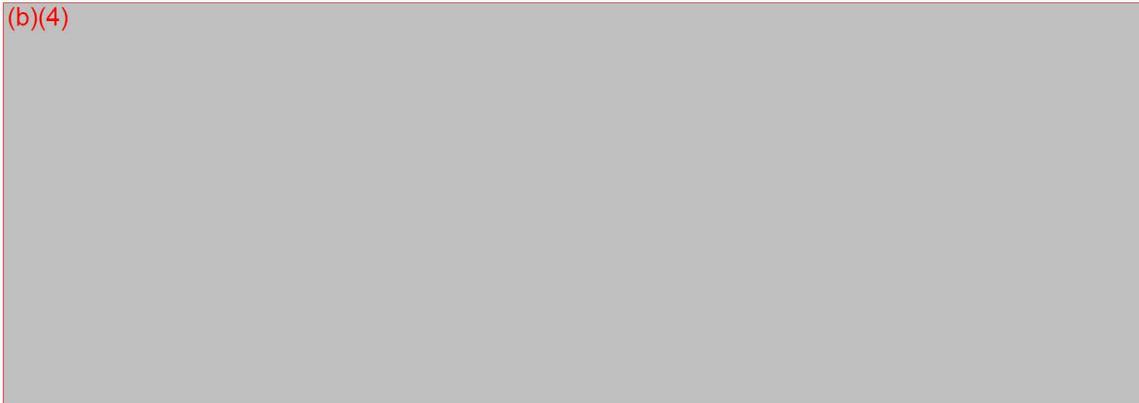
Discussion:

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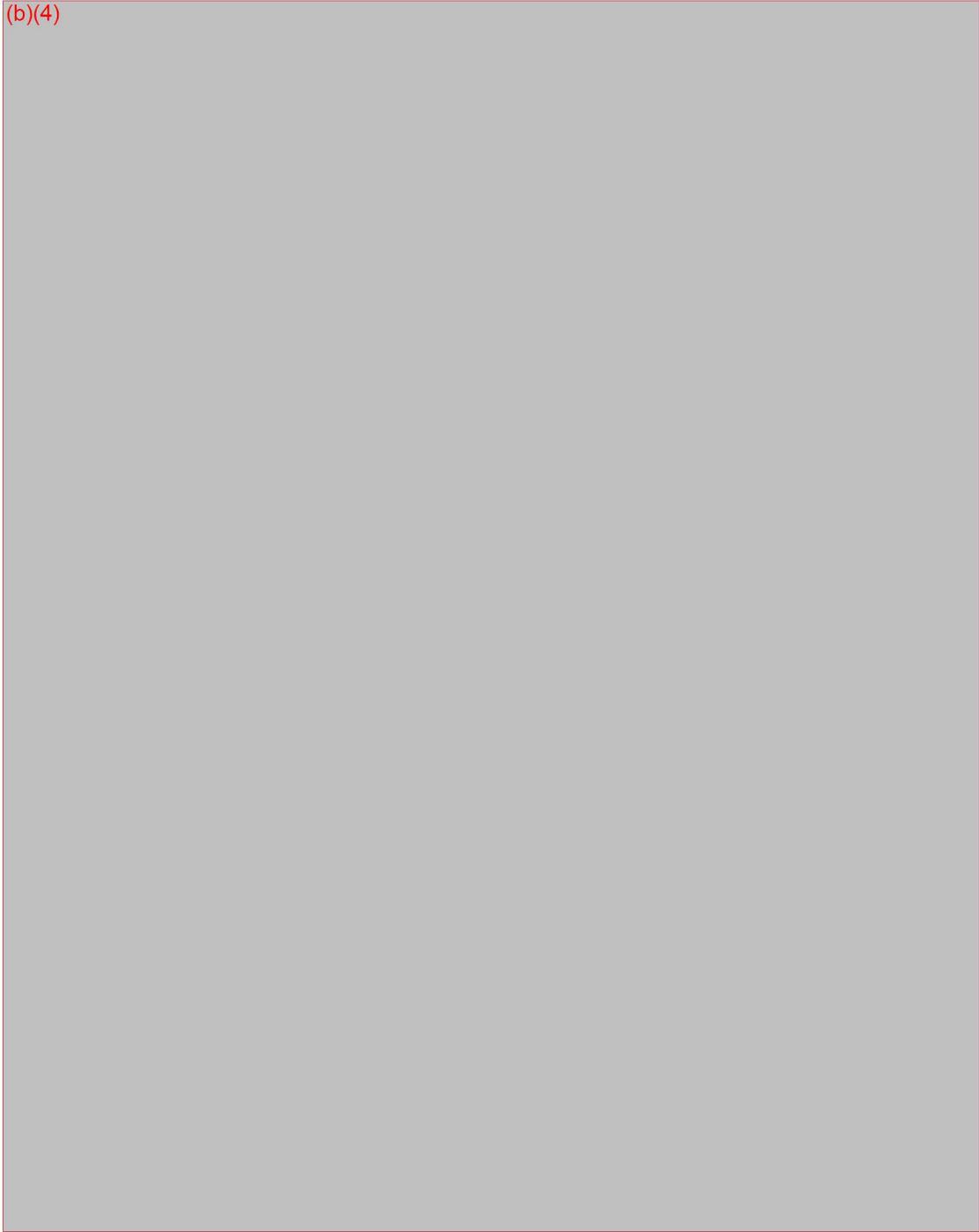


XII. Performance Testing - Bench

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XIII. Performance Testing - Human Factors

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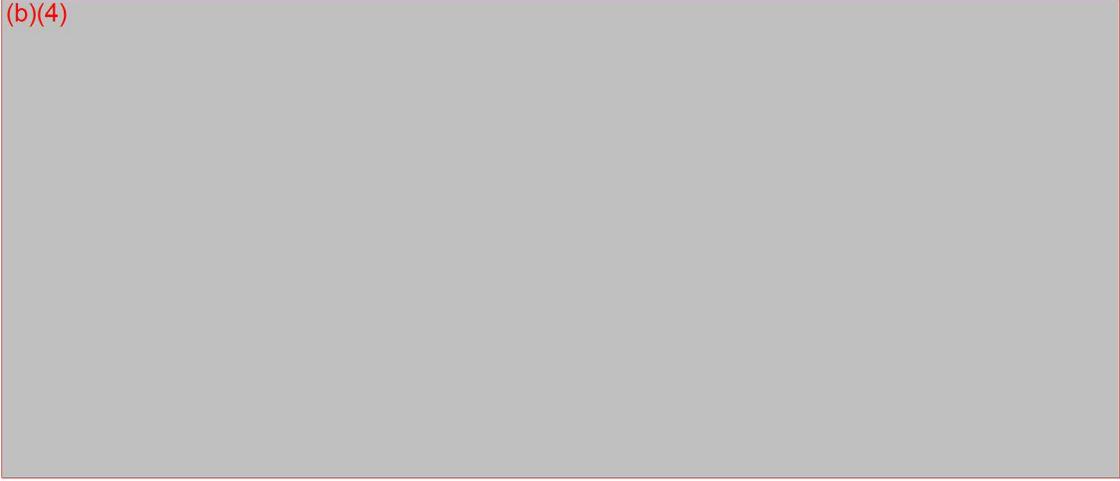
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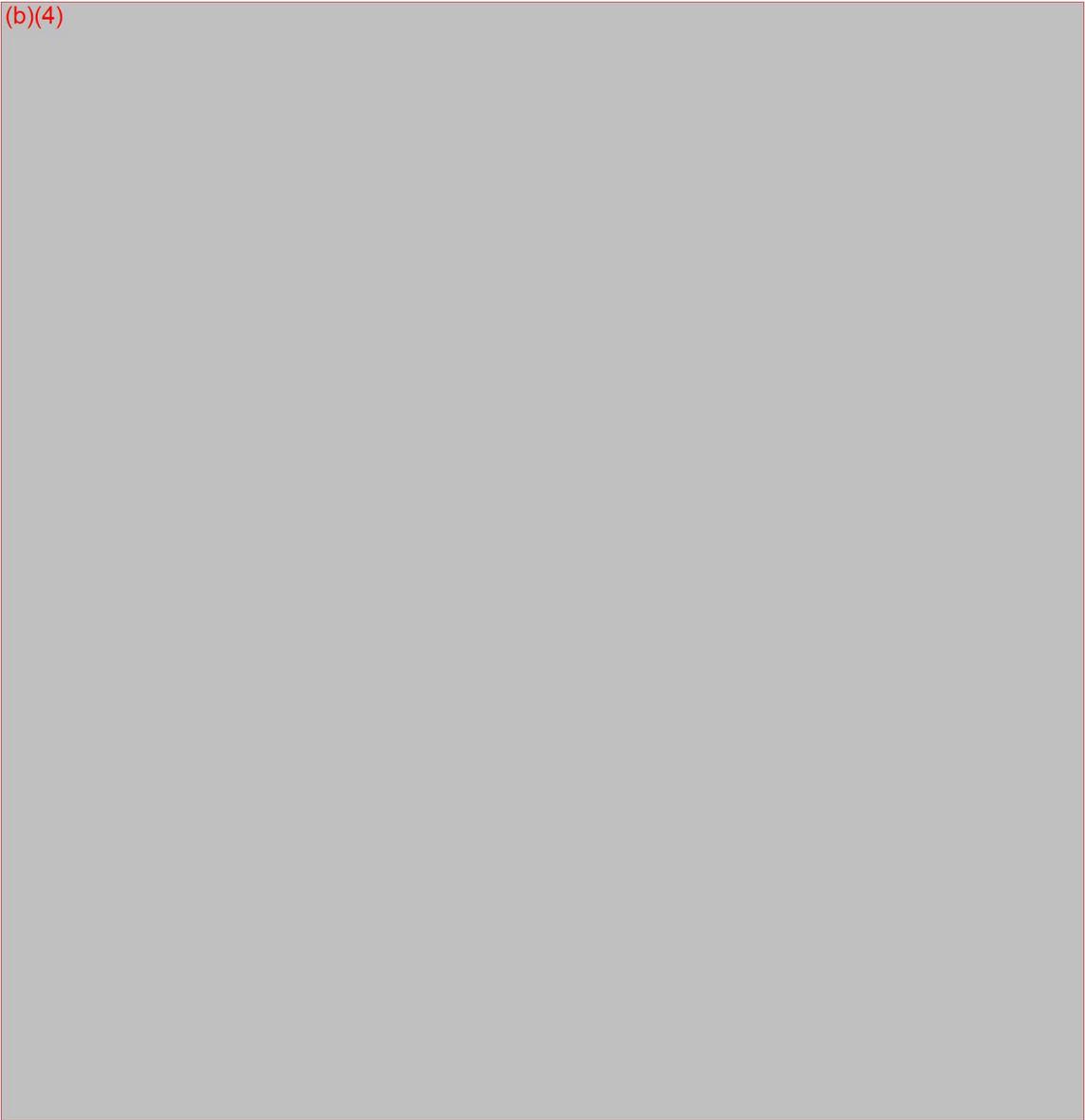
XIV. Performance Testing – Animal

(b)(4)



XV. Performance Testing – Clinical

(b)(4)



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XVI. Substantial Equivalence Discussion

	Yes	No
1. Same Indication Statement?	*	If YES = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?		If YES = Stop NSE
3. Same Technological Characteristics?	*	If YES = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?		If YES = Go To 6
5. Descriptive Characteristics Precise Enough?		* If NO = Go To 8 If YES = Stop SE
6. New Types Of Safety Or Effectiveness Questions?		If YES = Stop NSE
7. Accepted Scientific Methods Exist?		If NO = Stop NSE
8. Performance Data Available?	*	If NO = Request Data
9. Data Demonstrate Equivalence?	*	Final Decision: SE

Note: See http://erom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4148/ FLOWCHART%20DECISION%20TREE%20.DOC for Flowchart to assist in decision-making process. Please complete the following table and answer the corresponding questions. "Yes" responses to questions 2, 4, 6, and 9, and every "no" response requires an explanation.

1. Explain how the new indication differs from the predicate device's indication:
2. Explain why there is or is not a new effect or safety or effectiveness issue:
3. Describe the new technological characteristics:
4. Explain how new characteristics could or could not affect safety or effectiveness:
5. Explain how descriptive characteristics are not precise enough:
There are several concerns regarding the firm's labeling, performance testing, and sterilization methodology that could not be clarified based on the information provided in the submission.
6. Explain new types of safety or effectiveness question(s) raised or why the question(s) are not new:
7. Explain why existing scientific methods can not be used:
8. Explain what performance data is needed:
Deficiencies have been adequately addressed.
9. Explain how the performance data demonstrates that the device is or is not substantially equivalent:
The Sponsor has addressed all of the outstanding deficiencies. See Section XVII of this memorandum.

XVII. Sponsor's June 5, 2010, Response to FDA's March 4, 2010, Email Hold

510(k) Summary / 510(k) Statement

1. *FDA conducts a comprehensive review of the 510(k) Summary in accordance with 21 CFR 807.92 and the Required Elements for 510(k) Statements in accordance with 21 CFR 807.93. Based on our assessment of your 510(k) Summary in Section 5 of your submission, FDA believes that your Summary does not meet the regulation. Please address the following concerns regarding your 510(k) summary:*
 - a. *Please include a summary comparing the technological modifications made to your device as it relates to your predicate devices.*
 - b. *Please include a summary of the non-clinical testing data that was submitted, referenced or relied on to demonstrate that the Subject Device is safe and effective, and whose performance meets the requirements of its pre-defined acceptance criteria and intended uses.*
 - c. *Please include a summary of the clinical data that was submitted, referenced or relied on, including:*
 - i. *Description upon whom the device was tested*
 - ii. *Data obtained from the tests and especially*
 - iii. *Adverse events and complications*
 - iv. *Other information for SE determination*

Sponsor's June 7, 2010, Response:

The Sponsor updated their 510(k) summary to reflect the changes identified in FDA's deficiency. The Sponsor provided a copy of the revised 510(k) Summary on Page 4 of the response.

FDA Assessment of Sponsor's Response:

The response is adequate.

Labeling

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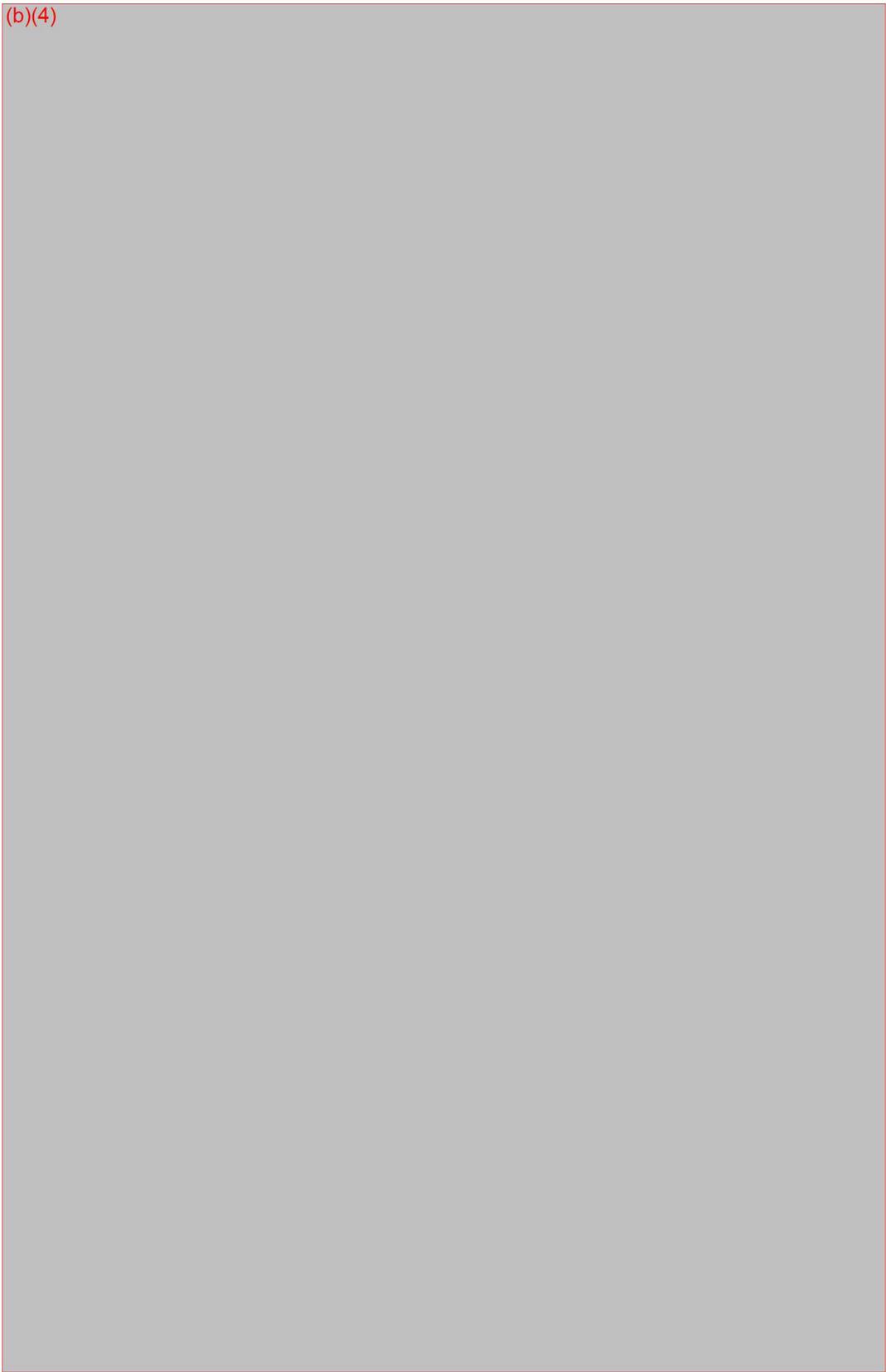


Sterilization/Shelf Life/Reuse

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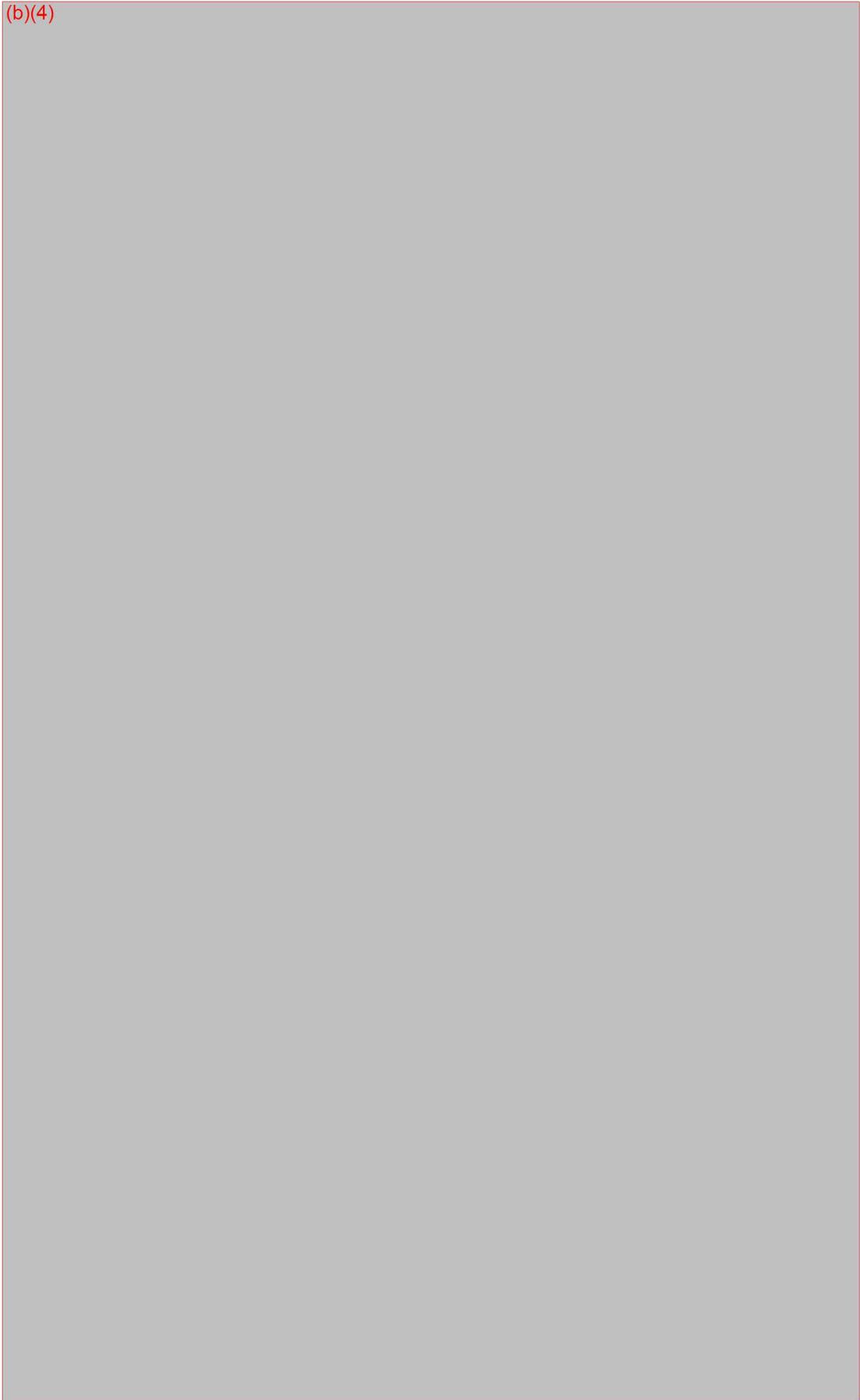


Sponsor's June 7, 2010, Response:

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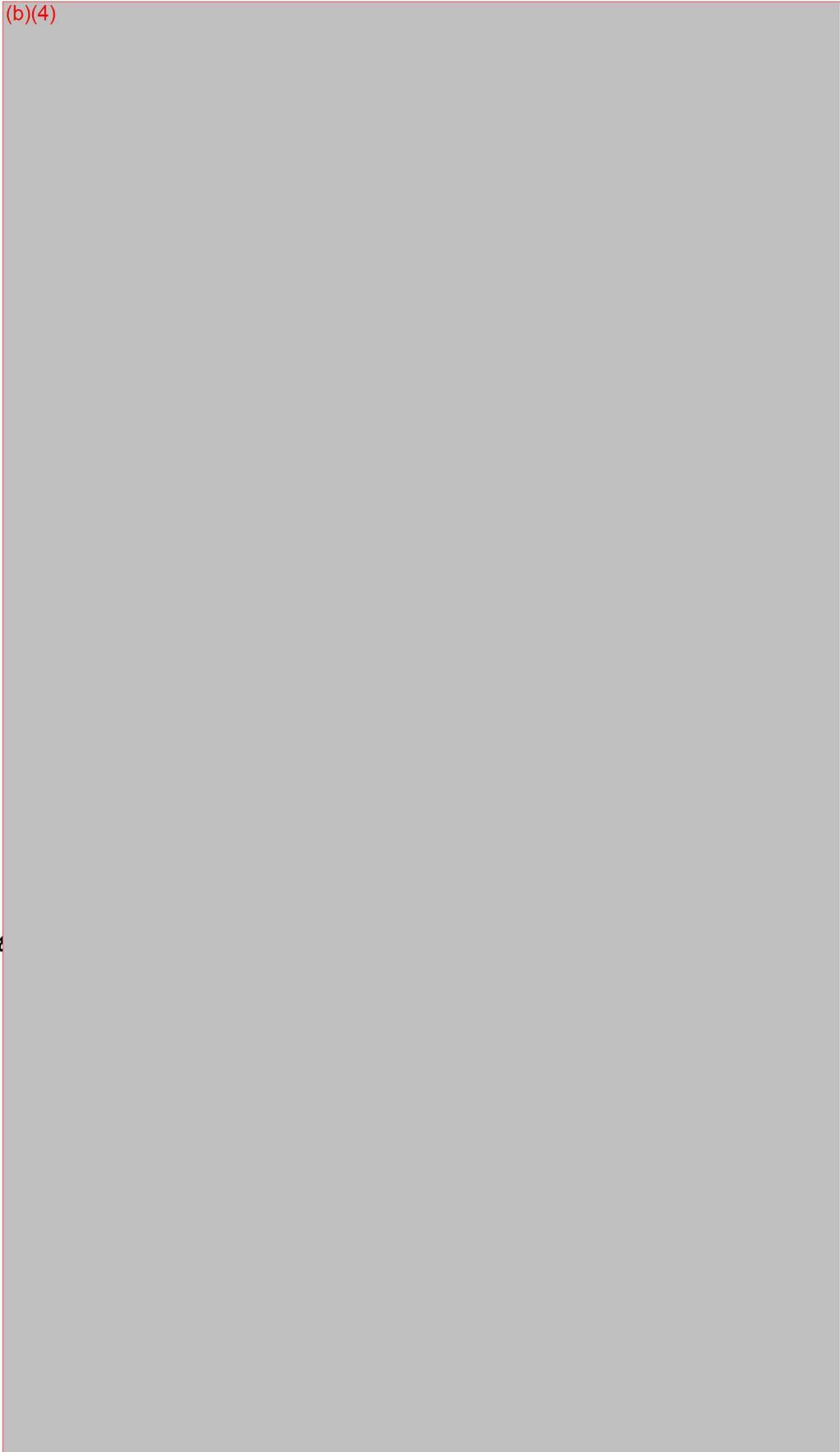
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Biocompatibility

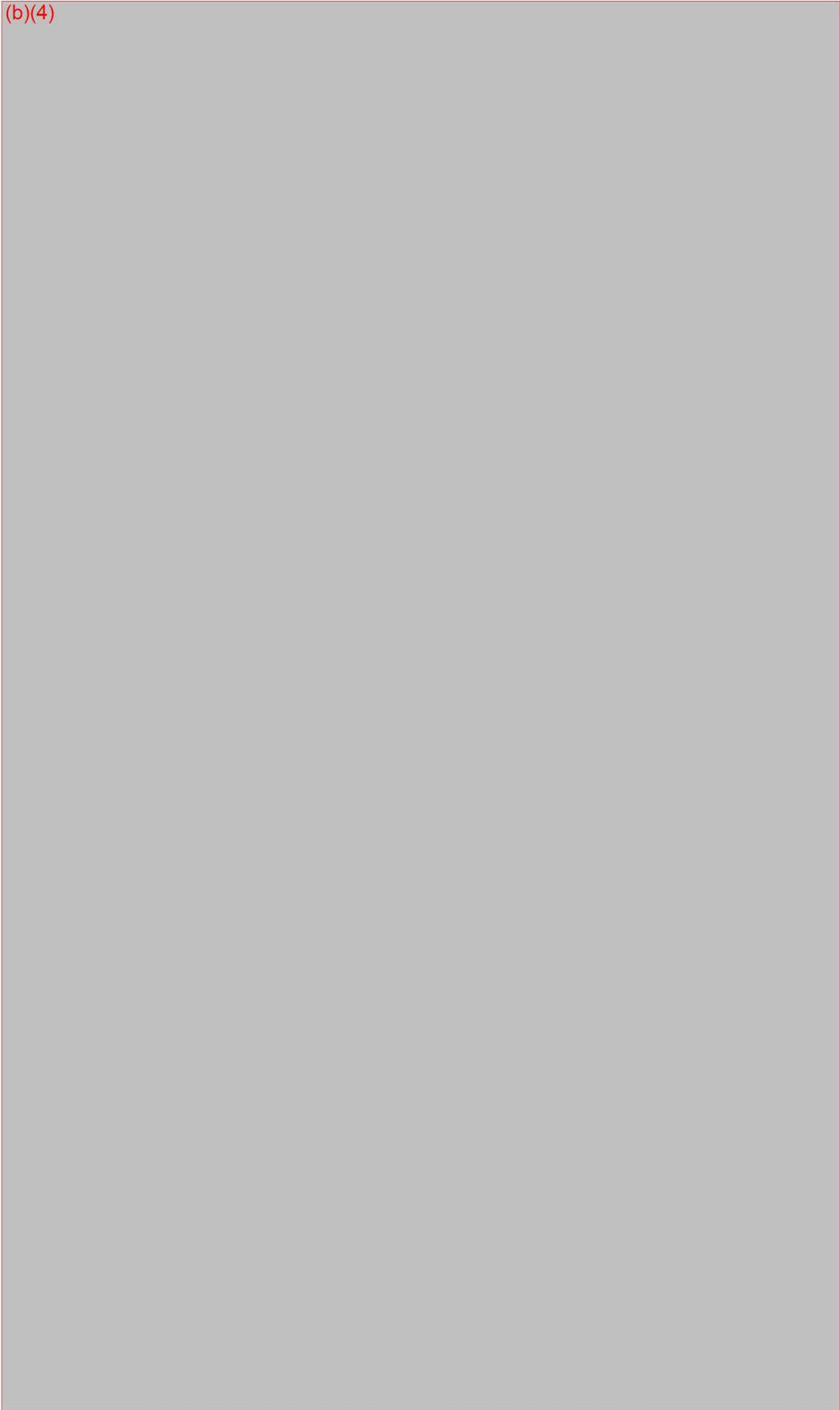
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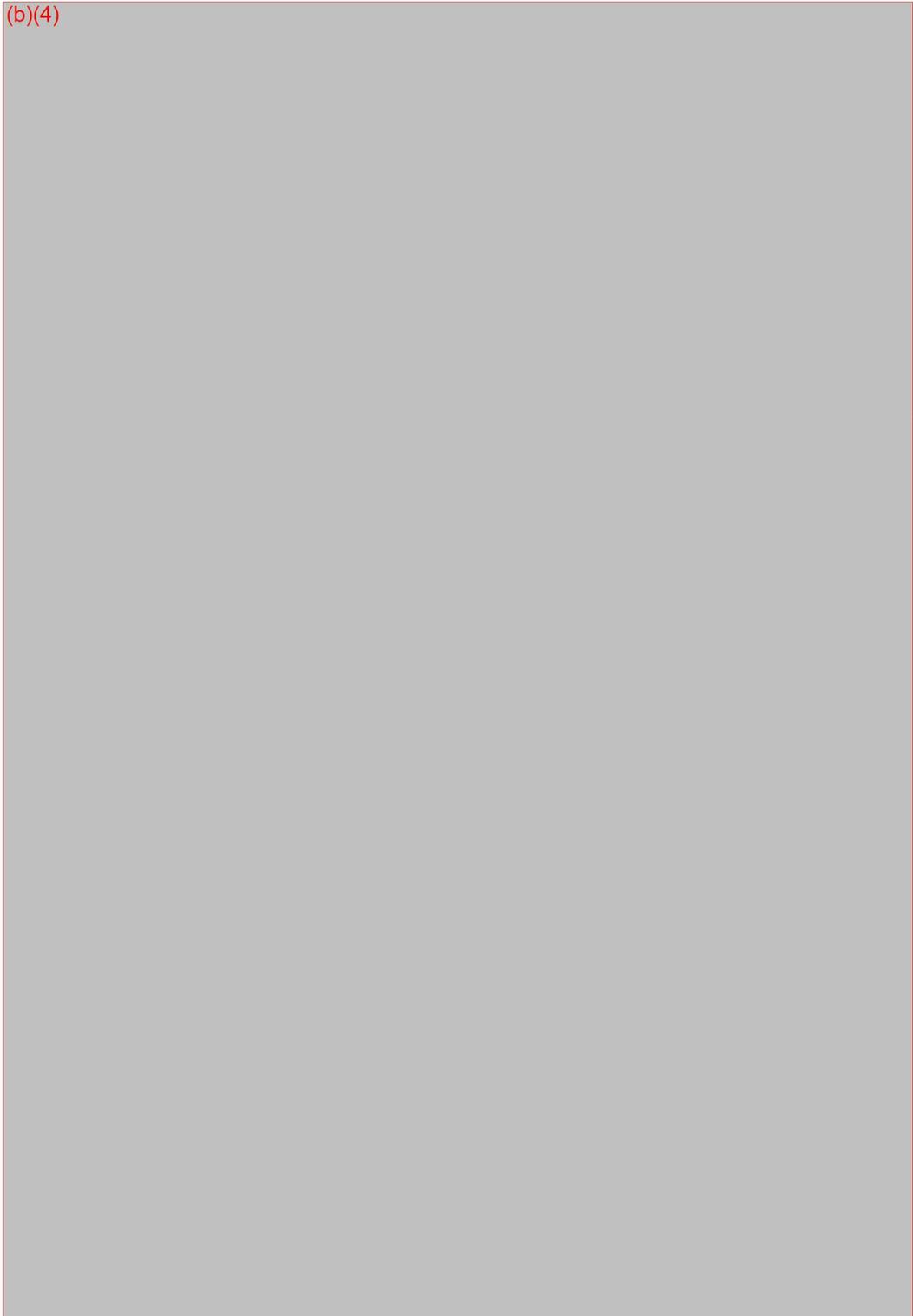


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Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

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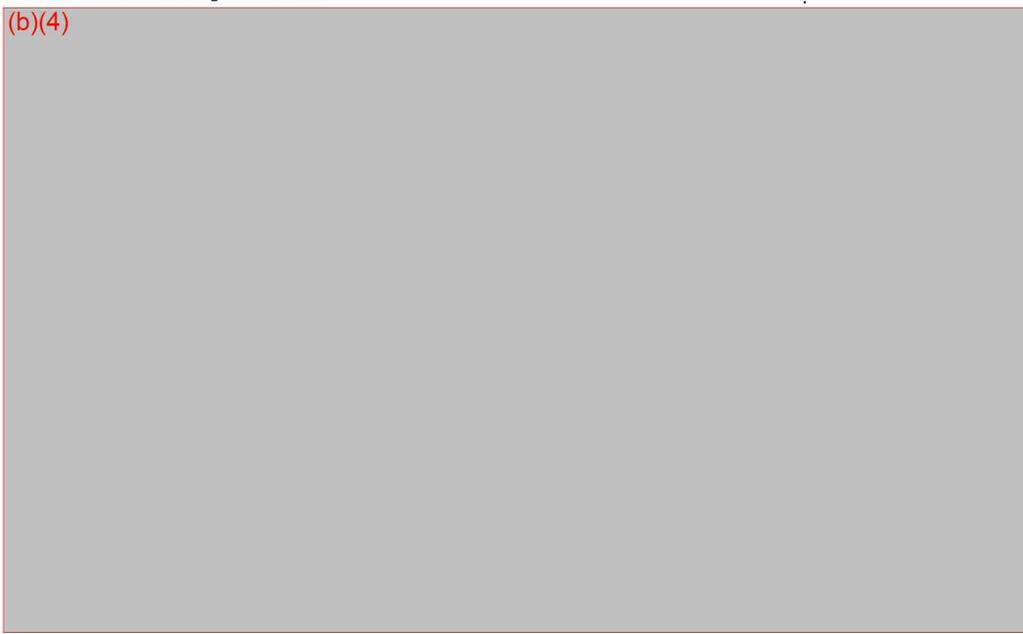
Section of standard	Description	Acceptance criteria	Results	Pass/Fail	Report #
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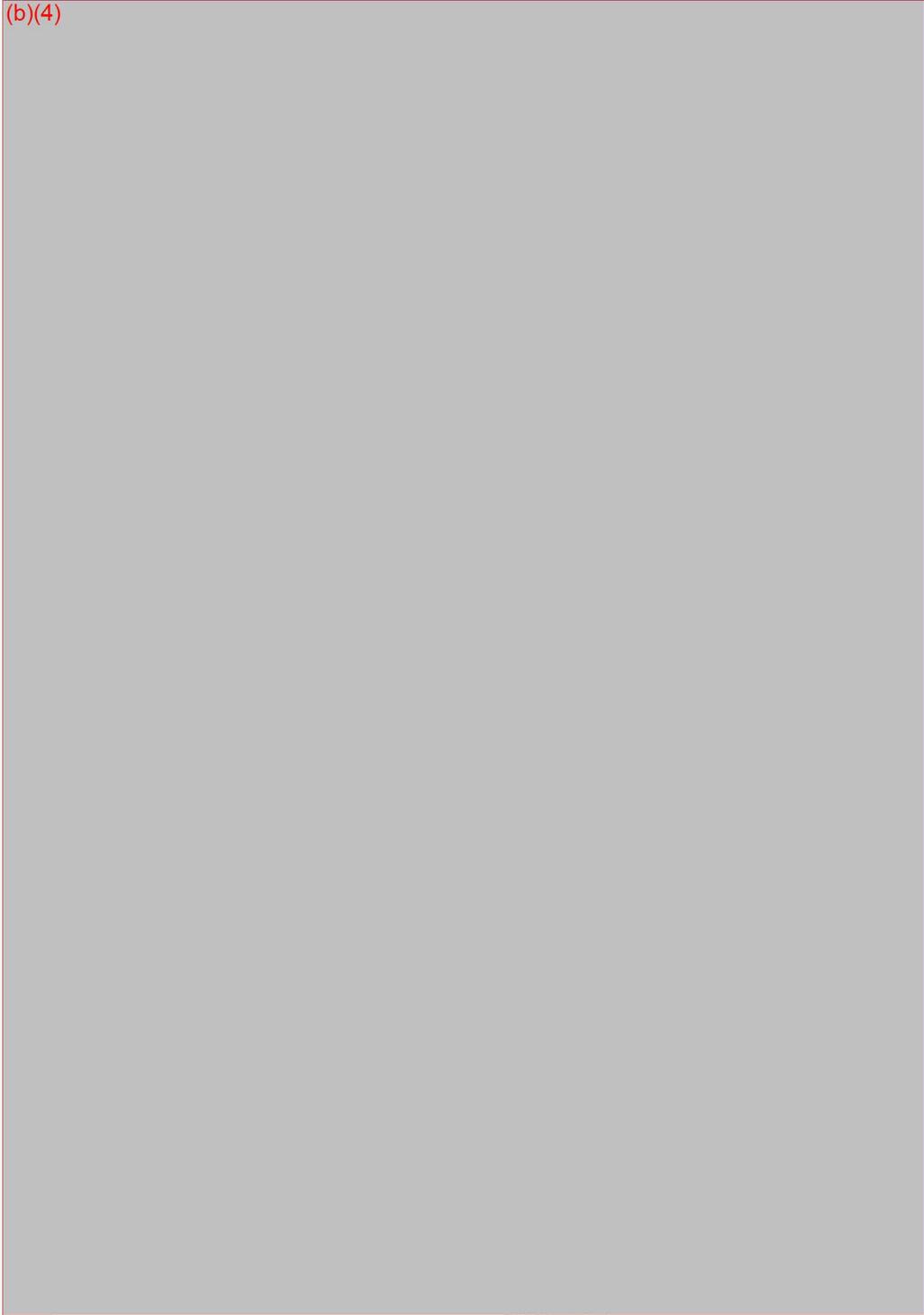
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Performance Testing - Bench

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Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
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Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
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Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
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Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
(b)(4)				

Performance Testing – Human Factors

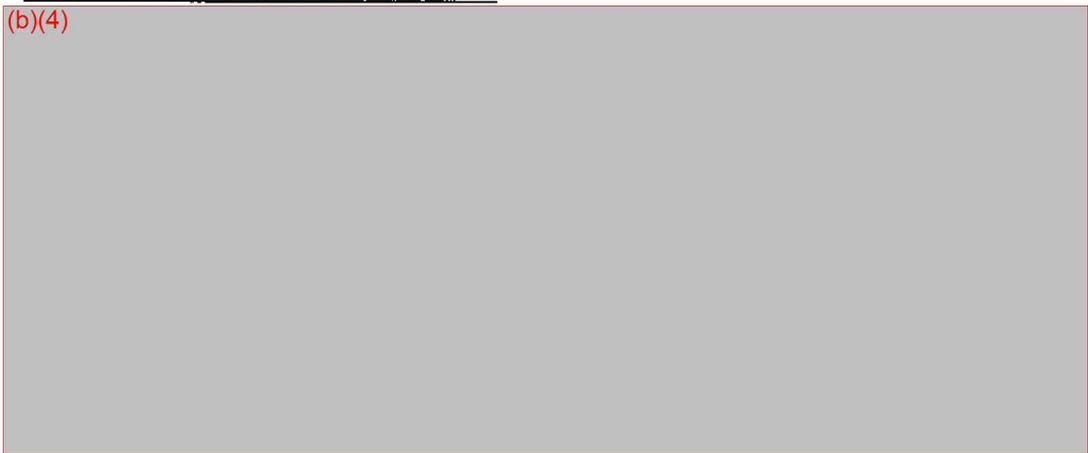
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Performance Testing – Animal & Clinical

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William J. ...
Reviewer

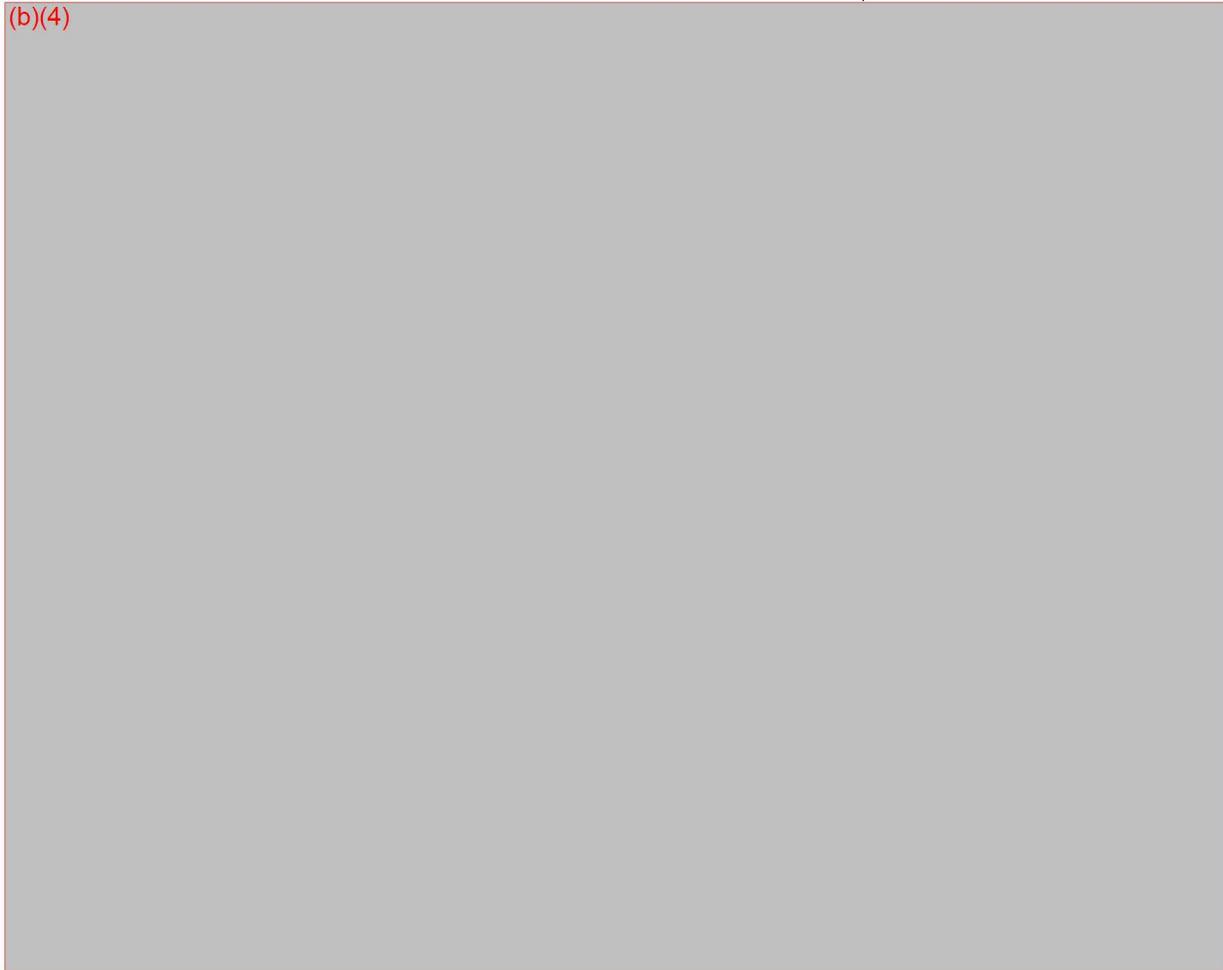
JUL 14, 2010
Date

R. C. Chapman
Branch Chief

7/15/10
Date

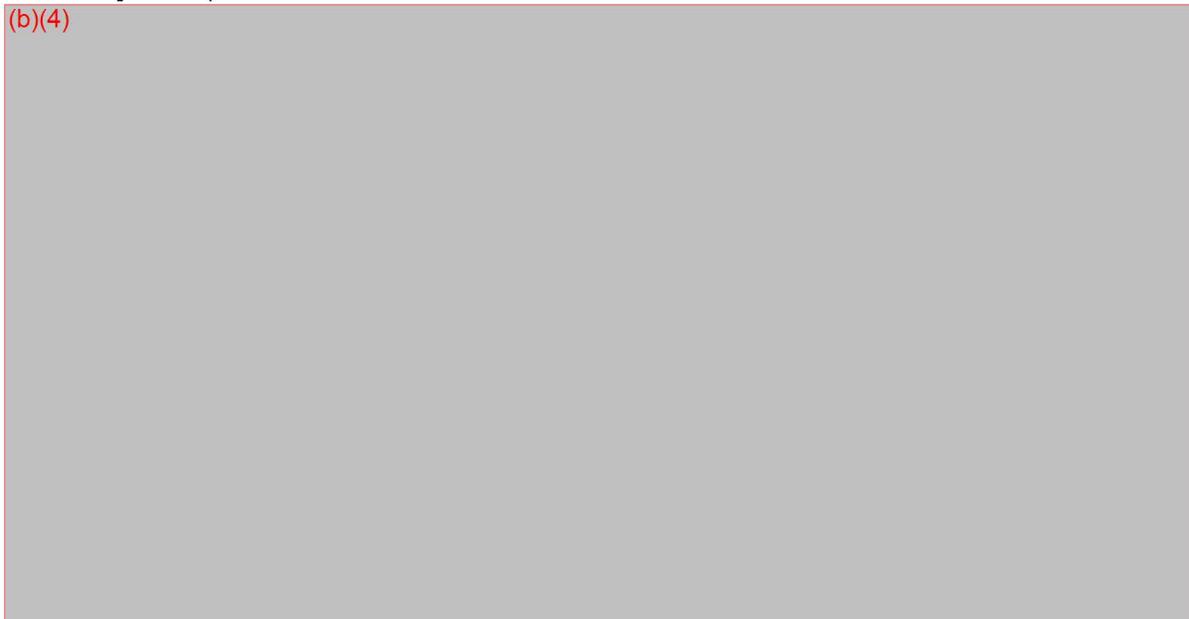
MEMORANDUM

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Biocompatibility

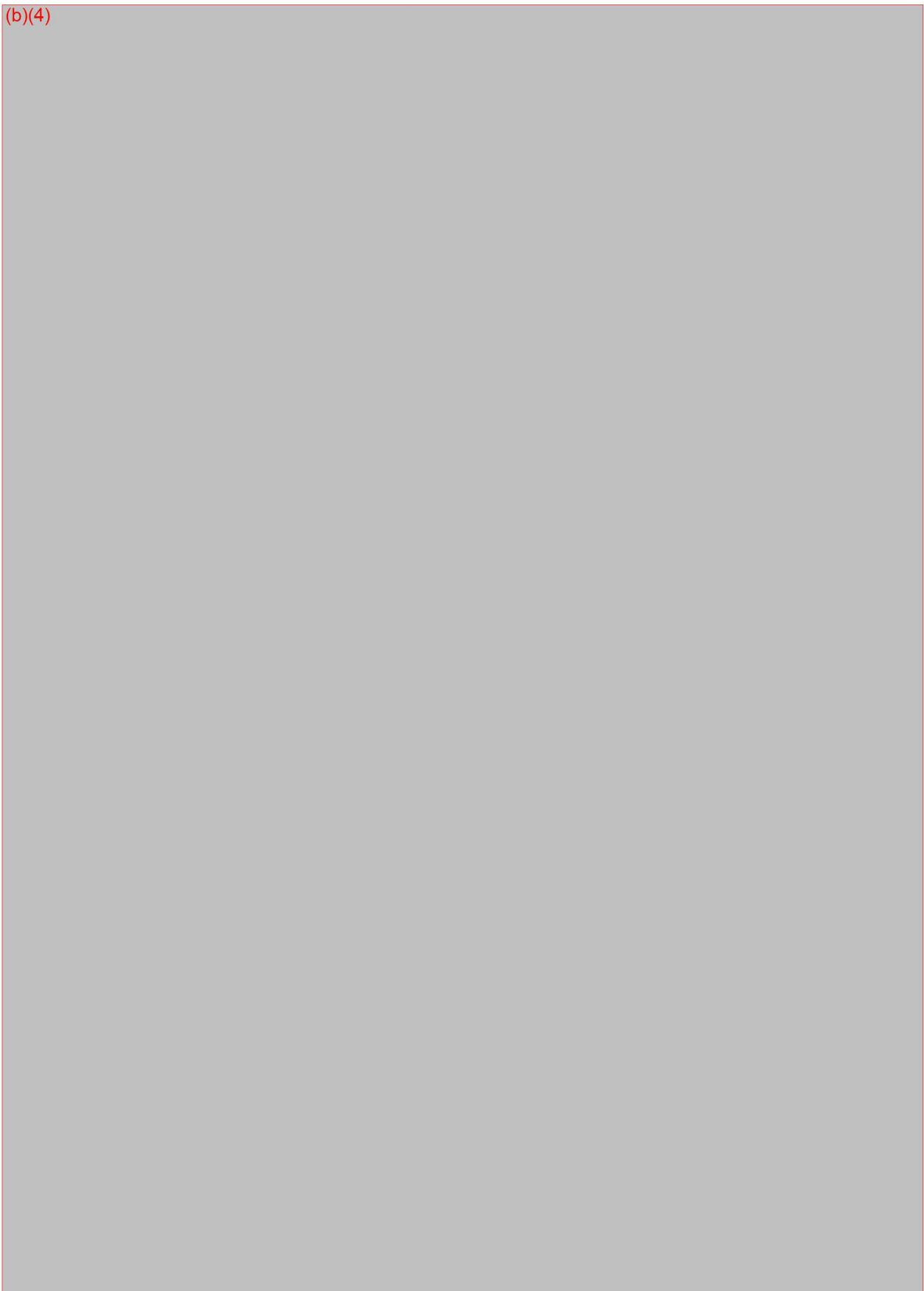
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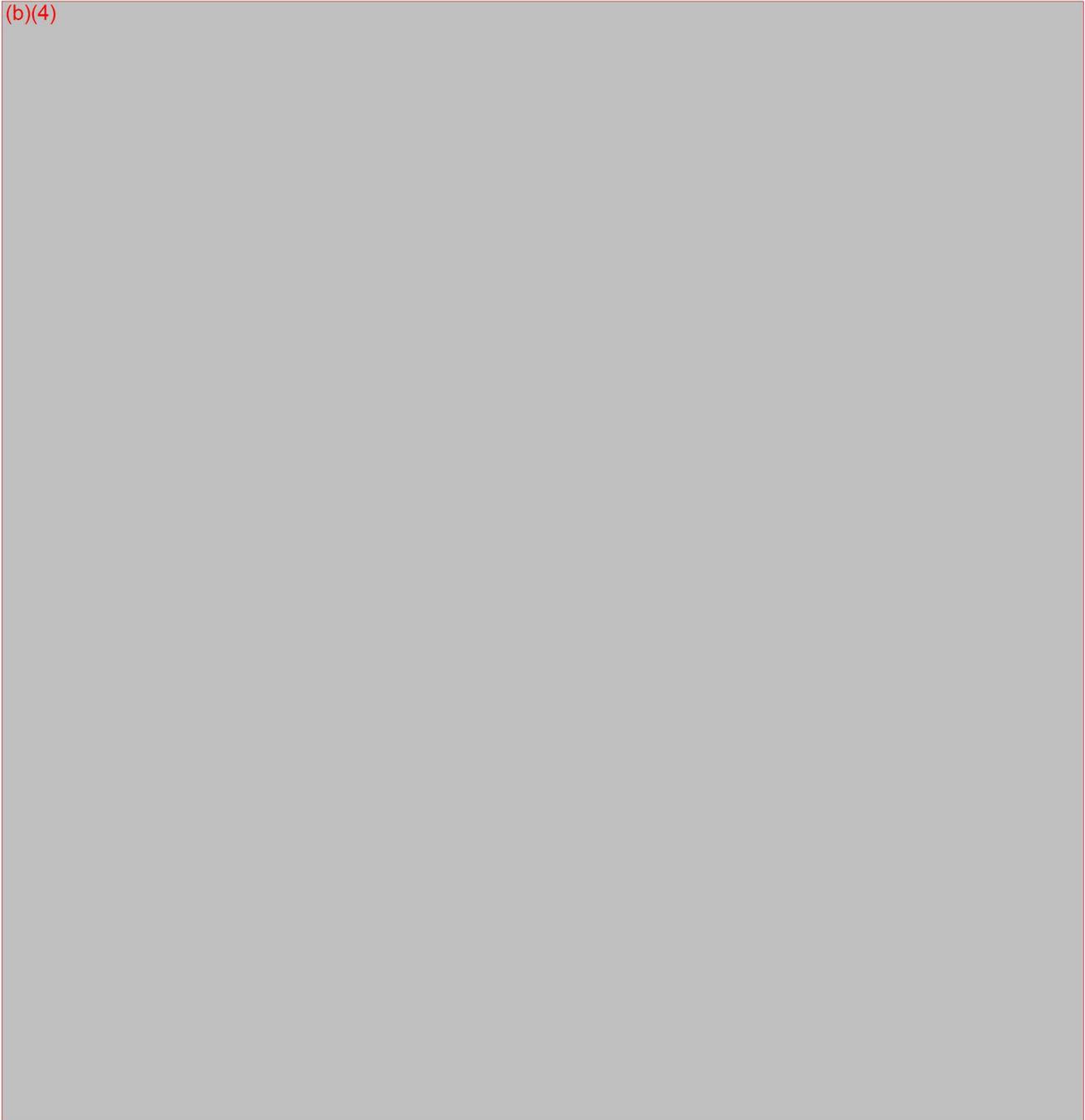
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K093775 Original:

Device Description:

The evGuide TLS consists of elements seen in the Figure 11.3, Section 11:

1. Sterile evGuide TLS Electrical Adaptor: ETO sterilization
2. Sterile evGuide TLS Saline Adaptor: ETO sterilization
3. Skin ECG electrodes (supplied by user)
4. evGuide TLS ECG module
5. ECG cable
6. PC/Laptop running evGuide TLS software
7. USB connection cable to the cardiac electrical signal (ECG) module
8. Label printer (optional)

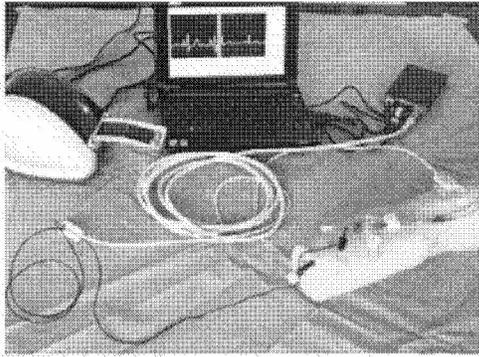


Figure 11.3 evGuide TLS system configuration

During the catheter placement procedure, one or several electrodes (7, on model hand) are connected to the patient's skin using non-sterile off-the-shelf electrodes and the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the patient's central veins per the institution's guidelines, an evGuide TLS adaptor either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. The sterile evGuide TLS adaptor transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (Figure 11.4) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated in Section 11 example, the user can estimate the location of the catheter tip. The construction and functionality of evGuide TLS is viewed by sponsor as substantially equivalent to "Sherlock 3CG" manufactured by Bard Access Systems (K091324).

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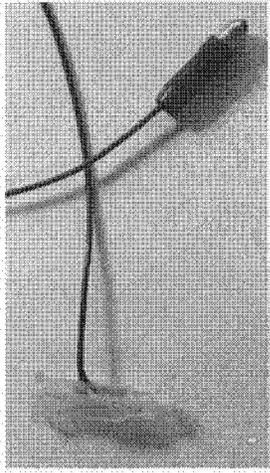
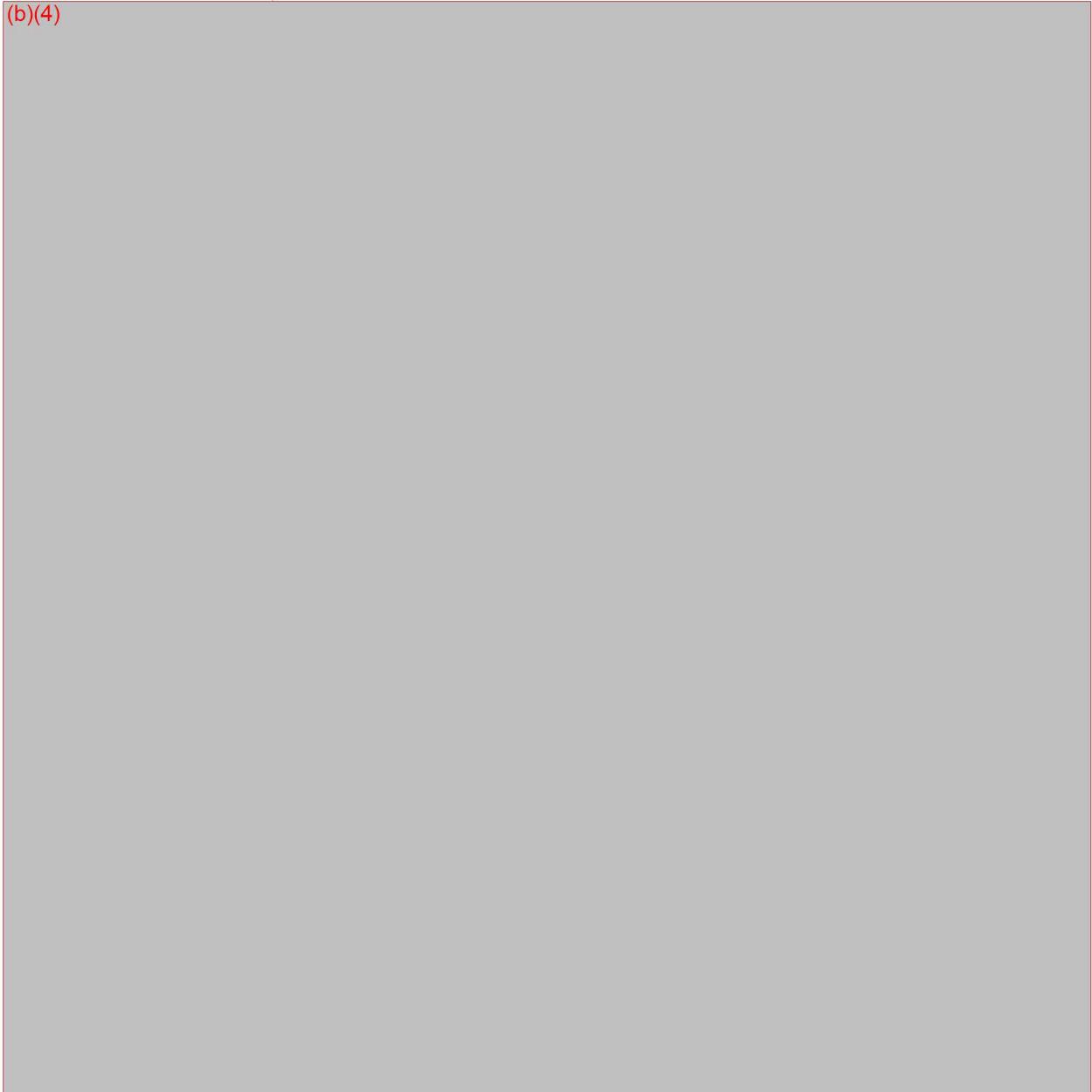


Figure 11.5 evGuide TLS Saline Adaptor

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End of review.

(Feb 3rd, 2010 Original Consult Email from Sajjad Syed)

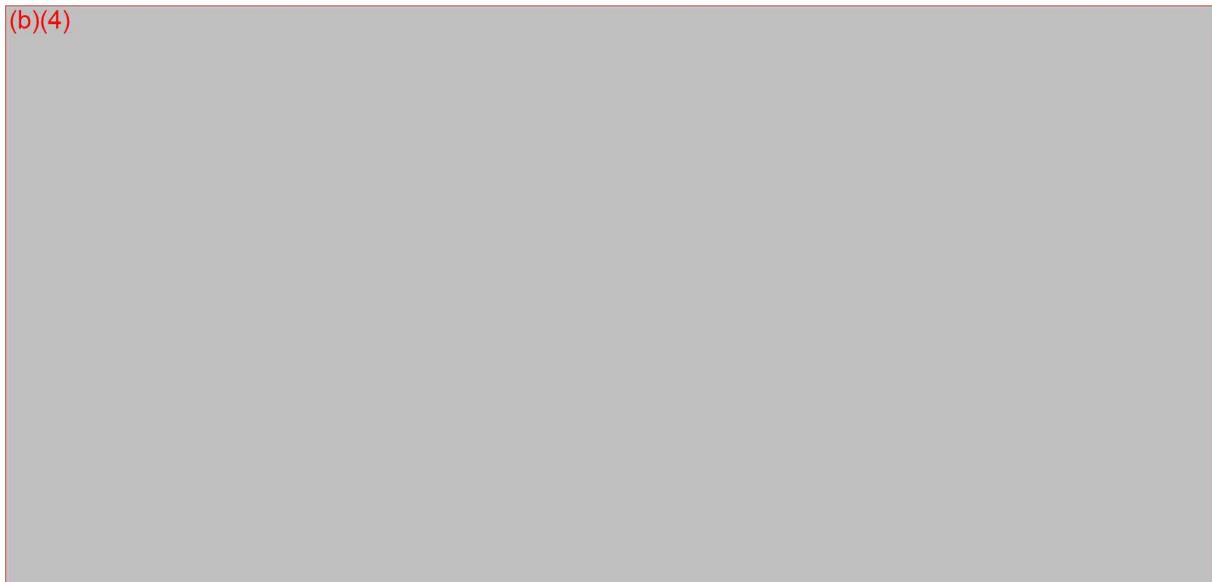
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Response (S001) of the sponsor to EMC question 9 on June 5th, 2010:

Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

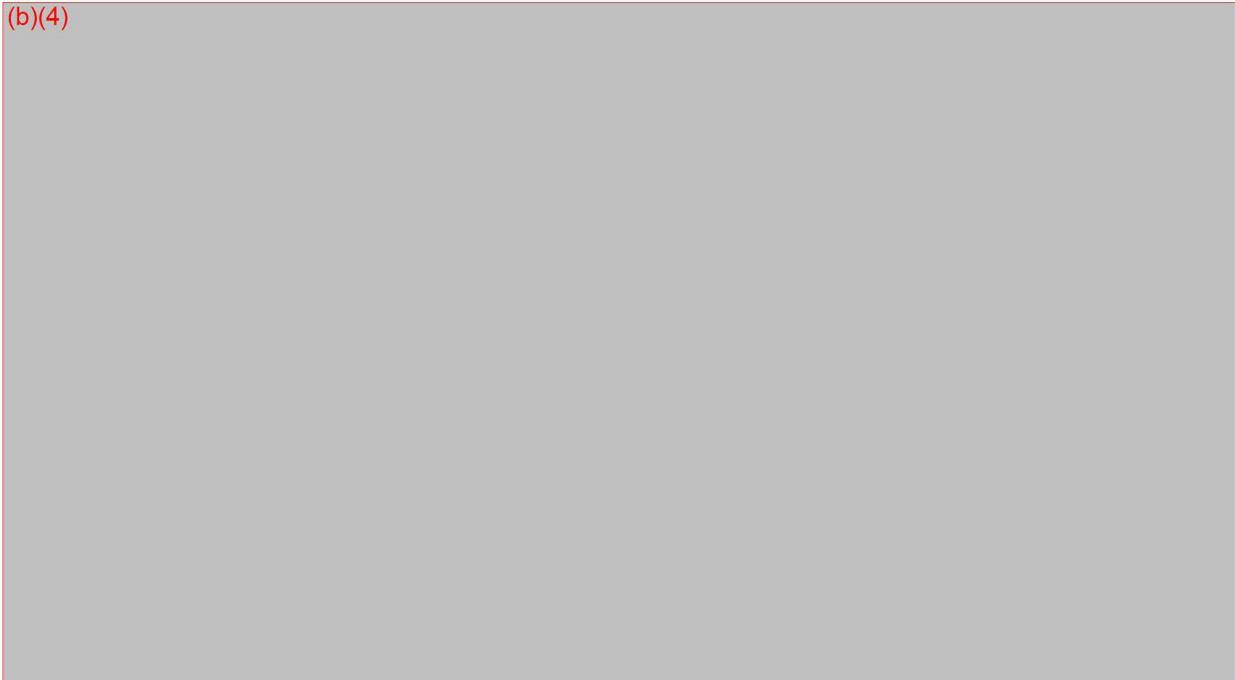
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Section of standard	Description	Acceptance criteria	Results	Pass Fail	Report #
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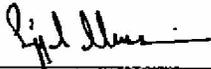
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Consultant's Comments reviewing June 5th, 2010 (S001) response of the sponsor above:

(b)(4)



 July 14, 2010
Sajjad H. Syed
Electrical Engineer
ODE-DAGID-GHDB

Human Factors Review

Name of the Device: evGuide-Sapiens™ TLS
Device Premarket Path: K093775/S001
ODE Coordinator: Nikhil Thakur
Applicant: Romedex International Srl
Kind of Device: Vascular access catheter accessories
Date sent: 7/12/2010
Consult: 108392
Reviewer: Ron Kaye

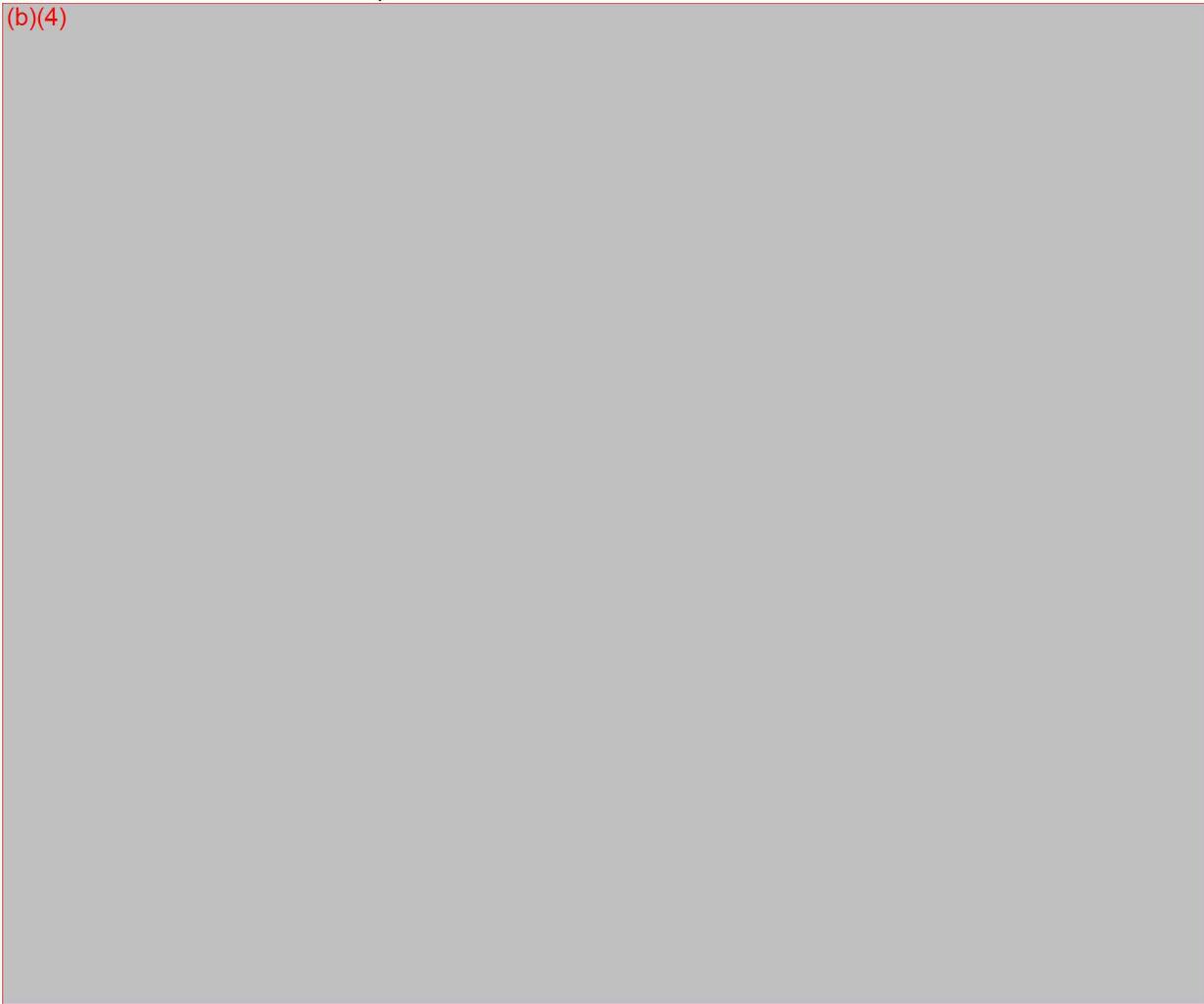
Conclusions

(b)(4)

A large rectangular area is redacted with a solid grey fill, obscuring the text under the 'Conclusions' heading.

Overview of the System

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A very large rectangular area is redacted with a solid grey fill, obscuring the text under the 'Overview of the System' heading.

(b)(4)

Materials Reviewed

(b)(4)

End of Review

 7/14/2020

Thakur, Nikhil

From: Samuels-Reid, Joy H.
Sent: Friday, June 11, 2010 12:37 PM
To: Thakur, Nikhil
Cc: Samuels-Reid, Joy H.
Subject: RE: CON108391 - Clinical Consult, K093775/S001

Nikhil,

The sponsor has addressed the concerns raised in Questions #16 through #18. The responses are acceptable; however, suggested revisions are shown below:

- Labelling has been revised to reflect appropriate indications and contraindications. ***This appears satisfactory; however, will need DCD (Cardiovascular Division) concurrence.***
- The sponsor should add that tip location accuracy was ***demonstrated in patients eighteen years and older*** (Table 16: Summary of evGuide/Sapiens TLS studies demographics).
- The sponsor has provided adequate clarification of when to use TLS electrical Adaptor and the TLS Saline Adaptor. ***(DCD concurrence needed)***
- The sponsor has provided a list of central venous access devices that can be successfully guided and positioned by the subject device as evidenced by the postmarket study (evGuide-Sapiens TLS Post-Market Clinical Study Report). The sponsor also cites a Human Factors Report (evGuide-Sapiens System Human Factors and Usability Validation Report). ***It may be necessary to list the specific types tested and have them captured in the labelling. Currently, the sponsor states all types of central venous catheters are compatible.***
- The 12 -subject study provided demonstrated the same level of accuracy as the predicate. No adverse events were reported. This appears reasonable.

Recommendation: Pending DCD's assessment, the responses appear adequate.

Joy

Joy Samuels-Reid, M.D.

CDRH/ODE/DAGID

Tel: 301-796-6266

From: Thakur, Nikhil

7/14/2010

Sent: Thursday, June 10, 2010 4:38 PM
To: Samuels-Reid, Joy H.
Subject: CON108391 - Clinical Consult, K093775/S001

Hi Joy,

You had provided a Clinical consult on K093775, Romodex International, Tip Location System. CDRH sent an Email Hold to the Sponsor on March 3, 2010. The Sponsor has provided a response.

Please review the sponsor's responses to Questions 16 to 18 from the email hold (Submission K093775/S001). I have an electronic copy of the submission, which I can give to you tomorrow.

Please note that I have missed my tier 1 goal for this submission. I would like, however, to not miss the tier 2 goal. This is the reason for the abbreviated response time for the submission. I apologize for the inconvenience that this will cause your branch. I appreciate your support.

Also, please note that I will be consulting Dr. Philippe Aguel within DCD to solicit his Division's experience with this device to determine whether there would be any additional clinical concerns.

Sincerely,
Nikhil

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
Silver Spring, MD 20993

Telephone: (301) 796 - 5536
Fax: (301) 847 - 8109

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7/14/2010

Thakur, Nikhil

From: Thakur, Nikhil
Sent: Wednesday, July 14, 2010 11:45 AM
To: Aguel, Felipe
Cc: Brockman, Randall
Subject: RE: Per our conversation.

Hi Felipe,

Thank you for your response. Yes. The Device is contraindicated in patients with cardiac arrhythmias.

**Sincerely,
Nikhil**

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
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From: Aguel, Felipe
Sent: Wednesday, July 14, 2010 11:44 AM
To: Thakur, Nikhil
Cc: Brockman, Randall
Subject: FW: Per our conversation.
Importance: High

Nikhil,

Thanks for sending me the executive summary and device description. I talked about this submission with Randy Brockman, and electrophysiologist in DCD. As long as no inappropriate claims regarding arrhythmia detection are made in the labeling, then I don't think we have any general concerns, assuming that the performance of the device has been validated. If I recall correctly, the device is contraindicated in patients with cardiac arrhythmias, correct?

Felipe

From: Thakur, Nikhil
Sent: Wednesday, July 14, 2010 11:27 AM
To: Aguel, Felipe
Subject: Per our conversation.
Importance: High

Hi Felipe,

Per our conversation, here are the reference files for the Romodex Tip Location System. I appreciate your opinion on this device.

Basically, to reiterate, GHDB was wondering if there are any general concerns regarding the technology that the Sponsor is using to locate central line catheter tips.

As you read these sections, please bare in mind that the Sponsor is no longer using the proprietary Saline Tip. They are using the Arrow-Johans Adapter which has been cleared by FDA on September 20, 1984 under K843263.

Thank you.

**Sincerely,
Nikhil**

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
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Silver Spring, MD 20993

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7/14/2010

59

Thakur, Nikhil

From: sorin@romedex.com
Sent: Wednesday, July 14, 2010 1:48 PM
To: Thakur, Nikhil
Cc: sorin@romedex.com
Subject: RE: K093775-S001

Hi Nikhil,

Yes, your understanding below regarding the interactions between the evGuide TLS system and the Arrow-Johans Saline Adaptor is correct.

Thank you very much for your support and for the productive dialog.

Best regards,

Sorin

Sorin Grunwald
Romedex International
Tel: 650.209.4838, Fax: 650.887.0348

From: Thakur, Nikhil [mailto:Nikhil.Thakur@fda.hhs.gov]
Sent: Wednesday, July 14, 2010 7:36 PM
To: sorin@romedex.com
Subject: RE: K093775-S001

Hi Sorin,

Thank you for clarifying my concerns regarding the interactions between the evGuide TLS system and the Arrow-Johans Saline Adaptor. Per our telephone discussion this morning, it is my understanding that the Arrow-Johans device is not packaged with the evGuide system. Rather, as a result of the agreements between Romodex Int'l and Teleflex (manufacturer of the Arrow Johans Adapter), you will be referencing the Arrow-Johans device in the instruction manual for your device, and recommending that the user follow the instructions on the Arrow-Johans device regarding installation, safety, etc.

Thank you. I will be in touch with you if there are any further questions regarding your submission.

**Sincerely,
Nikhil**

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

7/14/2010

60

Address:
10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
Silver Spring, MD 20993

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Thakur, Nikhil

From: sorin@romedex.com
Sent: Wednesday, July 14, 2010 5:26 PM
To: Thakur, Nikhil
Cc: sorin@romedex.com
Subject: RE: K093775-S001, Question about Labeling
Attachments: Att. 2 - evGuide-Sapines TLS adaptor instructions for use 1.pdf; Att. 1 - evGuide-Sapiens TLS users manual 1.pdf

Hi Nikhil,

Please see the attached documents in response to your concern below. The requested warning has been added in Att. 2 – Instructions for use, page 1, column 2, 4-th warning and in Att.1 – Users Manual, page 5, 5-th warning.

Please let me know if this addresses the FDA concerns and if you have any additional questions.

Best regards,

Sorin

From: Thakur, Nikhil [mailto:Nikhil.Thakur@fda.hhs.gov]
Sent: Wednesday, July 14, 2010 10:48 PM
To: sorin@romedex.com
Subject: K093775-S001, Question about Labeling
Importance: High

Hi Sorin,

I have one more question regarding K093775-S001. In Section 1.2 of Attachment 1 (evGuide TLS Instructions for Use), has a statement in the last paragraph that states "When an ECG monitor is connected to the endovascular electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node."

My medical officers have reviewed this statement and have stated that most patients without "cardiac arrhythmia" are in sinus rhythm in which case atrial activity (i.e. the P wave) originates from the sino-atrial node. It's possible that the origin of atrial activity is not the sino-atrial node, and in one respect this would fall under the broad category of "cardiac arrhythmia". However, it may not be obvious to a user that the origin of the rhythm is not the sino-atrial node if, for example, the rhythm were from an ectopic atrial focus. If that were the case, the relationship between the endovascular electrode (i.e. the tip of the catheter) and the atrial origin of electrical activity may be different that what would be expected, and the diagram of electrograms (relative to tip location within the endovascular system) may not predict catheter tip location (as presented in Figure 10.1 on the first page of the Executive Summary).

While by no means a perfect solution, if the labeling were to provide a Warning that stated that the evGuide TLS only works for a sinus rhythm, that would address the the FDA's concerns.

Please contact me so that we can discuss the FDA's concern, and your proposed solution. You may email a copy of the revised labeling to me. I will include the labeling as part of the response.

**Sincerely,
Nikhil**

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
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Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
White Oak Building 66
10903 New Hampshire Avenue
Silver Spring, MD 20993

**Premarket Notification [510(k)] Review for K093775
Traditional**

Date: March 3, 2010

To: The Record
From: Nikhil Thakur

Office: Office of Device Evaluation
Division: DAGID

510(k) Holder: Romodex International, Sri
Device Name: evGuide™ Tip Location System
Contact: Sorin Grunwald
Phone: (650) 209 – 4838
Fax: (650) 887 – 0348
Email: sorin@romodex.com

Dated: December 10, 2009
Received: December 10, 2009

Regulation Number: 21 CFR 880.5970
Regulation Name: Percutaneous, Implanted, Long Term Intravascular Catheter
Regulation Class: Class II (special controls)
Product Code: LJS

Predicate Device: K091324 (Bard Access Systems, Sherlock 3CG TPS)
K032613 (Peter Rothenberg, Transvenous Pacemaker Placement Assist Device)
K973371 (B. Braun Medical, Conduction Anesthesia Kit – Certodyn)
K843263 (Teleflex/Arrow International, Arrow-Johans ECG Adaptor)

Recommendation:

I. Purpose and Submission Summary

The 510(k) holder would like to introduce the evGuide™ Tip Location System (TLS) (Subject Device) into interstate commerce.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use page (Prescription Use Only): Section 4	✘		
Truthful and Accuracy Statement: Section 6	✘		

	Yes	No	N/A
510(k) Summary: Section 5	✘		
Standards Form: Appendix L	✘		

III. Device Description (Section 11)

	Yes	No	N/A
Is the device life-supporting or life sustaining?		✘	
Is the device an implant (implanted longer than 30 days)?		✘	
Does the device design use software?	✘		
Is the device sterile? (Only some components are marked as sterile)	✘		
Is the device reusable (not reprocessed single use)?	✘		
Are "cleaning" instructions included for the end user?	✘		

General Description

The evGuide Tip Location System (TLS) consists of a sterile electrical adaptor, a sterile saline adaptor (connection assemblies), an ECG module and data acquisition and display software running on a laptop. Optionally, a printer can be attached to evGuide TLS. The system is designed to aid in central venous catheter tip positioning through ECG signal information. The evGuide TLS detects and displays a cardiac electrical signal from three ECG electrodes, including the evGuide electrical or saline adaptor and two body electrodes, which provide catheter tip positioning information.

System Components

The evGuide TLS consists of the following elements (See Figure 1 below):

1. evGuide TLS ECG module
2. PC/Laptop running evGuide TLS software
3. USB connection cable to the cardiac electrical signal (ECG) module
4. Label printer (optional)
5. ECG cable
6. Sterile evGuide TLS Saline Adaptor & Sterile evGuide TLS Electrical Adaptor
7. Skin ECG electrodes (supplied by user)

Operational Description

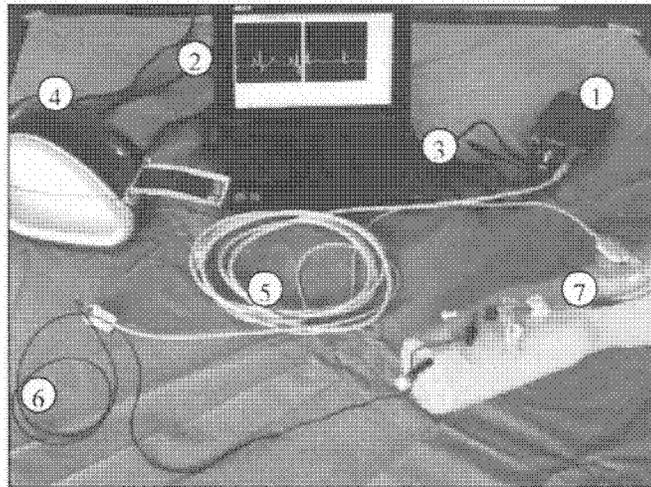


Figure 1 – evGuide Tip Location System

During the catheter placement procedure, one or several electrodes (7) are connected to the patient's skin using non-sterile off-the-shelf electrodes and the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the patient's central veins per the institution's guidelines, an evGuide TLS adaptor either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. (See Figure 3 for the Electrical Adaptor and Figure 4 for the Saline Adaptor) The sterile evGuide TLS adaptor transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (Figure 11.4) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated below, the user can estimate the location of the catheter tip. For example, in the Figure 2 below the yellow waveform on the right hand side of the screen is representative of a location very close to the sino-atrial node (the pacemaker of the heart) and the yellow waveform on the left hand side of the screen shows a waveform representative of the lower third of the superior vena cava. The white waveforms on both screens shows the skin ECG signal used for comparison.

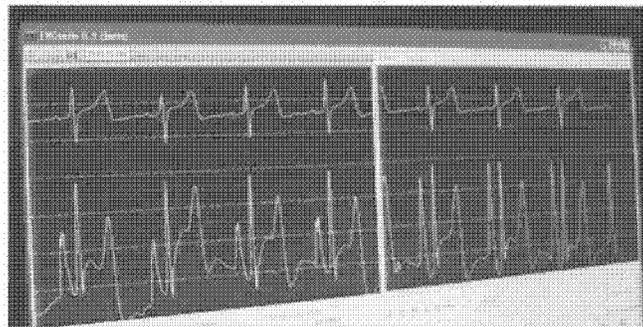


Figure 2 – evGuide TLS Graphical User Interface

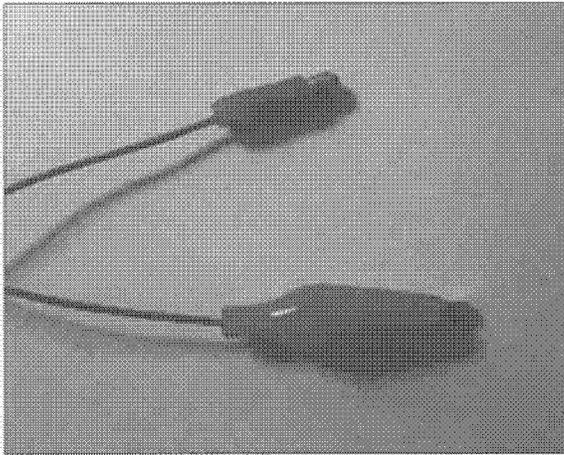


Figure 3 – evGuide TLS Electrical Adaptor

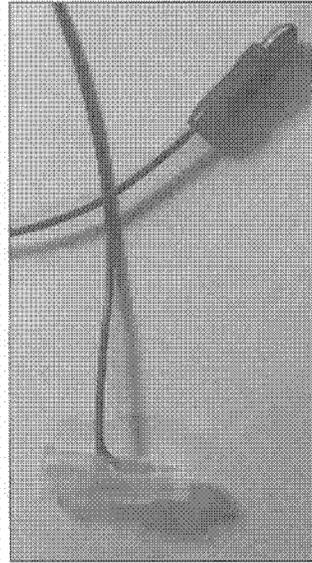


Figure 4 – evGuide TLS Saline Adaptor

IV. Indications for Use (Section 4)

Subject Device K093775

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide™ Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

Predicate Devices K091324 (Bard Access Systems, Sherlock 3CG TPS)

The Sherlock 3CG™ Tip Positioning System (TPS) is indicated for central venous catheter guidance and positioning during catheter placement. The Sherlock 3CG™ TPS provides real time catheter tip location information through the use of passive magnet and cardiac electrical signal detection.

Predicate Devices K032613 (Peter Rothenberg, Transvenous Pacemaker Placement Assist Device)

This device is designed to connect an intravascular electrode to a monitor through a standard EKG patient lead for the purpose of displaying an intravascular signal in real time. Only the black pinjack is "active". The red pinjack is electrically blind, and designed to isolate the proximal electrode from inadvertent stimulation.

Predicate Devices K973371 (B Braun Medical, Conduction Anesthesia Kit – Certodyn)

To aid in the accurate placement of central venous catheters using the RAECG technique.

Predicate Devices K843263 (Teleflex/Arrow International, Arrow-Johans ECG Adaptor)

The adaptor is to be used in the placement of central venous catheters and more accurately diagnosing atrial dysrhythmias.

Discussion: The Subject Device appears to have the same indications for use that were previously cleared for the stated Predicates.

V. Predicate Device Comparison (Section 12 and Appendix A)

Device Name → Manufacturer → 510(k) →	Subject Device: K093775 Romodex International Srl The evGuide™ Tip Location System (TLS)	Predicate Device: K091324 Berd Access Systems Sherlock 3CG TPS	Predicate Device: K032613 Peter Rothenberg Transvenous Pacemaker Placement Assist Device	Predicate Device: K973371 B Braun Medical Conduction Anesthesia Kit - Certodyn	Predicate Device: K843263 Teleflex/Arrow International Arrow-Johans ECG Adaptor
Characteristic ↓					
How does the device locate the tip?	Uses cardiac electrical signal through a guide wire OR a catheter filled with a saline column to determine tip location	Uses cardiac electrical signal and passive magnets to determine the tip location.	Uses cardiac electrical signal through a guide wire to determine the tip location.	Uses cardiac electrical signal through a guide wire to determine the tip location.	Uses cardiac electrical signals through a catheter containing a saline column to determine tip location.
evGuide TLS Electrical Adaptor					
Wire Length	39 in.	32 in.	39 in.	24 in.	No Electrical Lead Wire
Electrical Resistance	10 ohm	N/A	10 ohm	10 ohm	N/A
Materials of Construction (MOC)	<ul style="list-style-type: none"> • PVC insulated stainless steel threaded wire • PVC insulated stainless steel alligator clip • Solder paste • Stainless steel ECG cable connector 	<ul style="list-style-type: none"> • Medical grade Santoprene TPV wire insulation • Copper tinsel wire • Tin coated brass crimp 	<ul style="list-style-type: none"> • Isolated stainless steel threaded wire • Isolated stainless steel alligator clip • Solder paste • Stainless steel ECG cable connector 	<ul style="list-style-type: none"> • Isolated stainless steel threaded wire • Isolated stainless steel grabber • Solder paste • Stainless steel ECG cable connector 	N/A
evGuide TLS Saline Adaptor					
(b)(4)	(b)(4)	(b)(4)			(b)(4)
(b)(4)					(b)(4)
(b)(4)					
(b)(4)	(b)(4)				(b)(4)
evGuide TLS System					
Description of Electronic System and User Interface	<ul style="list-style-type: none"> • User interface running on laptop. ECG data acquisition 	<ul style="list-style-type: none"> • User interface and ECG data acquisition module 	This system does not have an integrated user interface or electronic	This system does not have an integrated user interface or electronic	This system does not have an integrated user interface or electronic

Device Name→ Manufacturer→ 510(k) →	Subject Device: K093775 Romodex International Srl The evGuide™ Tip Location System (TLS)	Predicate Device: K091324 Bard Access Systems Sherlock 3CG TPS	Predicate Device: K032613 Peter Rothenberg Transvenous Pacemaker Placement Assist Device	Predicate Device: K973371 B. Braun Medical Conduction Anesthesia Kit – Certodyn)	Predicate Device: K843263 Teleflex/Arrow International Arrow-Johans ECG Adaptor
Characteristic↓	<p>module is a separate component</p> <ul style="list-style-type: none"> • Standard ECG Cable (non-sterile) • Sterile evGuide electrical or Saline Adaptor connecting ECG cable with CVC in sterile field. • Sterile insertion of CVC to which the evGuide adaptor (electrical or saline) is connected. 	<p>integrated into one module.</p> <ul style="list-style-type: none"> • Also has ultrasound imaging and magnetic tip locator device. • Standard ECG Cable (non-sterile) • Sterile electrical wire connecting detection sensor beneath a sterile drape with CVC in sterile field. • Sterile insertion of CVC to which the sterile electrical wire under a sterile drape. 	<p>data acquisition module. The device is connected to a standard ECG device.</p>	<p>data acquisition module. The device is connected to a standard ECG device.</p>	<p>data acquisition module. The device is connected to a standard ECG device.</p>
Hardware Platform	PC-Based	PC-Based	N/A	N/A	N/A
Printing capability	Yes if printer is connected	Yes if printer is connected	N/A	N/A	N/A

Discussion:

(b)(4)

(b)(4)



VI. 510(k) Summary / 510(k) Statement (Section 5)

The sponsor has provided its 510(k) Summary in Section 5 of the Submission:

		YES	NO	N/A
Required Elements for 510(k) Summary (21 CFR 807.92)				
Clearly labeled "510(k) Summary"		*		
Submitter's name, address, phone #, a contact person		*		
Date the summary was prepared		*		
The name of the device/trade name/common name/classification name		*		
An identification of the legally marketed Predicate		*		
Description of the subject device		*		
Statement of intended use(identical to indications for use)		*		
Technological characteristics	if same, a summary of comparison of technological characters			*
	If different, a summary of how do they compare to the Predicate		*	
Performance Data	Brief discussion of non-clinical data submitted, referenced, or relied on		*	
	Brief discussion of clinical data submitted, referenced, or relied on, including: <ul style="list-style-type: none"> ▪ Description upon whom the device was tested, ▪ Data obtained from the tests and especially: ▪ Adverse events and complications ▪ Other information for SE determination 		*	
	Conclusion that data demonstrate SE	*		
Required Elements for 510(k) Statement (21 CFR 807.93)				

	YES	NO	N/A
Signed verbatim statement			*

Discussion:

(b)(4)



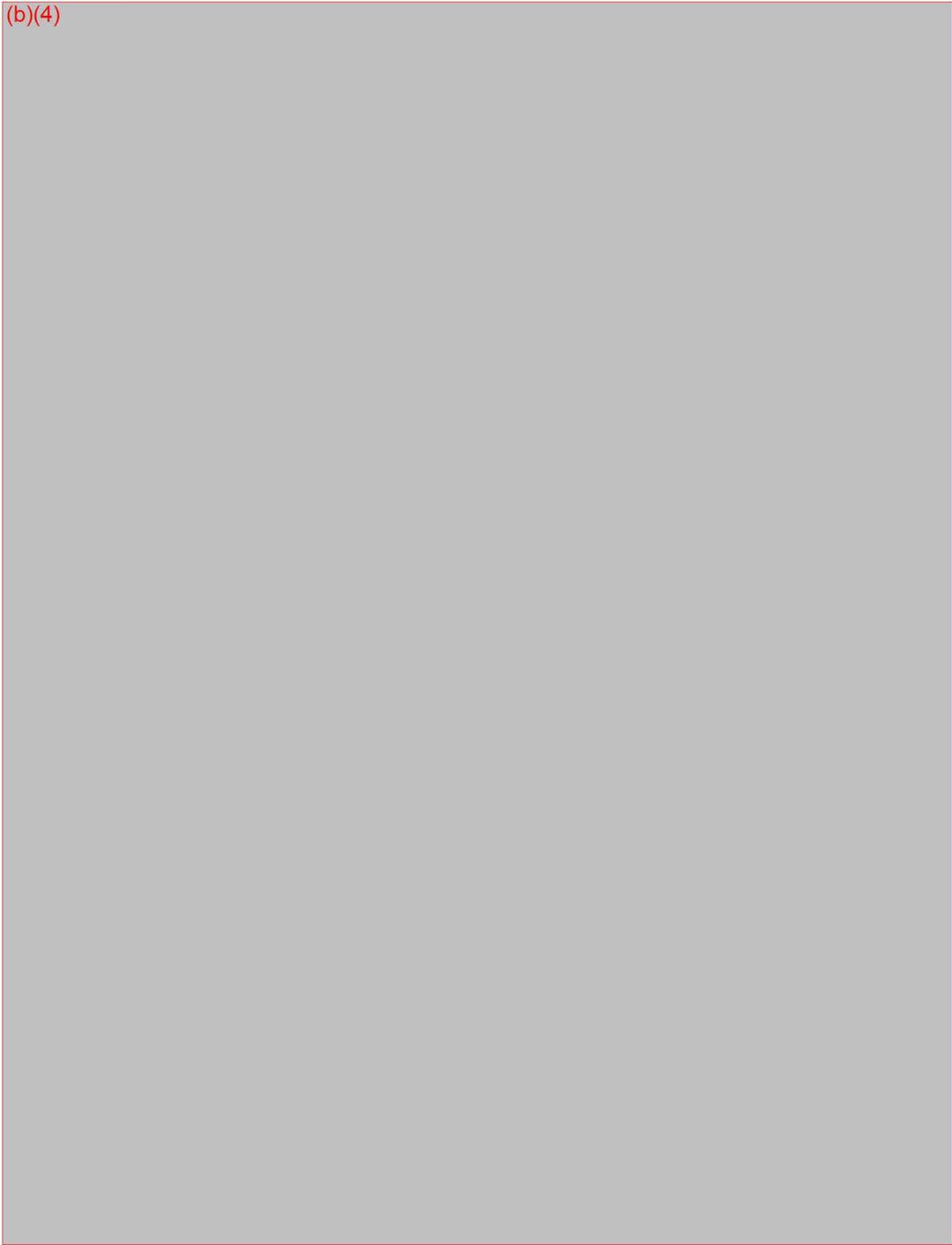
VII. Labeling (Section 13 and Appendix B)

Infusion Pump Guidance Labeling Recommendations	Yes	No
Does the submission contain proposed labels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for use?	*	
Does the labeling describe the intended uses?	*	
Does the labeling include adequate directions for use?	*	
Does the labeling include a prescription statement (21 CFR 801.109)?	*	
Labeling should include a list of device specifications including: reservoir volume, accuracy, residual volume, and the operational conditions (e.g., temperature and pressure) under which these are valid.	*	

Are route(s) of administration described as indicated in the statement of intended use?	*	
Are the fluid(s) to be administered by the device described as indicated in the statement of intended use?	*	
Does the labeling include comprehensive directions for preparation and use for all possible functions of the device?	*	
Does the labeling include a description of all warning and alarm features, and what actions to take for each alarm condition?	*	
MR/CT/X-ray warnings?		*

Discussion:

(b)(4)



(b)(4)

3. (b)(4)

VIII. Sterilization/Shelf Life/Reuse (Section 14 and Appendix K)

	(b)(4)	
(b)(4)		
	(b)(4)	
		(b)(4)
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	(b)(4)	
(b)(4)	(b)(4)	

Discussion:

(b)(4)



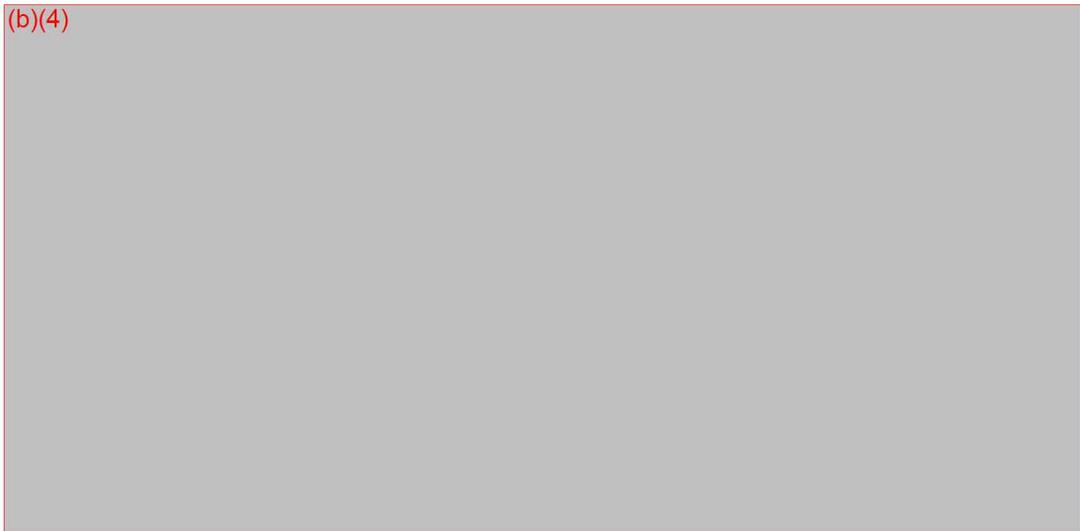
(b)(4)



IX. **Biocompatibility (Section 15)**

Discussion:

(b)(4)



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X. **Software (Section 14 and Appendices C & G)**

(b)(4)

Design Specifications: Appendix C	*	
Traceability Analysis/Matrix: Appendix G	*	
Development: Appendix C	*	
Verification & Validation Testing: Appendix G	*	
Revision level history: Section 16.3	*	
Unresolved anomalies: Sponsor states that there are No unresolved anomalies (Section 16.10)	*	

Discussion:

I consulted Mr. Lenning Shen, Software Engineer on December 30, 2009. Mr. Shen's, March 2, 2010, response to this consult identified concerns regarding the software testing performed on the device. A copy of this consult has been included at the end of this memorandum. Based on the consult, there were no software deficiencies identified.

XI. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety (Section 17 and Appendix D)

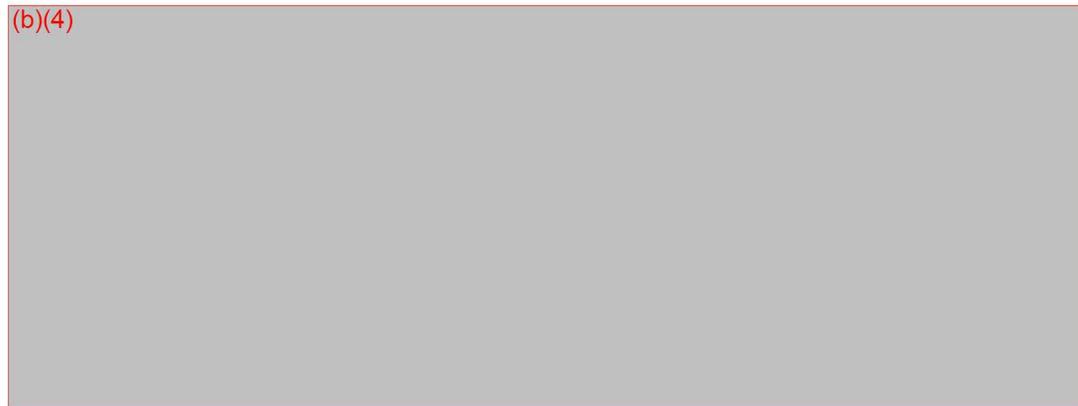
Discussion:

(b)(4)



XII. Performance Testing - Bench

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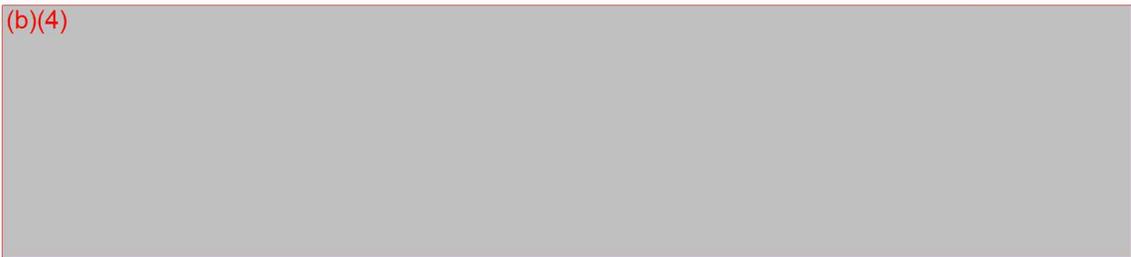


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XIII. Performance Testing - Human Factors

(b)(4)



328

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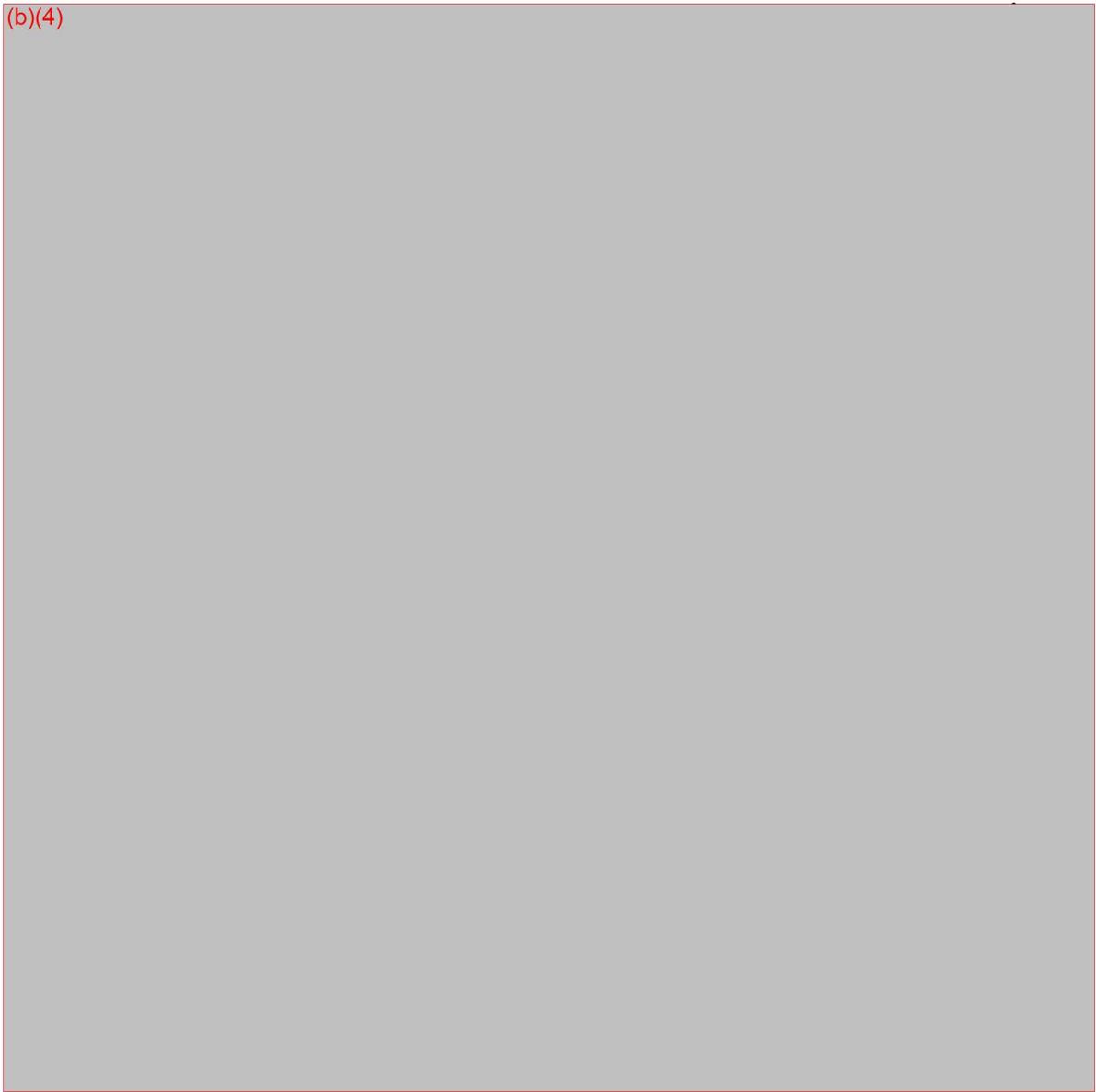
XIV. Performance Testing – Animal

(b)(4)



XV. Performance Testing – Clinical

(b)(4)



3. (b)(4)



XVI. Substantial Equivalence Discussion

	Yes	No	
1. Same Indication Statement?	✘		If YES = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If YES = Stop NSE
3. Same Technological Characteristics?	✘		If YES = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?			If YES = Go To 6
5. Descriptive Characteristics Precise Enough?		✘	If NO = Go To 8 If YES = Stop SE
6. New Types Of Safety Or Effectiveness Questions?			If YES = Stop NSE
7. Accepted Scientific Methods Exist?			If NO = Stop NSE
8. Performance Data Available?		✘	If NO = Request Data
9. Data Demonstrate Equivalence?			Final Decision: SE

Note: See

http://erom.fda.gov/eRoomReg/Files/CDRH3/CDRHPreMarketNotification510kProgram/0_4148/FLOWCHART%20DECISION%20TREE%20.DOC for Flowchart to assist in decision-making process. Please complete the following table and answer the corresponding questions. "Yes" responses to questions 2, 4, 6, and 9, and every "no" response requires an explanation.

1. Explain how the new indication differs from the predicate device's indication:
2. Explain why there is or is not a new effect or safety or effectiveness issue:
3. Describe the new technological characteristics:
4. Explain how new characteristics could or could not affect safety or effectiveness:
5. Explain how descriptive characteristics are not precise enough:
There are several concerns regarding the firm's labeling, performance testing, and sterilization methodology that could not be clarified based on the information provided in the submission.
6. Explain new types of safety or effectiveness question(s) raised or why the question(s) are not new:
7. Explain why existing scientific methods can not be used:
8. Explain what performance data is needed:
The information that I've requested regarding performance data, rationale behind some data, and other supporting information is identified in Section XVII of this memo, titled *Deficiencies*.
9. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

This question cannot be answered until the firm provides the information requested in Section XVI of this memo, titled *Deficiencies*.

XVII. Deficiencies

510(k) Summary / 510(k) Statement

1. *FDA conducts a comprehensive review of the 510(k) Summary in accordance with 21 CFR 807.92 and the Required Elements for 510(k) Statements in accordance with 21 CFR 807.93. Based on our assessment of your 510(k) Summary in Section 5 of your submission, FDA believes that your Summary does not meet the regulation. Please address the following concerns regarding your 510(k) summary:*
 - a. *Please include a summary comparing the technological modifications made to your device as it relates to your predicate devices.*
 - b. *Please include a summary of the non-clinical testing data that was submitted, referenced or relied on to demonstrate that the Subject Device is safe and effective, and whose performance meets the requirements of its pre-defined acceptance criteria and intended uses.*
 - c. *Please include a summary of the clinical data that was submitted, referenced or relied on, including:*
 - i. *Description upon whom the device was tested*
 - ii. *Data obtained from the tests and especially*
 - iii. *Adverse events and complications*
 - iv. *Other information for SE determination*

Labeling

(b)(4)



(b)(4)



Sterilization/Shelf Life/Reuse

(b)(4)



(b)(4)



Biocompatibility

(b)(4)



(b)(4)

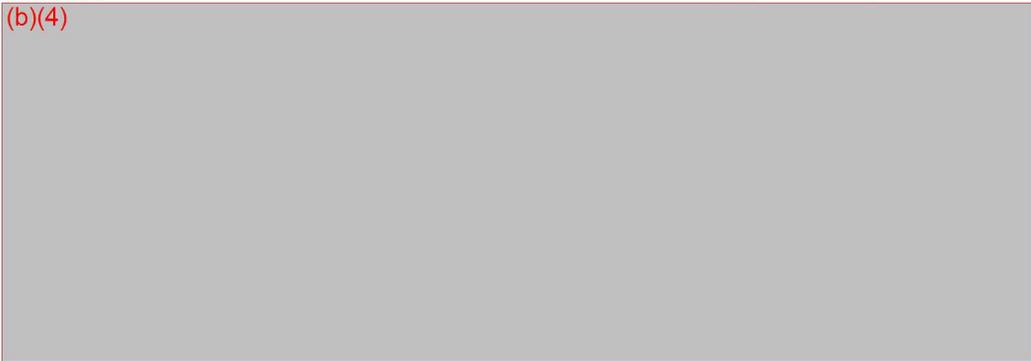


(b)(4)



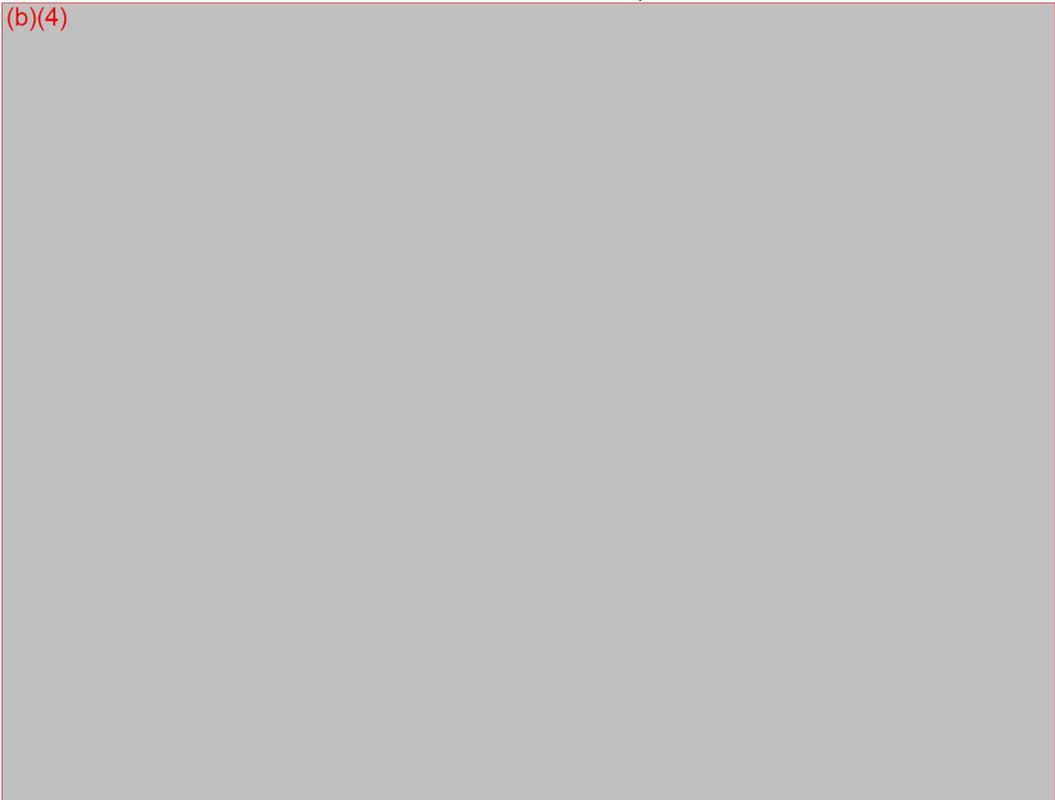
Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

(b)(4)



Performance Testing - Bench

(b)(4)

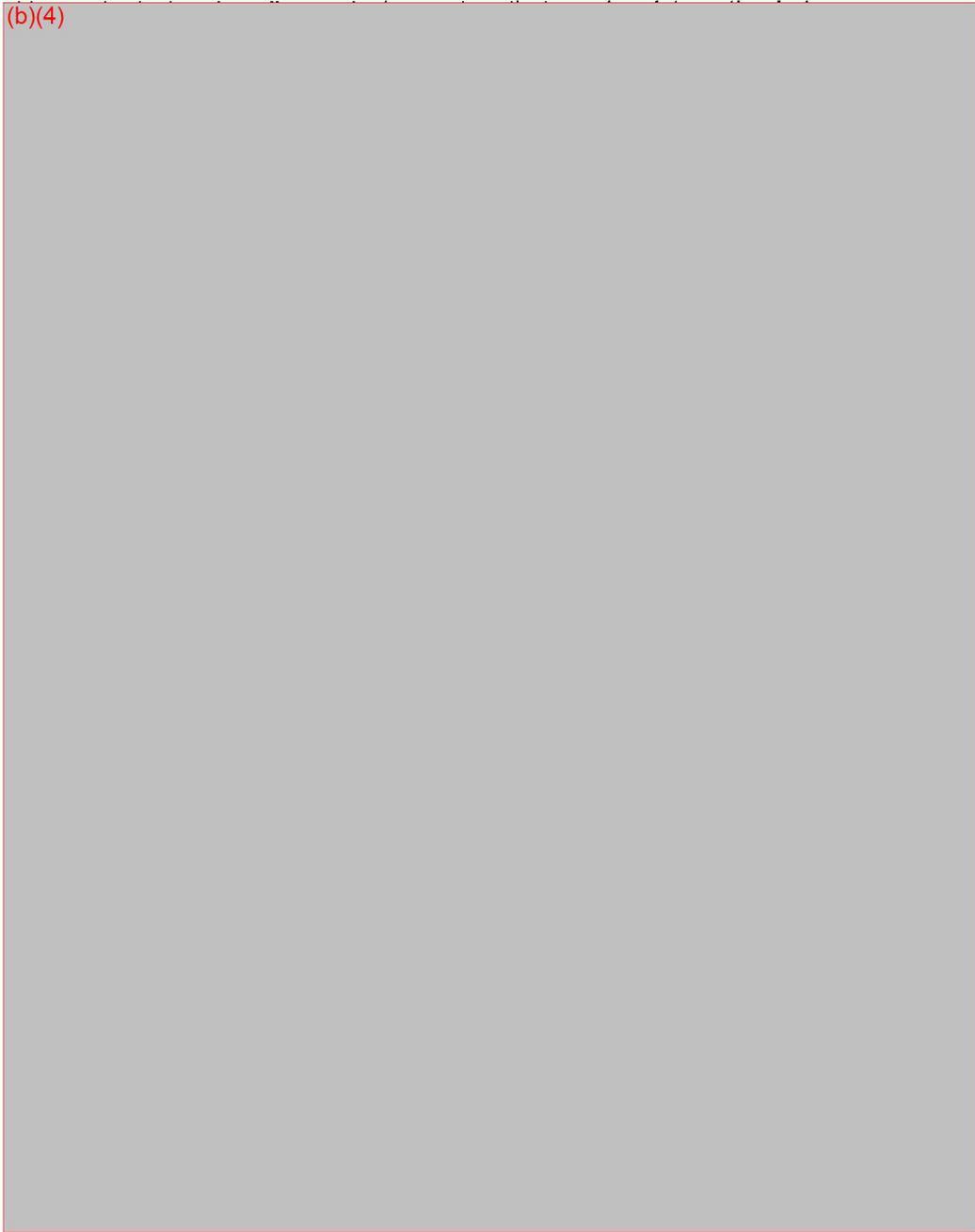


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Performance Testing – Human Factors

(b)(4)

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(b)(4)

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Performance Testing – Animal & Clinical

(b)(4)

A large rectangular area of the document is redacted with a solid grey fill. This redaction covers the entire middle and lower half of the page, including the section header.

XVIII. Contact History

**XIX. Recommendation EMAIL HOLD
Substantially Equivalent to**

Regulation Number:
Regulation Name:
Regulatory Class:
Product Code:



Reviewer

3/3/2010
Date

 for Chip Zimliski

Branch Chief

3/3/10
Date

Thakur, Nikhil

From: Thakur, Nikhil
Sent: Wednesday, March 03, 2010 8:30 PM
To: 'sorin@romedex.com'
Cc: Stevens, Alan M; Zimliki, Charles L* (CDRH)
Subject: K093775: Email Hold

Dear Mr. Grunwald,

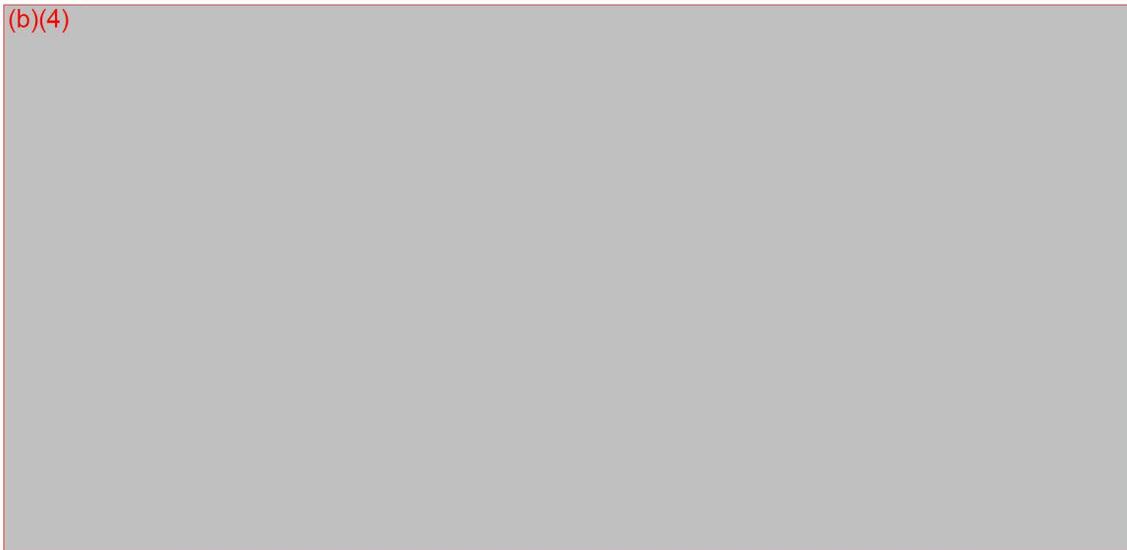
We have reviewed your 510(k) submission regarding the evGuide Tip Location System (Subject Device). We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, we require the following additional information:

510(k) Summary / 510(k) Statement

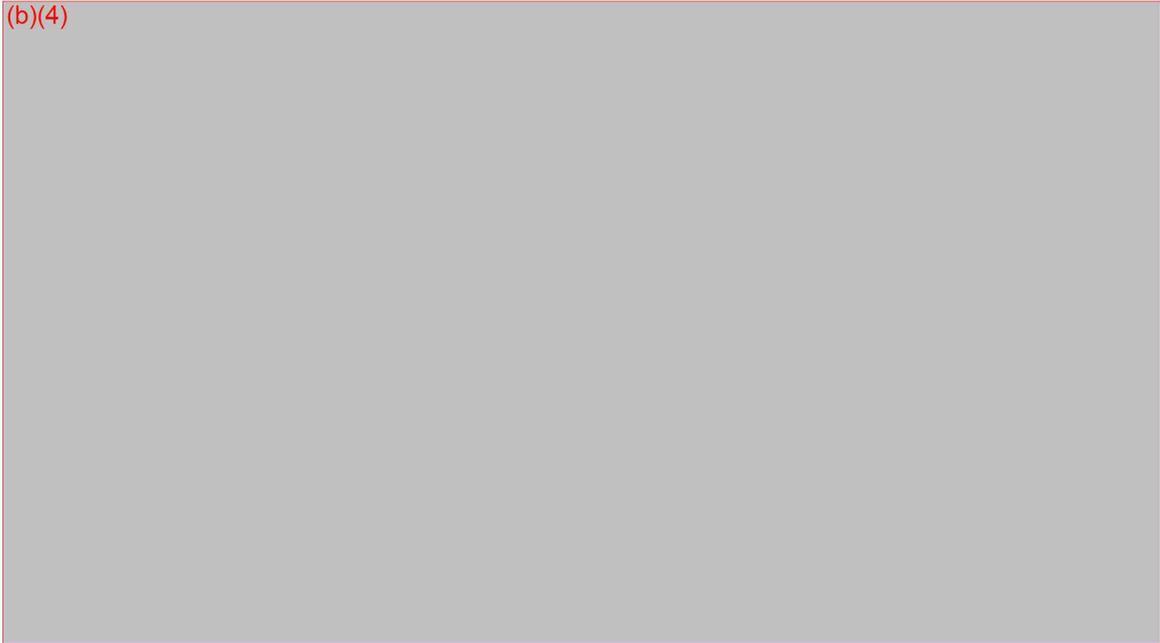
1. *FDA conducts a comprehensive review of the 510(k) Summary in accordance with 21 CFR 807.92 and the Required Elements for 510(k) Statements in accordance with 21 CFR 807.93. Based on our assessment of your 510(k) Summary in Section 5 of your submission, FDA believes that your Summary does not meet the regulation. Please address the following concerns regarding your 510(k) summary:*
 - a. *Please include a summary comparing the technological modifications made to your device as it relates to your predicate devices.*
 - b. *Please include a summary of the non-clinical testing data that was submitted, referenced or relied on to demonstrate that the Subject Device is safe and effective, and whose performance meets the requirements of its pre-defined acceptance criteria and intended uses.*
 - c. *Please include a summary of the clinical data that was submitted, referenced or relied on, including:*
 - i. *Description upon whom the device was tested*
 - ii. *Data obtained from the tests and especially*
 - iii. *Adverse events and complications*
 - iv. *Other information for SE determination*

Labeling

(b)(4)

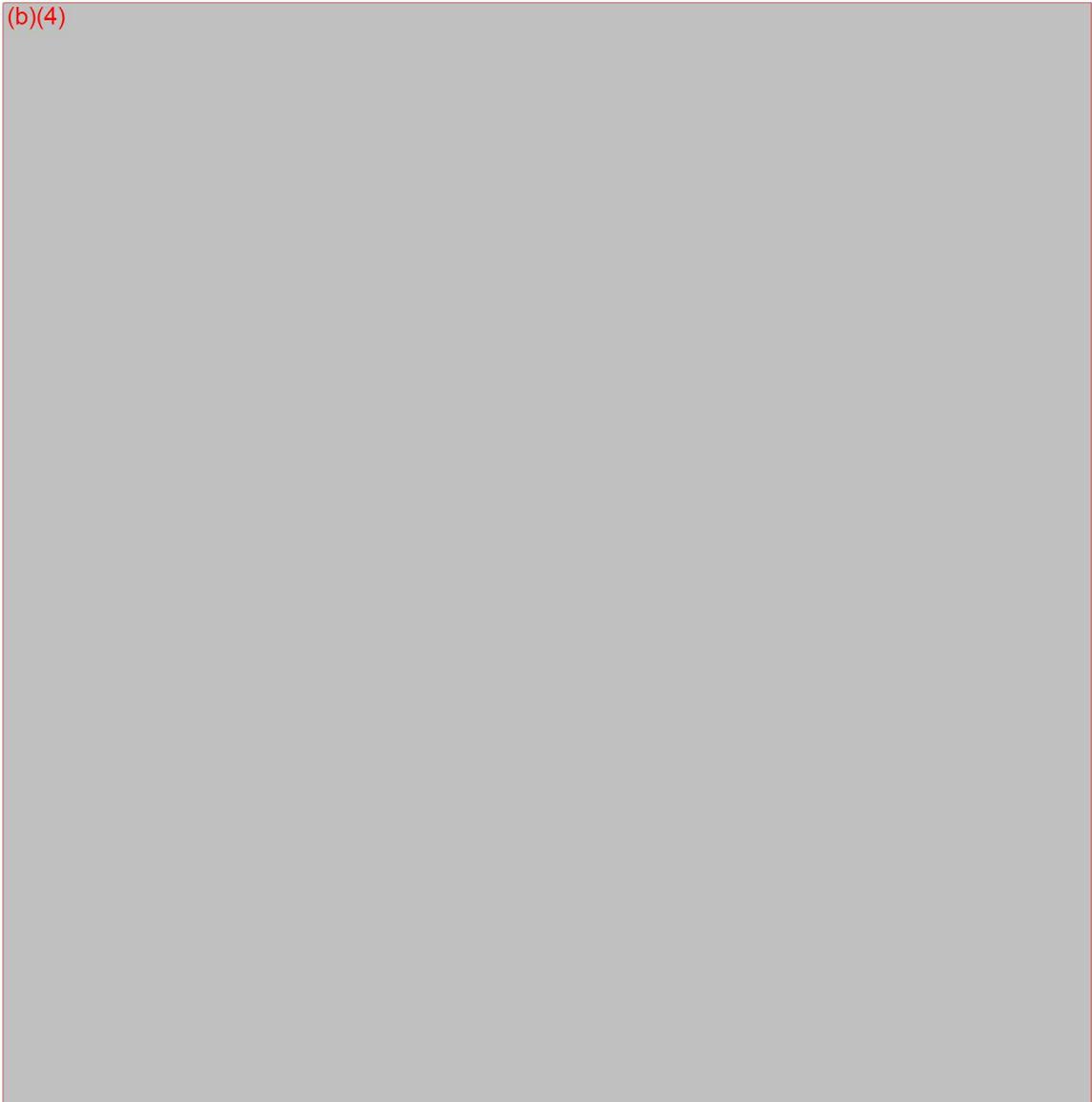


(b)(4)



Sterilization/Shelf Life/Reuse

(b)(4)

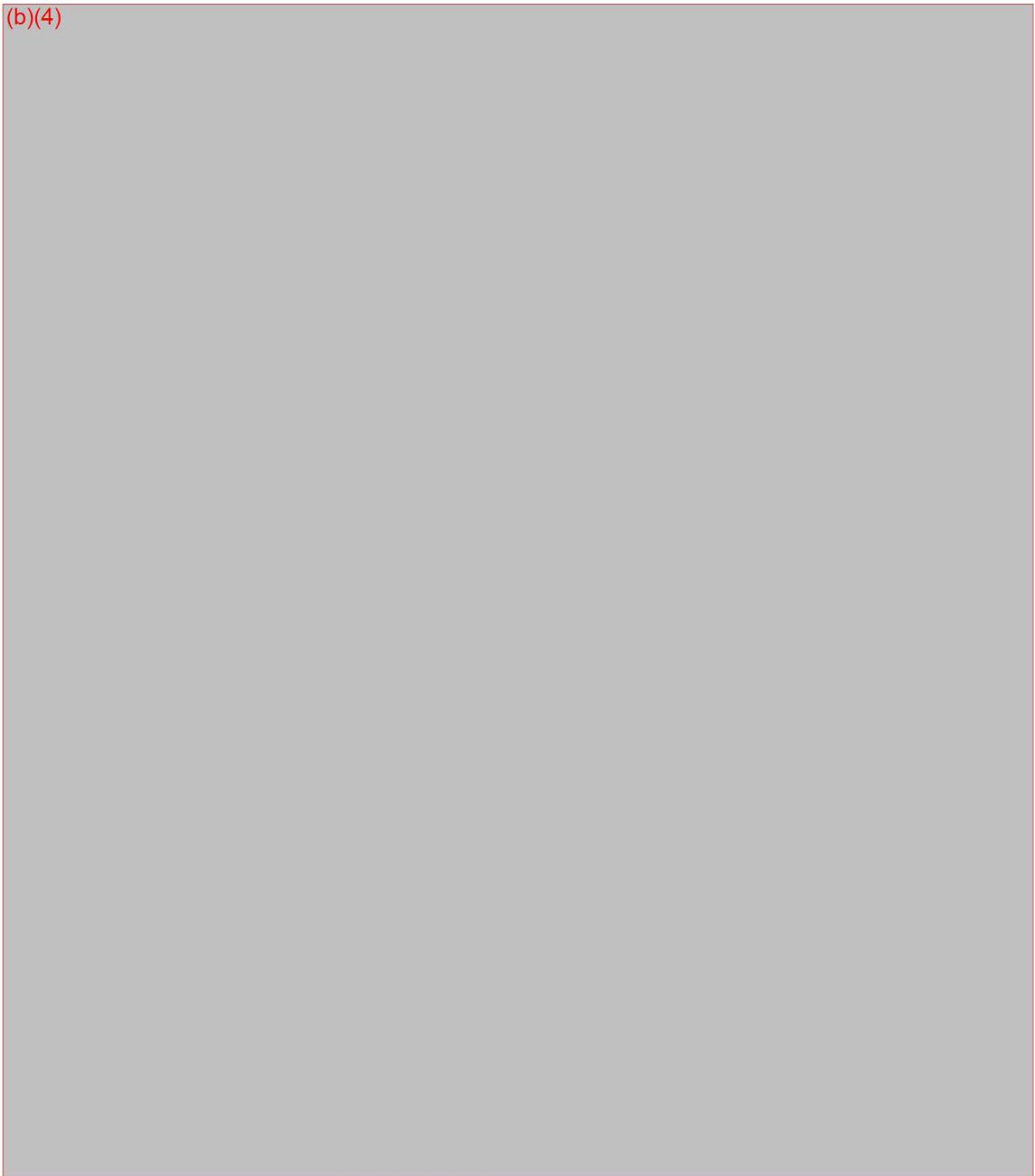


(b)(4)

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Biocompatibility

(b)(4)

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(b)(4)



(b)(4)

Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

(b)(4)

Performance Testing - Bench

(b)(4)

Performance Testing – Human Factors

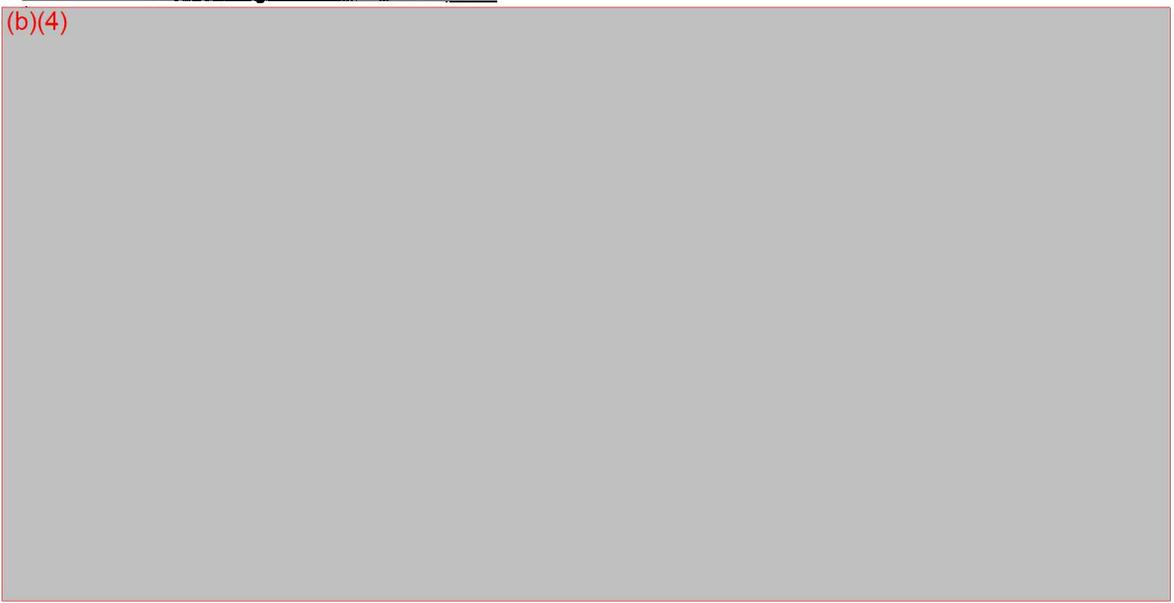
(b)(4)

(b)(4)

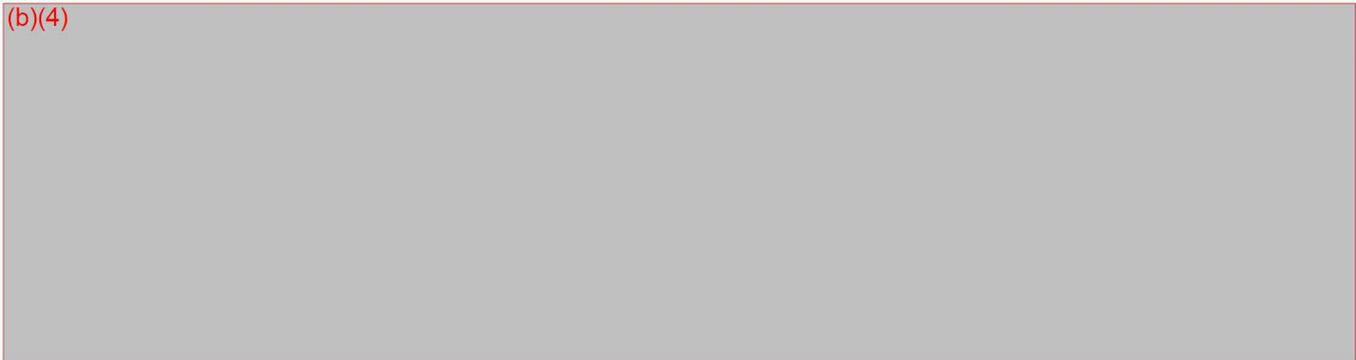
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Performance Testing – Animal & Clinical

(b)(4)

A rectangular area below the section header is redacted with a solid grey fill. This redaction covers the text under the 'Performance Testing – Animal & Clinical' heading.

(b)(4)



Review of your 510(k) will be placed on hold until your response to the above deficiencies is received. Please submit your response to the CDRH Document Mail Center at the following address:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Please feel free to contact me with any questions.

Sincerely,
Nikhil

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
Silver Spring, MD 20993

Telephone: (301) 796 - 5536
Fax: (301) 847 - 8109

This e-mail message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information. If you are not the intended recipient, any dissemination, distribution or copying is strictly prohibited. If you think you have received this e-mail message in error, please e-mail the sender immediately at nikhil.thakur@fda.hhs.gov.

MEMORANDUM

Date: January 25, 2010

To: Mr. Nikhil Thakur, GHDB, DAGID

From: Rakhi Dalal, Ph.D.
Toxicologist, INCB, DAGID

CC: Ms. Elizabeth F. Claverie., Acting Branch Chief, INCB, DAGID
Charles L. Zimliki, Ph.D., Acting Branch Chief, GHDB, DAGID

Re: 510K number: K093775

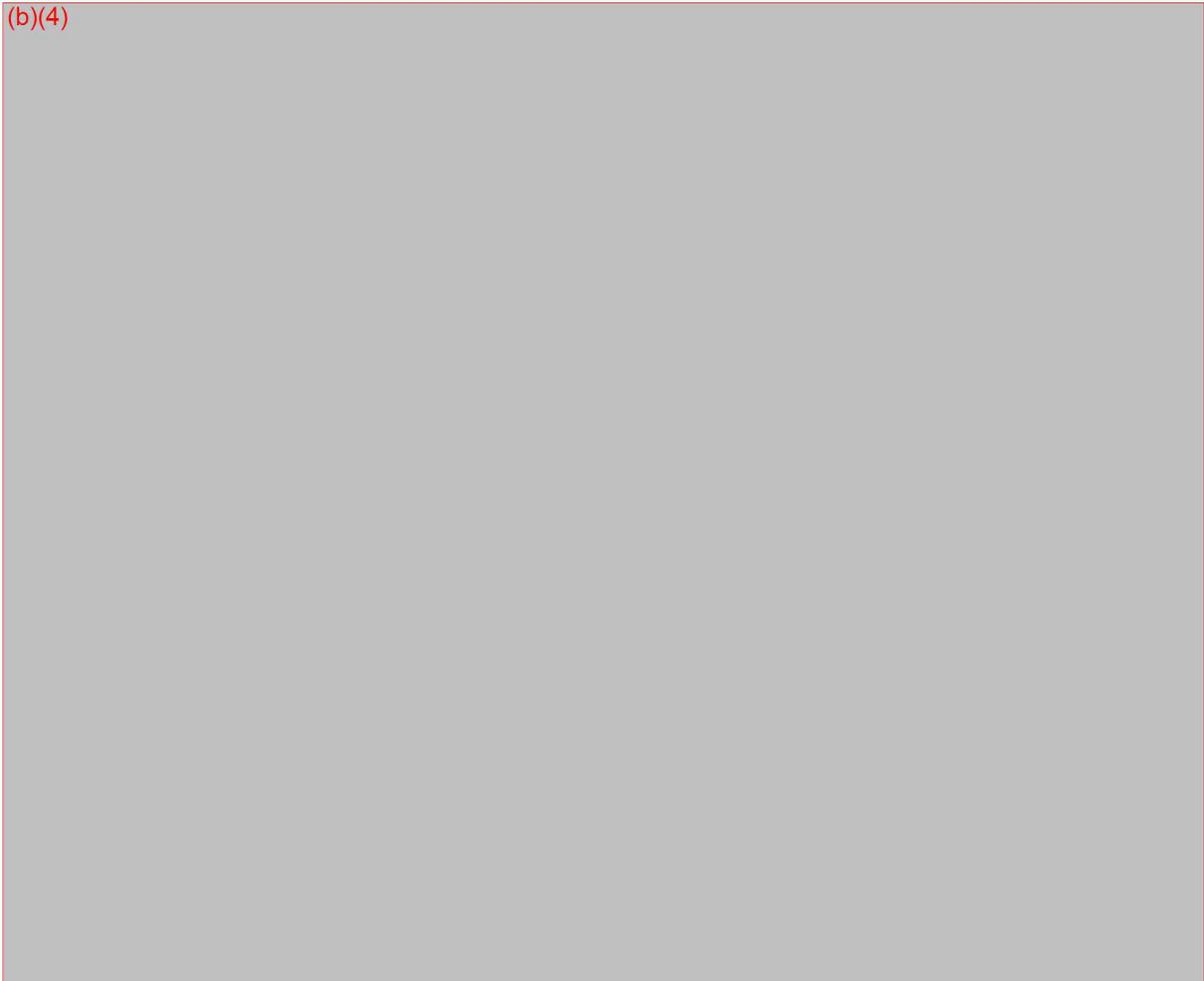
Trade Name: evGuide™ Tip Location System (TLS) also known as Sapiens™ Tip Location System (TLS)

Sponsor: Romedex International Srl
58 Aleea Arubium
Bucharest, 022944, Romania


1/26/10

Recommendation: AI, Please see the recommended deficiency.

(b)(4)



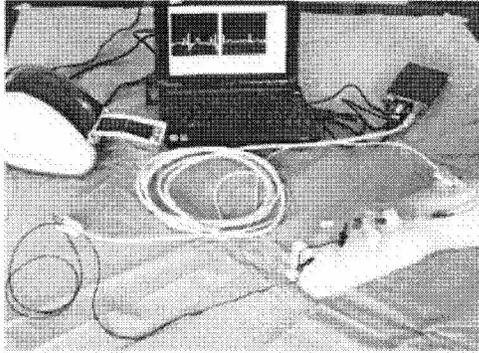


Figure 11.3 evGuide TLS system configuration

During the catheter placement procedure, one or several electrodes (7, on model hand) are connected to the patient's skin using non-sterile off-the-shelf electrodes and the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the patient's central veins per the institution's guidelines, an evGuide TLS adaptor either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. The sterile evGuide TLS adaptor transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (Figure 11.4) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated in Section 11.1 example, the user can estimate the location of the catheter tip. The construction and functionality of evGuide TLS is viewed by sponsor as substantially equivalent to "Sherlock 3CG" manufactured by Bard Access Systems (K091324).

Saline adaptor description:

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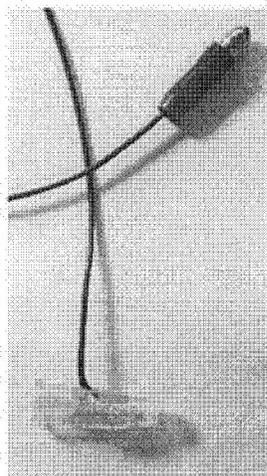


Figure 11.5 evGuide TLS Saline Adaptor

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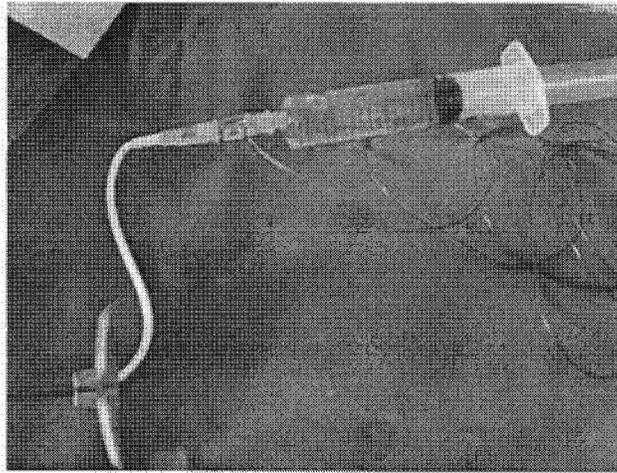


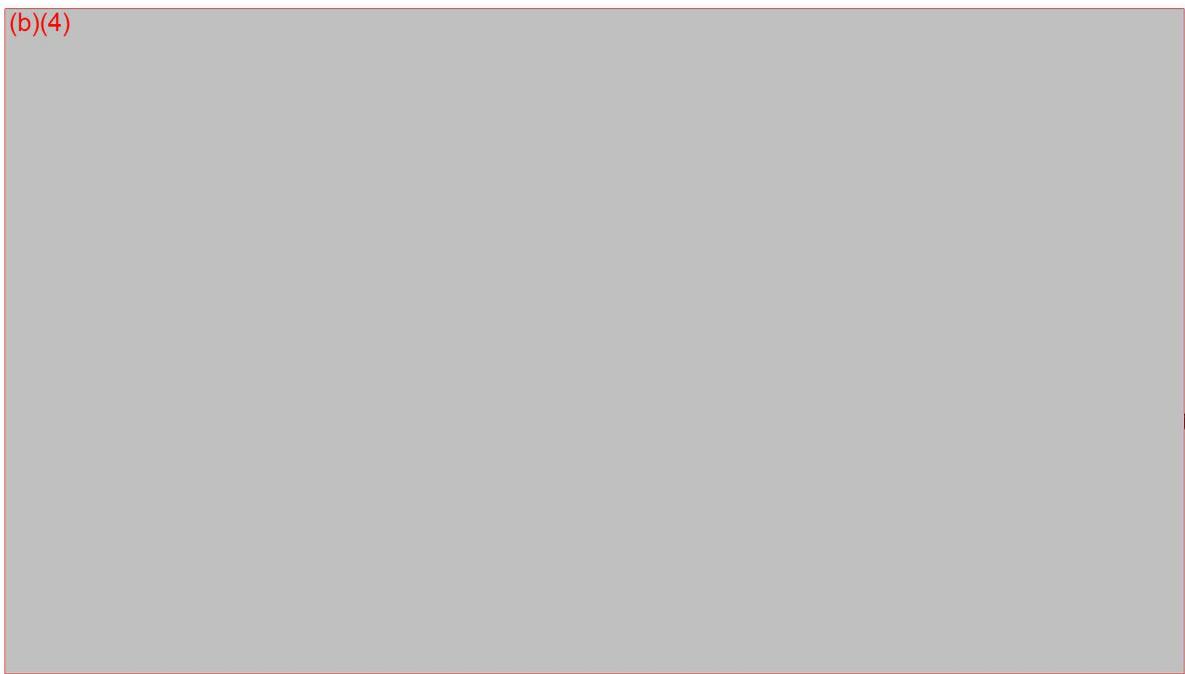
Figure 11.6 evGuide TLS Saline Adaptor in clinical use

(b)(4)



Figure 11.7: evGuide Saline Adaptor – Detail

(b)(4)



1.

(b)(4)



2. (b)(4)

3.

(b)(4)



End of review.

MEMO OF SOFTWARE REVIEW

510(K): K093775 / CON015119

FROM: Lening Shen, Software Engineer (CDRH General Hospital Devices Branch), 301-796-6291, lening.shen@fda.hhs.gov

TO: Nikhil Thakur (ODE/DAGID/GHDB)

DATE: Thursday, January 25, 2010

SUBJECT: Software Review of **evGUIDE TIP LOCATION SYSTEM**

General description of device:

When a central venous catheter or its associated stylet is connected to the evGuide TLS system via the evGuide TLS Saline or Electrical Adaptors, the evGuide TLS PC/Laptop screen displays cardiac electric or endovascular ECG signals acquired at the location of the tip of the catheter. The waveforms provided by evGuide TLS can be used for guiding the placement of the central venous catheter. The evGuide TLS must be used in accordance to the evGuide TLS User's Manual and the Instructions for Use. The central venous catheter must be used in accordance to the manufacturer's Instructions for Use.

The evGuide TLS consists of the following elements seen in the Figure 11.3:

1. Sterile evGuide TLS Electrical Adaptor (6)
2. Sterile evGuide TLS Saline Adaptor
3. Skin ECG electrodes (supplied by user) (7)
4. evGuide TLS ECG module (1)
5. ECG cable (5)
6. PC/Laptop running evGuide TLS software (2)
7. USB connection cable to the cardiac electrical signal (ECG) module (3)
8. Label printer (optional) (4)

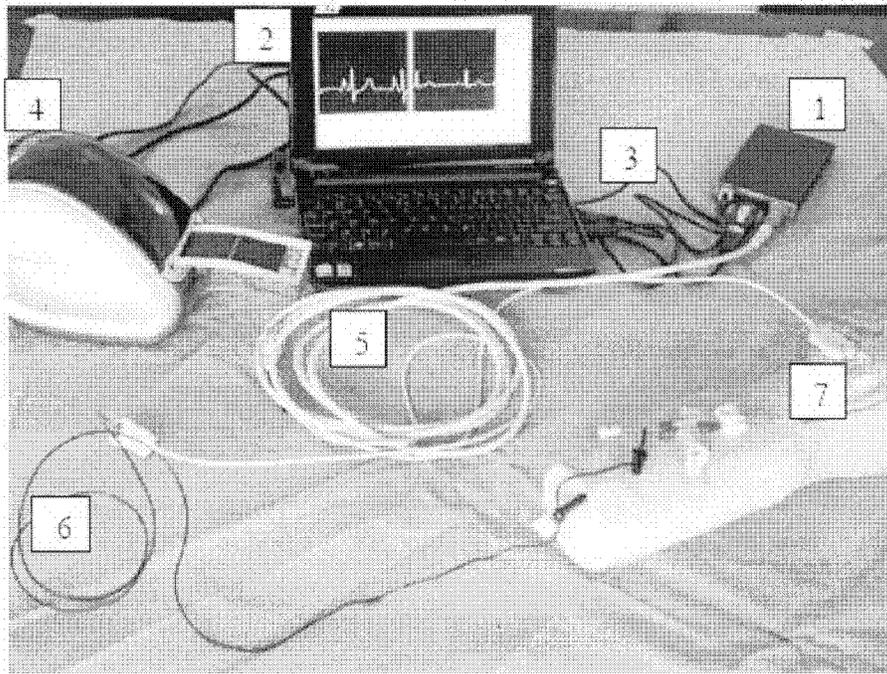
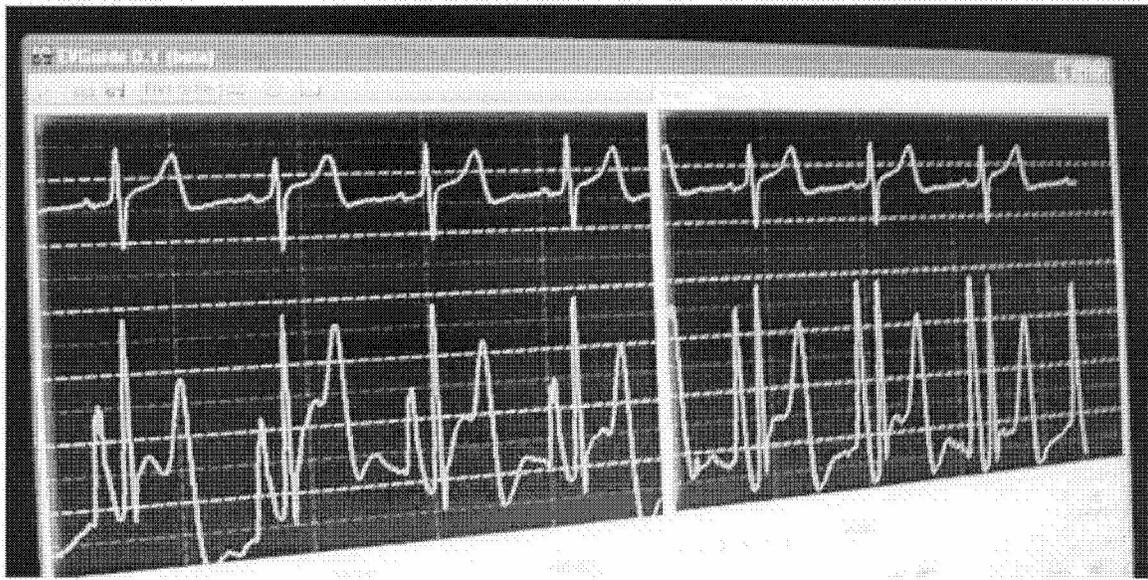


Figure 11.3 evGuide TLS system configuration

During the catheter placement procedure, one or several electrodes (7) are connected to the patient's skin using non-sterile off-the-shelf electrodes and the standard ECG cable (5) provided with the evGuide system. The ECG cable is connected to the ECG module (1) outside the sterile field. After a commercially available central venous catheter has been inserted in the patient's central veins per the institution's guidelines, an evGuide TLS adaptor either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. The sterile evGuide TLS adaptor transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable (3) to the laptop (2) running the evGuide TLS application software. An optional printer (4) can be connected to the laptop in order to document placement procedure results. During the case, the laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen (Figure 11.4) endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes illustrated below, the user can estimate the location of the catheter tip. For example, in the Figure 11.4 the yellow waveform on the right hand side of the screen is representative of a location very close to the sino-atrial node (the pacemaker of the heart) and the yellow waveform on the left hand side of the screen shows a waveform representative of the lower third of the superior vena cava. The white waveforms on both screens shows the skin ECG signal used for comparison.



Indications for Use:

The evGuide™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters during insertion and placement. The evGuide Tip Location System provides real-time catheter tip location information by using the patient's cardiac electrical activity.

Software Consultation (including Description, Comments, Deficiencies):

(b)(4)



(b)(4)

Deficiency to the Sponsor

None.



3/2/10

Lening Shen, General Engineer
General Hospital Devices Branch
Division of Anesthesiology, General Hospital, Infection Control, and Dental Devices
Center for Devices and Radiological Health
U.S. Food and Drug Administration
Tel: (301) 796-6291
Fax: (301) 796-8109

Syed, Sajjad H

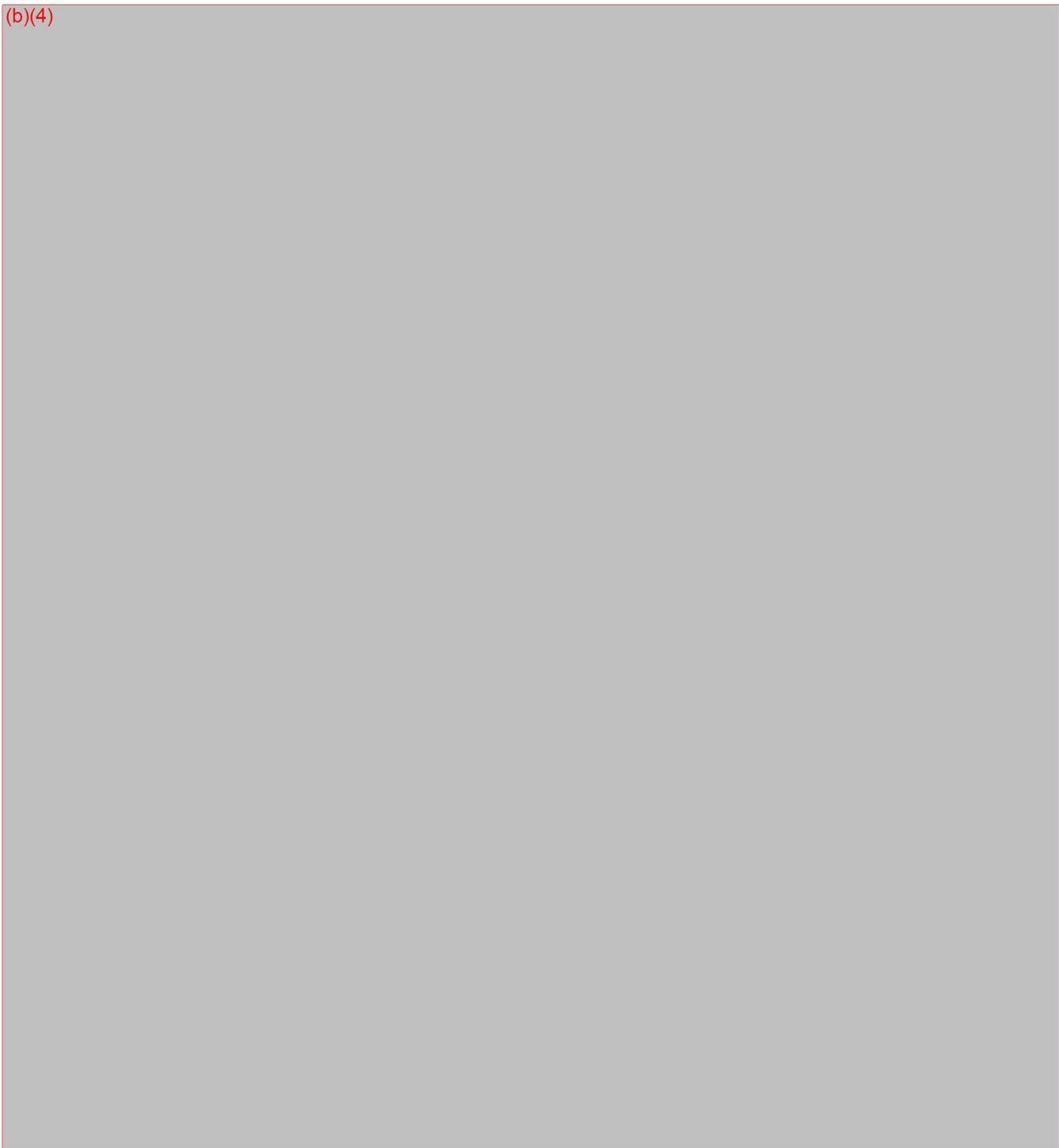
From: Syed, Sajjad H

Sent: Wednesday, February 03, 2010 4:29 PM

To: Thakur, Nikhil

Subject: RE: K093775 - Romodex International, Tip Location System

(b)(4)



Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
Silver Spring, MD 20993

Telephone: (301) 796 - 5536
Fax: (301) 847 - 8109

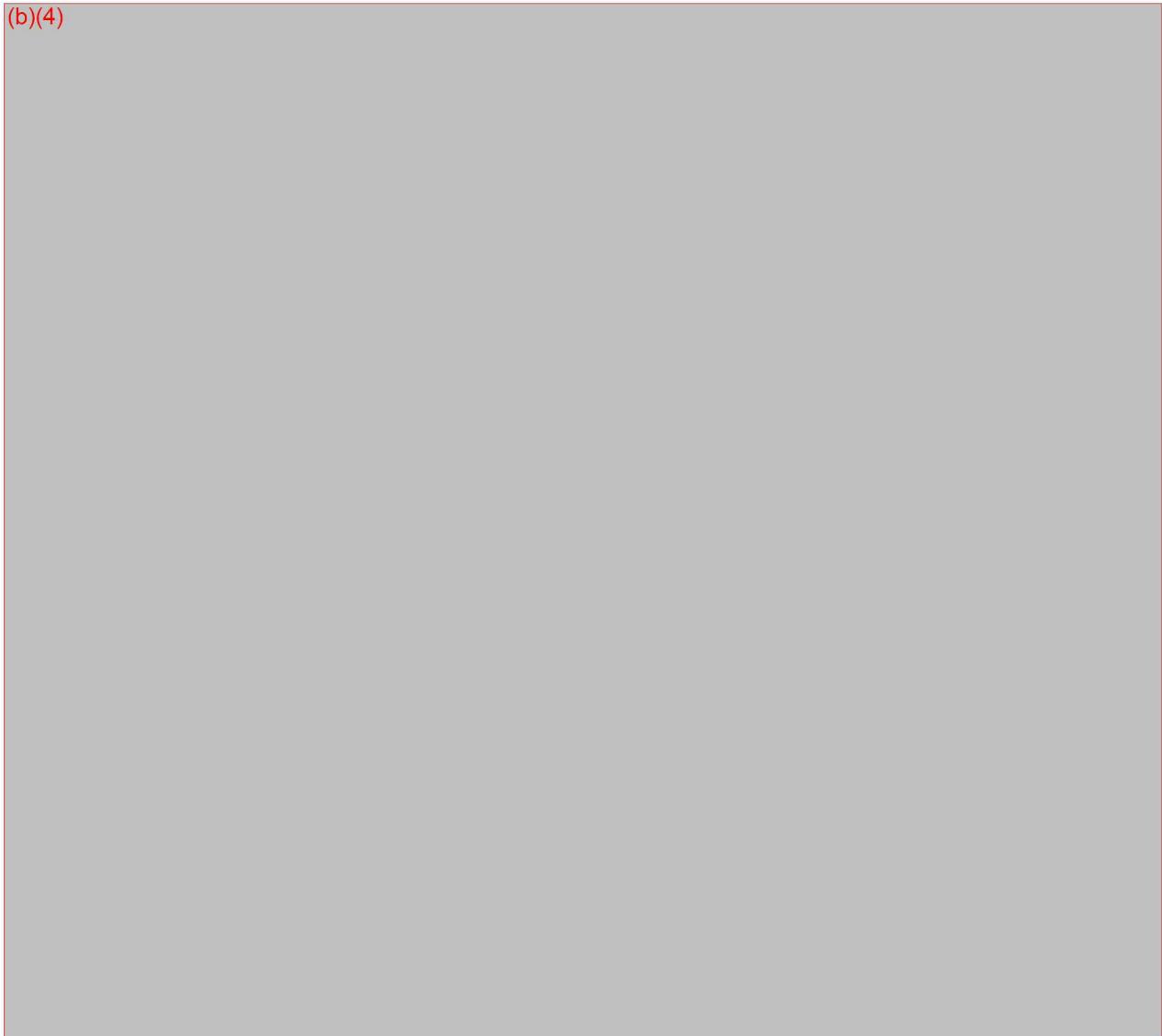
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Human Factors Review

Name of the Device: Vasular access catheter accessories
Device Premarket Path: K093775
ODE Coordinator: Nikhil Thakur
Applicant: Romedex International Srl
Kind of Device: Vascular access catheter accessories
Date sent: 1/26/2010
Consult: 0915120
Reviewer: Ron Kaye *[Signature]* For Ron KAYE 3/3/2010

Conclusions

(b)(4)



Recommendations

(b)(4)



Overview of the System

(b)(4)

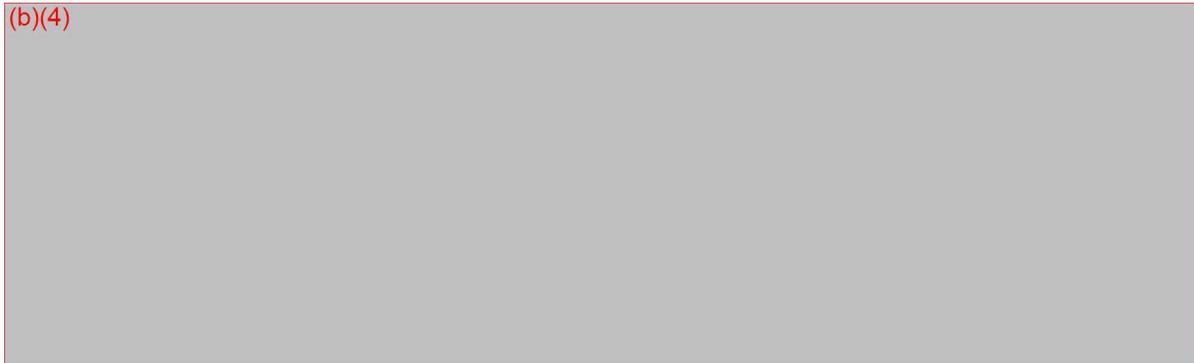


(b)(4)



Materials Reviewed

(b)(4)



End of Review

Thakur, Nikhil

From: Thakur, Nikhil
Sent: Tuesday, March 02, 2010 12:49 PM
To: Kaye, Ron D.
Subject: Romedex HF review K093775

Attachments: RomedexK093775rdk.doc

Hi Ron,

You had provided the following consult to me a while ago. I seemed to have misplaced the signed copy of your consult. Can you please give me another signed copy? Thank you.

Sincerely,
Nikhil

Nikhil Thakur
LCDR, USPHS

Reviewer

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:

10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
Silver Spring, MD 20993

Telephone: (301) 796 - 5536

Fax: (301) 847 - 8109

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From: Kaye, Ron D.
Sent: Tuesday, January 26, 2010 11:37 AM
To: Thakur, Nikhil
Subject: Romedex HF review K093775



RomedexK093775r
dk.doc (62 KB)

Hi Nikhil,

Let me know if you have any questions. Will give you a signed copy tomorrow.

Thanks,
Ron Kaye

Human Factors and Device Use-Safety Team Leader
FDA/CDRH/ODE/DAGID
301.796.6289

Samuels-Reid, Joy H.

From: Samuels-Reid, Joy H.
Sent: Wednesday, January 27, 2010 4:32 PM
To: Thakur, Nikhil
Subject: evGuide

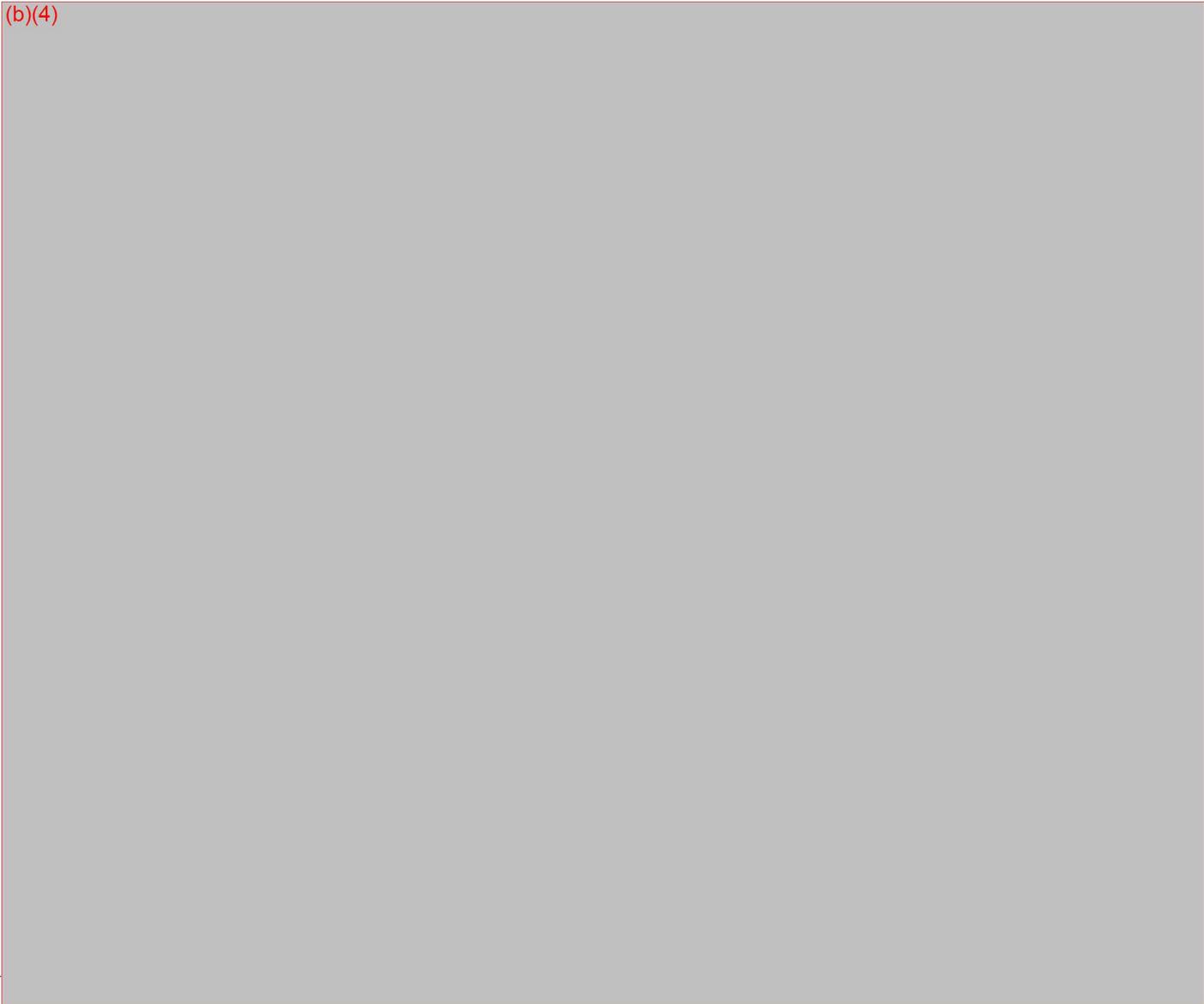
To: LCDR Nikhil Thakur

From: Joy Samuels-Reid, M.D.

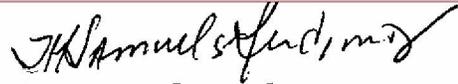
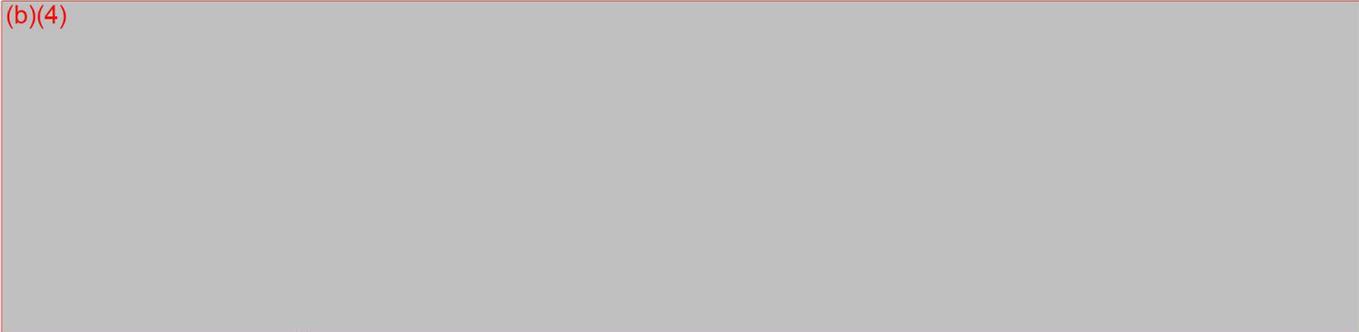
Date: January 27, 2010

Re: K093775 – evGUIDE Tip Location System

(b)(4)



(b)(4)



Joy Samuels-Reid, M.D., FAAP

Chief Medical Officer,

Division of Anesthesiology, General Hospital,

Infection Control and Dental Devices

Center for Devices and Radiological Health

US Food and Drug Administration

Office of Device Evaluation-White Oak - Bldg 66-2608

10903 New Hampshire Avenue, Silver Spring,

Maryland, 20993

Tel: 301-796-5580

Fax: 301-847-8109

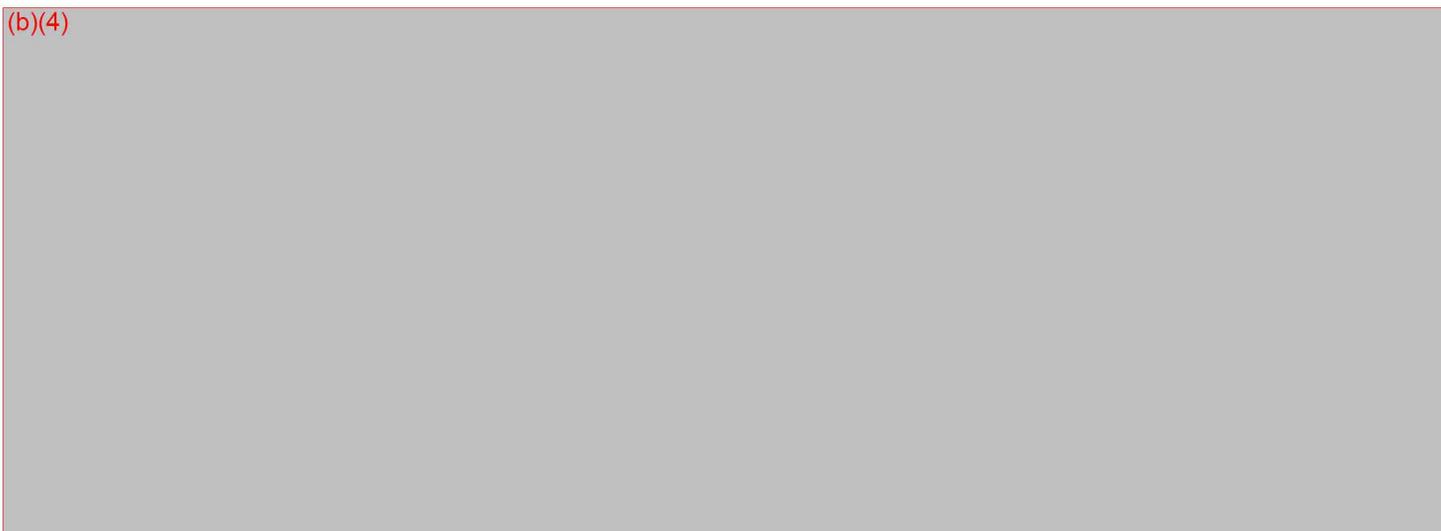
Joy.Samuels-Reid@fda.hhs.gov

Thakur, Nikhil

From: Samuels-Reid, Joy H.
Sent: Wednesday, March 03, 2010 8:16 AM
To: Thakur, Nikhil
Subject: RE: Consult for K093775, Romodex evGuide Tip Location System

Nikhil,

(b)(4)

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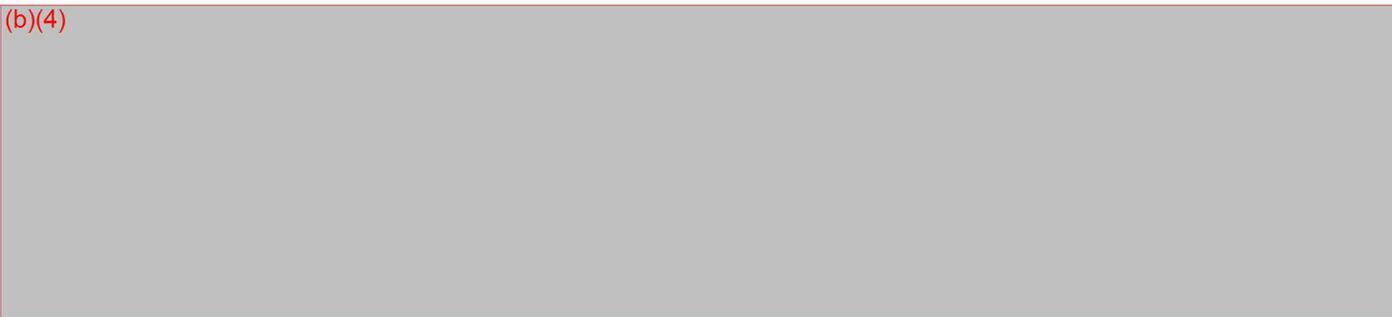
Joy

Joy Samuels-Reid, M.D.
CDRH/ODE/DAGID
Tel: 301-796-6266

From: Thakur, Nikhil
Sent: Tuesday, March 02, 2010 9:25 AM
To: Samuels-Reid, Joy H.
Subject: Consult for K093775, Romodex evGuide Tip Location System

Hi Joy,

(b)(4)

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Thank you.

3/3/2010

366

Sincerely,
Nikhil

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
Silver Spring, MD 20993

Telephone: (301) 796 - 5536
Fax: (301) 847 - 8109

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From: Samuels-Reid, Joy H.
Sent: Wednesday, January 27, 2010 4:32 PM
To: Thakur, Nikhil
Subject: evGuide

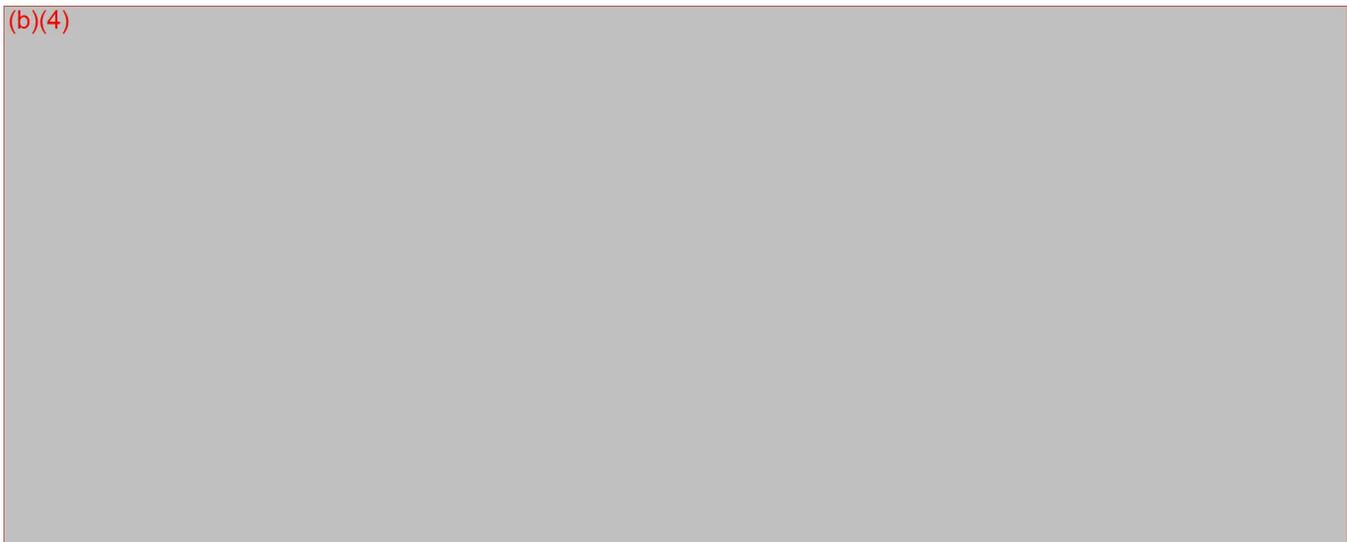
To: LCDR Nikhil Thakur

From: Joy Samuels-Reid, M.D.

Date: January 27, 2010

Re: K093775 – evGUIDE Tip Location System

(b)(4)



(b)(4)



Joy Samuels-Reid, M.D., FAAP

Chief Medical Officer,

Division of Anesthesiology, General Hospital,

Infection Control and Dental Devices

Center for Devices and Radiological Health

US Food and Drug Administration

Office of Device Evaluation-White Oak - Bldg 66-2608

10903 New Hampshire Avenue, Silver Spring,

Maryland, 20993

Tel: 301-796-5580

Fax: 301-847-8109

Joy.Samuels-Reid@fda.hhs.gov

Thakur, Nikhil

From: Samuels-Reid, Joy H.
Sent: Wednesday, March 03, 2010 7:02 PM
To: Thakur, Nikhil
Subject: RE: Draft Clinical Questions for K093775, Romodex

Nikhil,

Only a minor edit; I think that you have captured my comments well.

Joy.

*Joy Samuels-Reid, M.D.
CDRH/ODE/DAGID
Tel: 301-796-6266*

From: Thakur, Nikhil
Sent: Wednesday, March 03, 2010 5:35 PM
To: Samuels-Reid, Joy H.
Subject: Draft Clinical Questions for K093775, Romodex
Importance: High

Hi Joy,

(b)(4)



(b)(4)



*** **

Sincerely,
Nikhil

Nikhil Thakur
LCDR, USPHS
Reviewer
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation

Address:
10903 New Hampshire Avenue,
Bldg: WO66, Rm 2562
Silver Spring, MD 20993

Telephone: (301) 796 - 5536
Fax: (301) 847 - 8109

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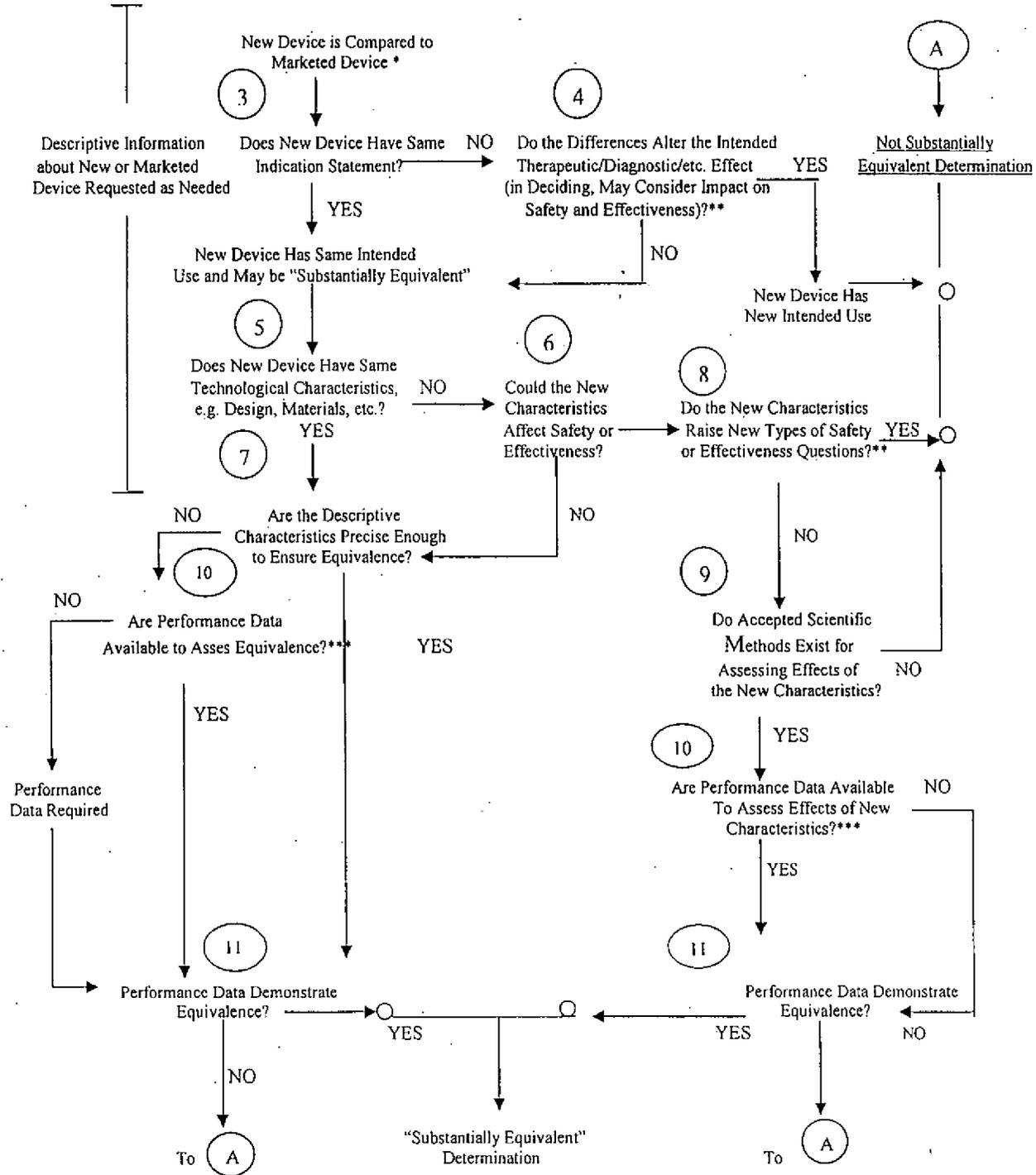
COVER SHEET MEMORANDUM

From: Reviewer Name NICHIL THAKOR
Subject: 510(k) Number K093775
To: The Record

- Please list CTS decision code ~~KT~~ TH
- Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%20%202%2007.doc)
 - Hold (Additional Information or Telephone Hold).
 - Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

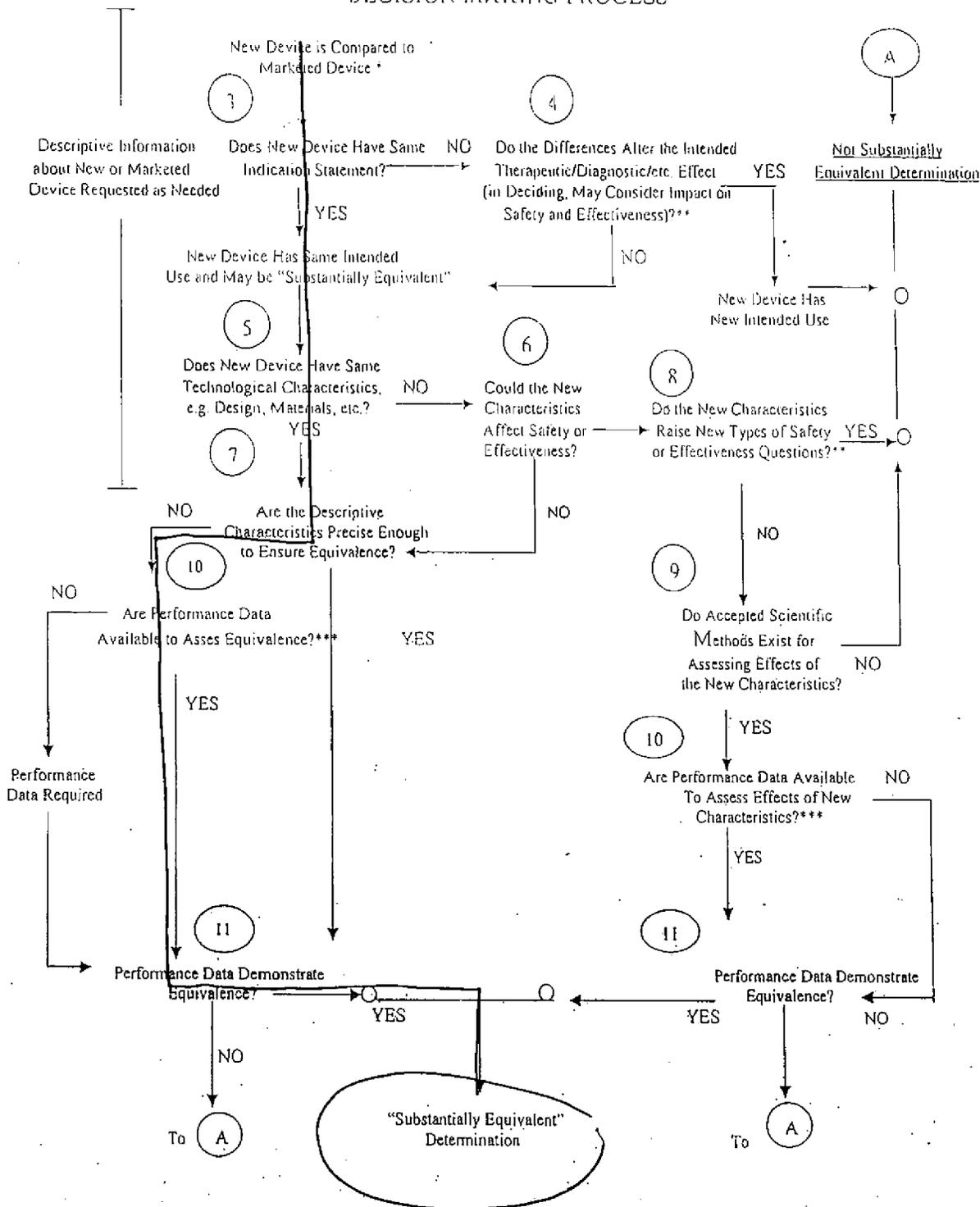
Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	Attach IFU	X	
510(k) Summary /510(k) Statement	Attach Summary	X	
Truthful and Accurate Statement.	Must be present for a Final Decision	X	
Is the device Class III? If yes, does firm include Class III Summary?	Must be present for a Final Decision		X
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)		X	
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/CO-MBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC)			X
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			X
Is this device intended for pediatric use only?			X
Is this a prescription device? (If both prescription & OTC, check both boxes.)		X	
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?			X
Is clinical data necessary to support the review of this 510(k)? Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If not, then applicant must be contacted to obtain completed form.)		X	X
Does this device include an Animal Tissue Source?			X
All Pediatric Patients age <=21			
Neonate/Newborn (Birth to 28 days)			
Infant (29 days - < 2 years old)			
Child (2 years - < 12 years old)			
Adolescent (12 years - < 18 years old)			
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)			

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



- ❖ 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.
- ❖❖ This decision is normally based on descriptive information alone, but limited testing information is sometimes required.
- ❖❖❖ Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



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Romedex International

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June 5, 2010

Nikhil Thakur, Reviewer
U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

FDA CDRH DMC

JUN 07 2010

Received

14-27

Subject: K093775
Response to your request for additional information from 3/4/2010

Dear Mr. Thakur:

Romedex International Srl is submitting this response to your March 4, 2010 request for additional information for the 510(k) submission referenced above. Your requests (*italics*) and our responses follow. Please note that on March 29, 2010 Romedex applied for and since received a 90 day extension to respond to the request for additional information.

In reference to the teleconference from April 9th, 2010 at 10:00 AM between the Agency's review team and Romedex, the evGuide™ TLS Saline Adaptor has been replaced in this submission by the evGuide™ TLS Electrical Adaptor used in combination with the Arrow-Johans Adaptor (K843263).

An updated CDRH Premarket Review Submission Cover Sheet is provided in Attachment 12.

(b)(6)

Sorin Grunwald, Ph.D.
Managing Director
Romedex International Srl

Confidential Information

sorin@romedex.com

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ATTACHMENTS

1. EVGUIDE-SAPIENS TLS USERS MANUAL
2. EVGUIDE-SAPIENS TLS ADAPTOR INSTRUCTIONS FOR USE
3. ROMEDEX-STERIGENICS STERILIZATION VALIDATION PROTOCOL
4. ROMEDEX-STERIGENICS STERILIZATION VALIDATION REPORT
5. EVGUIDE-SAPIENS STERILIZATION TEST RESULTS
6. BIOBURDEN VALIDATION FOR ROMEDEX - PROTOCOL
7. BIOBURDEN VALIDATION FOR ROMEDEX - REPORT
8. EVGUIDE-SAPIENS SHELF-LIFE TEST PROTOCOL
9. BIOCOMPATIBILITY SUMMARY FOR THE ARROW-JOHANS ADAPTOR
10. EVGUIDE-SAPIENS SYSTEM HUMAN FACTORS AND USABILITY VALIDATION REPORT
11. EVGUIDE-SAPIENS POST-MARKET CLINICAL STUDY REPORT
12. K093775 – UPDATED SUBMISSION COVER SHEET
13. K093775 – UPDATED SECTION 4 – INDICATIONS FOR USE
14. EVGUIDE-SAPIENS ECG WAVEFORM ACCURACY TEST REPORT
15. ELECTROCARDIOGRAM (EKG) GUIDED PERIPHERALLY INSERTED CENTRAL CATHETER PLACEMENT AND TIP POSITION: RESULTS OF A TRIAL TO REPLACE RADIOLOGICAL CONFIRMATION, BY NANCY MOUREAU ET AL. PUBLISHED IN THE JOURNAL OF THE ASSOCIATION FOR VASCULAR ACCESS IN 2010, JAVA VOL. 15 No. 1 2010, pp. 9-15
16. THE ECG METHOD FOR POSITIONING THE TIP OF PICCS: RESULTS FROM TWO PRELIMINARY STUDIES, BY MAURO PITTIRUTI ET AL. PUBLISHED IN THE JOURNAL OF THE ASSOCIATION FOR VASCULAR ACCESS IN 2008, JAVA VOL. 13 No. 4 2008, pp. 112-119

evGuide-Sapiens™ TLS USER'S MANUAL

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evGuide-Sapiens™ TLS USER'S MANUAL

Note: The names evGuide™ TLS and Sapiens™ TLS will be used interchangeably in this document.

1. Overview

1.1 Indications for Use

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

1.2 The ECG Method for Catheter Guidance

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health care institutions and as documented in many papers including:

- a. *Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation*, by Nancy Moureau et al. published in the Journal of the Association for Vascular Access in 2010, JAVA Vol. 15 No. 1 2010, pp. 9-15
- b. *The ECG method for positioning the tip of PICCs: results from two preliminary studies*, by Mauro Pittiruti et al. published in the Journal of the Association for Vascular Access in 2008, JAVA Vol. 13 No. 4 2008, pp. 112-119

Figure 1 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community. The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the “red” or “right shoulder“ electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode,

the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A “giant” P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface ECG, the tip of the electrode is in the superior cava vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava).

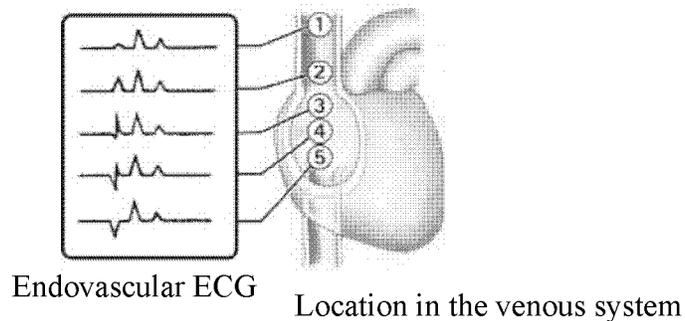


Figure 1: Changes in the ECG waveform as function of location in the vasculature

Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy.

1.3 Sapiens™ TLS Description

The Sapiens™ TLS consists of the Sapiens™ TLS Electrical Adaptor, an ECG Module and an ECG cable, a laptop, and the Sapiens™ TLS application software. The Sapiens™ TLS components excluding the Sapiens™ TLS Adaptors are also referred to as the Sapiens™ TLS System. An optional printer can be connected to the laptop for documentation purposes. The Sapiens™ TLS Saline Adaptor can be connected to an Arrow-Johans Adaptor (Teleflex) to be used according to the saline column method as described herein. The Sapiens™ TLS Saline Adaptor with the Arrow-Johans Adaptor can be connected to any commercially available central venous catheters and the Sapiens™ TLS Electrical Adaptor to any commercially available stylets or guidewires used for the placement of central venous catheters. The Sapiens™ TLS system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, or intracavitary ECG) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and

acquired in real time through the Sapiens adaptors. Thus, the waveforms presented on the Sapiens™ TLS graphical user interface can aid the placement of central venous catheters.

The Sapiens™ TLS System is shipped in two subsystems: laptop running the Sapiens™ TLS software and the Sapiens™ TLS ECG module together with the corresponding cables.

Store the Sapiens™ TLS System indoors at room temperature and condition.

Figure 2 shows the system components:

1. PC/Laptop running Sapiens™ TLS software
2. ECG module
3. USB connection cable to the ECG module
4. ECG cable
5. Sterile Sapiens™ TLS Electrical Adaptor connected to an Arrow-Johans Adaptor placed between a syringe and a catheter
6. Skin ECG electrodes
7. Optional label printer
8. Optional remote control

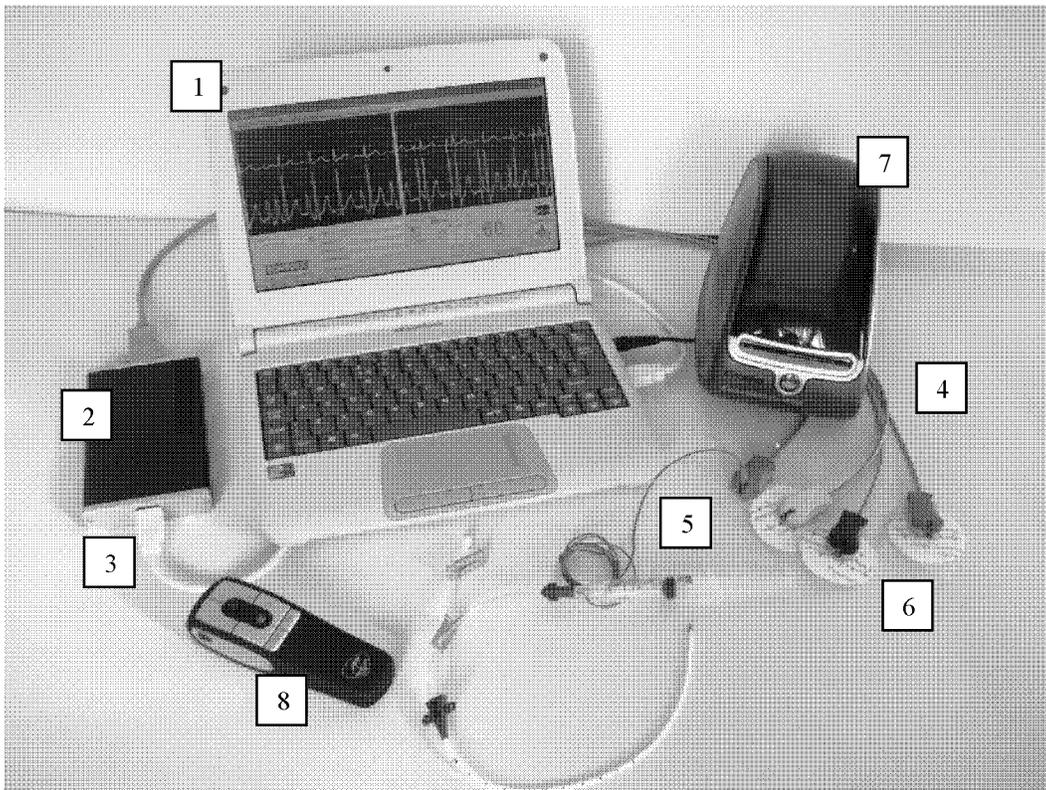


Figure 2: Sapiens TLS System Configuration

1.4 Warnings and Precautions

A Warning indicates that the personal safety of the patient or physician may be involved. Disregarding a Warning could result in injury to the patient or physician. A Caution indicates that particular service procedures or precautions must be followed to avoid possible damage to the product.

Warnings

- Warning:** Before using the Sapiens™ TLS System for the first time, be sure to read and understand all of the information in this User's Manual.
- Warning:** Failure to abide by the precautions detailed below causes the system and its use to be out of compliance with regulations and places the patient and the user at risk of injury or death.
- Warning:** When using the Sapiens™ TLS System with the Sapiens™ TLS Adaptors, always follow the Instructions for Use provided with the Sapiens™ TLS Adaptor. When using the Arrow-Johans Adaptor, always follow the Instructions for Use provided with the Arrow-Johans Adaptor.
- Warning:** The Sapiens™ TLS System should only be used by physicians and nurses trained in central lines placement procedures and in assessing the ECG information provided by the Sapiens™ TLS System.
- Warning:** The Sapiens™ TLS User's Manual provides information about ECG waveforms and their correspondence with specific locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** Place skin electrodes carefully at locations indicated by this User's Manual and ensure good skin-electrode contact. Failure to do so may cause unstable ECG waveforms and/or ECG waveforms which are not described in this Manual. In such a case, the use of an additional and/or different method may be required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** In patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** In patients undergoing central venous catheterization using venous access through the saphenous or the femoral veins, the catheter tip will typically not reach the right atrium and the caval atrial junction. In such a situation, the ECG waveforms described by this manual cannot be used for catheter

guidance and placement and the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In certain patients, unstable ECG waveforms may be detected because of the manipulation of the Sapiens™ TLS Adaptor by the user. Verify that the connection between the Sapiens™ TLS Adaptor and the central venous catheter and the connection between the Sapiens™ TLS Adaptor and the ECG cable are free from contact with any other material and refrain from touching the Sapiens™ TLS Adaptor and any of its connections. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In certain patients, no ECG waveforms may be detected because of very specific impedance mismatch between the patient and the ECG electrodes. Be sure to use the Instructions for Use provided by the manufacturer of the skin electrodes. Verify the connection between the patient's skin and the electrodes, between the electrodes and Sapiens™ TLS ECG cable, and between the Sapiens™ TLS Adaptor and the Sapiens™ TLS ECG cable. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In neonates, unstable ECG waveforms may be detected because of patient's movements or manipulation by the user. In such a situation, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: The Sapiens™ TLS system is not intended to diagnose or treat disease.

Warning: Monitor catheter tip placement during insertion procedure and verify catheter tip location placement using your institution's guidelines.

Warning: Do not place and/or use the Sapiens™ TLS system in the presence of strong magnetic fields such as Magnetic Resonance Imaging (MRI) devices. The high magnetic fields created by an MRI device will attract the equipment with a force sufficient to cause death or serious personal injury to persons between the equipment and the MRI device. This magnetic attraction may also damage the equipment. The magnetic and the RF fields associated with the MRI environment may interfere with the display of ECG waveforms. Consult the MRI manufacturer for more information.

Warning: Do not use the Sapiens™ TLS system at the same time with a defibrillator. Disconnect any Sapiens™ TLS Adaptor from any catheter and any Sapiens™ TLS ECG cable connection from any ECG skin electrode before using a defibrillator.

- Warning:** Always use controls, make adjustments and perform procedures with Sapiens™ TLS as specified in this User's Manual.
- Warning:** The Sapiens™ TLS system is password protected to avoid accidental changes in the software and system configuration. Do not install any software on the Sapiens™ TLS System unless instructed to do so by qualified Romedex personnel and under the guidance of qualified Romedex personnel. Failure to do so may result in patient and user harm and system damage.
- Warning:** The Sapiens™ TLS system must be powered only by the batteries provided with the Sapiens™ TLS Laptop. Batteries may not be charged while using the Sapiens™ TLS system in a medical procedure.
- Warning:** Charge the Sapiens™ TLS system only when the system is Off using a medical grade power adaptor.
- Warning:** All optional system components including the optional printer must be powered by, and only by a medical grade power adaptor if they are connected to the Sapiens™ TLS system during the clinical procedure.
- Warning:** Do not use additional cables, extension cords or outlets with the Sapiens™ TLS System.
- Warning:** This device is not to be used in the presence of combustible or flammable gases, anesthetics, or cleaners/disinfectants.
- Warning:** Do not remove system covers. To avoid electrical shock, use only the power cord supplied with the system and connect only to properly grounded wall outlets. Only Romedex qualified personnel should service the system.
- Warning:** Maximum care should be taken in checking that all connecting cables and connections, such as alligator clips, are electrically insulated and do not come into contact with other electrical cables or metal surfaces
- Warning:** No part of the body of the patient must be in direct or indirect uninsulated contact with metal surfaces.

Cautions

- Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician
- Caution:** Active electric motor driven equipment, such as pumps, may interfere with the display of the ECG waveforms. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Caution:** Equipment such as CT scanners, X-rays and fluoroscopy systems, cauterizers and diathermy equipment, operating in close proximity may emit strong electromagnetic or radio frequency interference (RFI) which

could interfere with the display of ECG waveforms by Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Caution: Electric equipment which requires direct contact with the patient may interfere with the display of ECG waveforms by Sapiens™ TLS. Do not use electric cauterization, electric scalpels, and ablation equipment while using Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

1.5 Sapiens TLS System Limitations

When using the Sapiens™ TLS Electrical Adaptor, a stylet or a guidewire typically provided with the kit of the vascular access device must be used in order to ensure an electrically conductive path between the proximal and the distal ends of the vascular access device.

When using the saline adaptor configuration of Sapiens™ TLS, the user needs to ensure that the catheter lumen is constantly filled with saline and in contact with the Arrow-Johans Adaptor, such that electrical conductivity through the catheter lumen is ensured from the proximal to the distal end of the vascular access device.

When using the saline adaptor configuration, instability of the endovascular electrical signal baseline may occur if the user makes hand contact with the proximal end connection of the Arrow-Johans Adaptor.

The Sapiens™ TLS system must be battery powered when used in a clinical case, i.e., as long as ECG electrodes are connected to the patient. The system battery lasts for approximately two hours. Recharging the battery must be done in between clinical cases.

The Sapiens™ TLS system uses data processing algorithms to enhance the quality of the endovascular ECG signal. In situations when electrodes have been disconnected and reconnected again, e.g., when the red clip electrode is connected to the sterile adaptor, it may take several seconds for the system to transition from a no-signal to a stable signal state. Please wait while the system makes this transition and do not touch the electrical connections of the adaptor during this time.

The Sapiens™ TLS system uses a serial communication protocol and a USB-Serial converter between the laptop and the ECG module. If the USB connector is not connected when the Sapiens software application starts up or if the USB connector is

disconnected before shutting down the Sapiens software application, under certain circumstances the Sapiens application must be restarted.

In order to prevent accidental installation of software on the Sapiens™ TLS laptop computer, the user does not have administrative rights to install software. Only Romedex personnel have the administrative rights to perform software installation on the Sapiens™ TLS laptop.

2. Sapiens™ TLS procedure workflow

2.1 System setup

Find an appropriate location for the system. Ensure the Sapiens™ TLS System is placed no more than 4 feet away from the patient outside the sterile field.

Ensure that all the individual power switches to the Laptop, optional printer, and medical grade power supply, where appropriate, are turned OFF. Connect the ECG module to the Laptop via the USB cable provided with the system. Connect the ECG cable to the ECG module via the ECG cable connector.

The laptop and the ECG module can run on the laptop battery. If the optional printer is not used, then there is no need to connect the medical grade power supply to the power outlet. Fully charging the laptop battery should be accomplished before any procedure if the system runs on battery. A full battery charge lasts for approximately two hours.

Turn the system on by turning on the power switches on of the individual systems in the following order:

- a. Optional printer
- b. Laptop

Once the Laptop power up sequence is finished, the Sapiens™ TLS software will be launched automatically. The startup screen is shown in Figure 3.

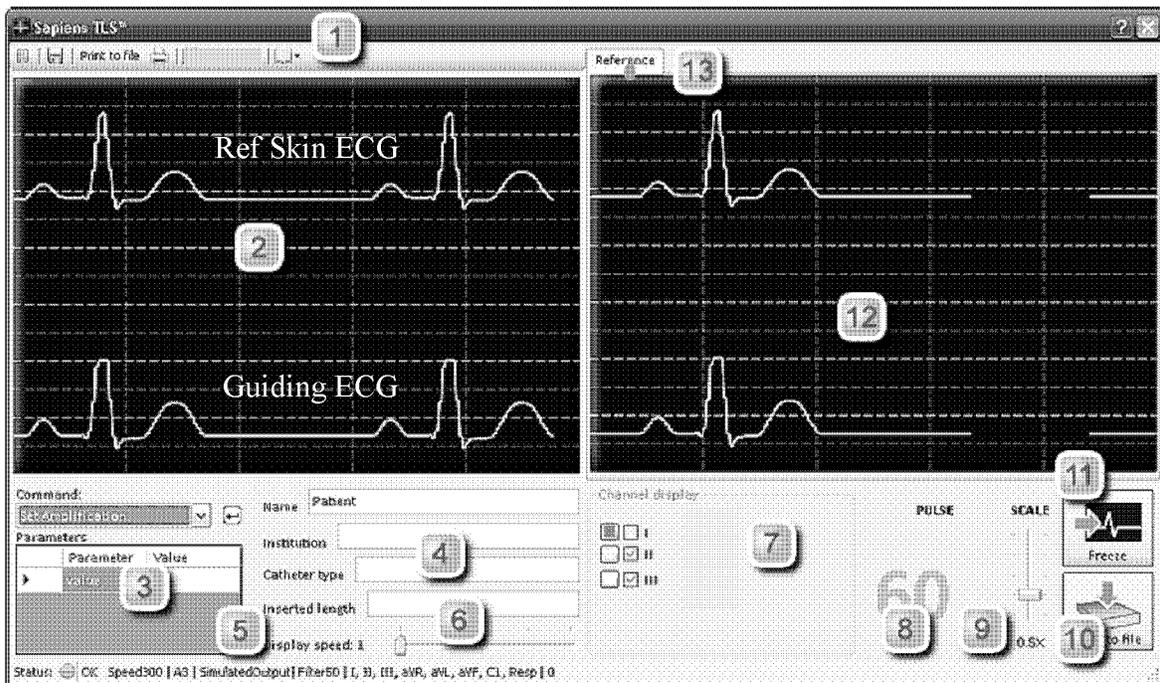


Figure 3: Sapiens™ TLS Screen Layout

- 1 - Toolbar containing controls for play / pause the data acquisition, load / save ECG files, printing to file / printer, settings and help. The following functions are available on the toolbar:
- Pause/Play the ECG waveform in acquisition and playback modes.
 - Save the case to file. When clicking the “Save” icon, all ECG waveforms for the entire duration since the beginning of the case or since last save are saved in a file. The default name of the file is the name of the patient to which the date and time are appended. The default directory is C:/Data created when installing the Sapiens™ TLS application.
 - Print to file. Click on the button to select (highlight) it, click again to unselect it. When this button is selected, the printer output will be redirected to a file using a default name and location.
 - Print. By clicking the printer icon, the print preview will be displayed. The desired information needs to be first frozen on the right hand side screen before it can be printed. The printer output will be redirected to the default printer. A default label printer is preinstalled on the system.
 - Clicking on the Help button brings up the User's manual and information about the Sapiens™ TLS software.
 - By dragging the question mark to a screen location, certain hints will be provided depending on the location.
 - Closes the Sapiens™ TLS application before turning off the computer. If the user accidentally closes it and needs to reopen it again, double click on the Sapiens TLS icon on the desktop.

- 2 - Main screen where the real-time ECG waveforms are displayed: the reference skin ECG waveform (lead III in Einthoven's reference system) and the guiding ECG waveform at the tip of the catheter (lead II in Einthoven's reference system).
- 3 - Available commands accepted by the device and respective parameters
- 4 - 'Patient name', 'institution', 'catheter type' and 'inserted length' information that will be shown on printed label.
- 5 - Status bar displaying information about the ECG module status
- 6 - Scroll bar used for changing the scroll speed of the ECG waveform display
- 7 - Color and visibility setting for channels.
- 8 - Frequency of R-Peaks measured in number of peaks / minute.
- 9 - Scale setting used to amplify the signals received from device.
- 10 - Pressing this button will save the current image shown in Main screen.
- 11 - Pressing this button will copy the current image shown in Main screen to Secondary screen.
- 12 - Secondary screen used for freezing ECG waveforms for comparison.
- 13 - Tab container displays the 'Reference' page.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

To power off the system:

- a. Close the Sapiens™ TLS application
- b. Power down the Windows operating system on the laptop
- c. Turn off the optional printer

2.2 Patient preparation and vein puncture

Connect the ECG cable to the patient:

1. Before preparing the sterile field, take the ECG cable supplied with the Sapiens™ TLS System and wipe the cable down according to hospital's guideline.
2. Locate three new off-the-shelf ECG snap electrode patches and place one on the patient's lower left abdomen, one on the patient's lower right abdomen, and one on the patient's left shoulder or arm per the ECG electrodes instructions for use.
3. Connect the green clip connector of the provided ECG cable to the electrode snap on the patient's left lower abdomen.
4. Connect the black clip connector of the provided ECG cable to the electrode snap on the patient's left lower abdomen.
5. Connect the yellow clip connector of the provided ECG cable to the electrode snap on the patient's left shoulder or arm.

6. Leave the red clip connector of the provided ECG cable in a reachable location for the connection with the sterile adaptor during the procedure.

With the Sapiens™ TLS system running, the reference skin ECG waveform should be at this time visible and stable. It should be possible to unambiguously identify the ECG waveform elements, e.g., the P-wave and the R-wave, as represented in this User's Manual. If this is not the case, do not attempt to use Sapiens™ TLS for catheter guidance and positioning and use another method for catheter tip location verification as indicated by the institutional guidelines, e.g., chest X-ray or fluoroscopy.

Prepare the patient for central venous catheterization per institution's guidelines.

Perform vein puncture and venous access per institution's guidelines, if applicable under ultrasound imaging guidance.

2.3 Connecting the Sapiens™ TLS Adaptor or the Arrow-Johans adaptor

In order to obtain ECG waveforms at the tip of the central venous catheter, the non-sterile red clip connector of the provided ECG cable must be connected to the sterile central venous catheter. This connection is achieved using the Sapiens™ TLS Electrical Adaptor and/or the Arrow-Johans Adaptor. Please refer to the Instructions for Use of these adaptors for details.

When using the Sapiens™ TLS Electrical Adaptor, connect the alligator clip end of the Sapiens™ TLS Adaptor to the proximal end of the stylet or guidewire which is packaged with your venous access device or pre-inserted in one of the lumens of your venous access device. Connect the red clip connector of the provided ECG cable to the plug end of the sterile Sapiens™ TLS Electrical Adaptor.

When using the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor, connect the Arrow-Johans Adaptor similarly to the Sapiens™ TLS Saline Adaptor. Then connect the alligator clip of the Sapiens™ TLS Electrical Adaptor to the snap nipple connector of the Arrow-Johans Adaptor and then connect the red clip connector of the provided ECG cable to the plug end of the sterile Sapiens™ TLS Electrical Adaptor.

2.4 Electrical vs. saline adaptors

The choice between using the Sapiens™ TLS Electrical Adaptor or the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor is a matter of user preference and workflow optimization and is potentially subject to institutional guidelines. Please refer also to the Instructions for Use of the respective adaptors.

Typical situations for using the Sapiens™ TLS Electrical Adaptor are:

1. Placement of open-ended PICCs with pre-inserted stylets and luer-locks which allow for stylet position control
2. Implantable ports using open vein access with over-the-guidewire catheter placement
3. Any central venous catheter inserted over a guidewire with centimeter markings

Typical situations for using the combination between the Arrow-Johans Adaptor and the Sapiens TLS Electrical Adaptor are:

1. Any post-procedural tip location verification of any central venous catheter type
2. Placement of closed-end PICCs
3. Placement of central venous catheters using the modified Seldinger technique (MST) which do not have pre-inserted stylets, e.g., tunneled catheters like Broviac catheters.
4. Any central venous catheter inserted over a guidewire without centimeter markings, e.g., CVCs.
5. Hemodialysis catheters which may require tip location verification for both ends: the long distal end in the right atrium and the short distal end at the caval-atrial junction.

2.5 Display ECG waveforms

As soon as the Sapiens™ TLS adaptors and/or the Arrow-Johans Adaptor are connected to the catheter and to the ECG cable, the guiding ECG waveform is displayed (Figure 3).

The waveforms on the top in Figure 3 on both left and right hand side display windows represent the skin ECG or reference ECG. The waveforms on the bottom in Figure 3 on both left and right hand side display windows represent the electrical signal detected at the tip of the central venous catheter.

The right hand side window in Figure 3 is labeled “Reference”. The reference window allows for saving the ECG waveforms at a desired location for further comparison. Clicking on the “Freeze” button below the Reference window or using the left arrow key on the keyboard freezes the display, such that the frozen ECG waveform can be used as a reference.

The scroll speed of the ECG waveform can be selected by using the scroll bar “Display speed” (6 in Fig 3). The amplitude scale for the ECG waveform can be manually selected by using the Scale scrollbar (9 in Fig 3) or the up/down arrow keys on the keyboard.

2.6 Document the catheter tip location

The ECG waveforms can be recorded real-time during the procedure by clicking on the “Record” button. The ECG waveforms are recorded in a file. The file name is

automatically generated by the computer if a patient ID is not input. If a patient ID is input the file name is generated based on the patient ID. The file can be copied to a USB memory stick or memory card as a removable storage device.

Clicking the “Print/Save” button sends a screen shot to the printer if attached and save the screen shot in a file in JPG format. The file name is assigned automatically if no patient ID is input and a name is assigned based on the patient ID if a patient ID is input.

Using Sapiens™ TLS it is possible to print the ECG waveforms at the chosen tip location in order to attach the print to the patient chart and document the catheter tip location. The alphanumeric information input by the user and the ECG waveforms displayed in the Reference window are printed using the print layout illustrated in Figure 4. The print layout is displayed when clicking on the printer icon on the command toolbar at the top of the screen. The reference skin ECG and the guiding ECG waveforms are displayed on the right hand side and respectively on the left hand side of the print layout. Between the two waveforms a heart symbol is printed in order to allow the user to mark with a pen on printed paper the location of tip where the corresponding ECG waveforms have been obtained.

The patient name, institution name, catheter type and length, are displayed as well as they were input in the corresponding fields of the graphical user interface.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

This information is printed out in the corresponding fields of the print layout in Figure 4.

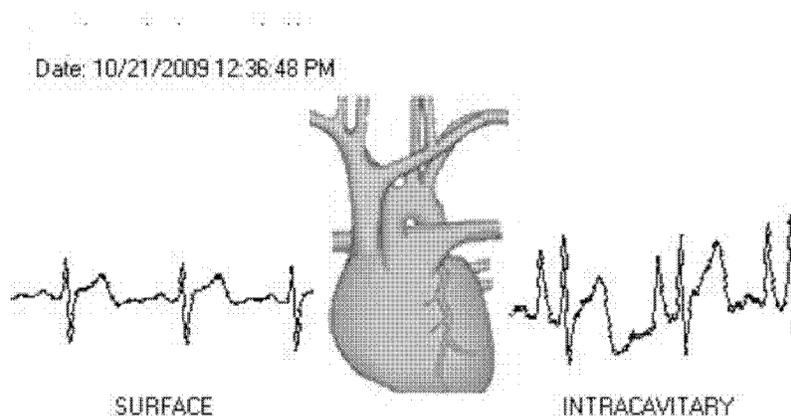


Figure 4: Print layout

To copy any file from the Sapiens™ TLS laptop to a removable storage medium, exit the Sapiens™ TLS application and use the Windows XP operating system to copy the desired file to the desired location.

3. Sapiens™ TLS Catheter Guidance

3.1 Outside the thoracic cavity

Outside the thoracic cavity the ECG signals are similar to the ones at the skin level. Figure 5 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located outside the thoracic cavity relative to the reference skin ECG.

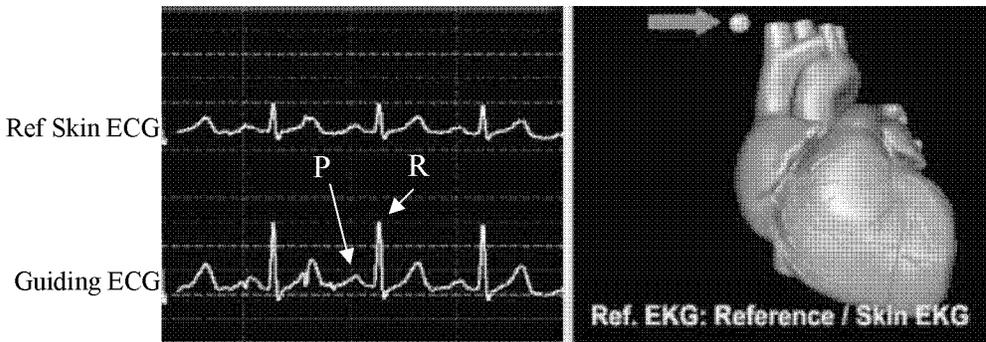


Figure 5: ECG waveform at the tip of the catheter outside the thoracic cavity.

3.2 Superior vena cava

Figure 6 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the upper superior vena cava (SVC). Compared to Figure 5 one can notice that the reference skin ECG waveform has not changed since this waveform does not depend on the location of the tip of the catheter. The amplitude and energy of the guiding ECG waveform have increase in Figure 6 when compared to Figure 5 indicating that the catheter tip is approaching the heart, i.e., a region of high electrical activity. Still, the shape of the ECG waveform has not changed significantly indicating that the catheter tip is not yet close to the sino-atrial node and the caval-atrial junction.



Figure 6: ECG waveform at the tip of the catheter in the upper SVC

3.3 Lower third of the superior vena cava

Figure 7 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in lower third of the upper superior vena cava. The P-wave has increased visibly when compared to Figure 6. The amplitude of the P-wave is about half size of the amplitude of the R-wave.

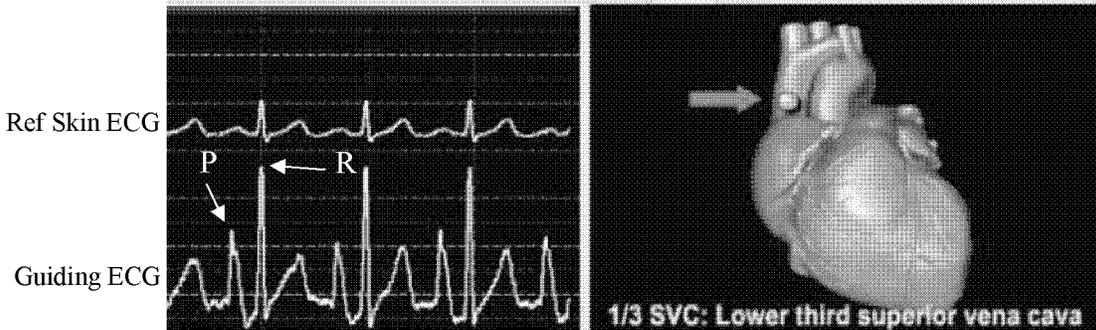


Figure 7: ECG waveform at the tip of the catheter in the lower third of the SVC

3.4 Caval-atrial junction

Figure 8 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located at the caval-atrial junction (CAJ) right below the sino-atrial node (SAN). The P-wave is bi-phasic, i.e., has a negative component. A negative component of the P-wave appears when the tip of the catheter is below the sino-atrial node (SAN). Since the P-wave has a negative component but the amplitude of the P-wave has not increased much compared to Figure 7, the ECG waveform in Figure 8 is typical of the caval-atrial junction with the tip of the catheter just below the SAN.

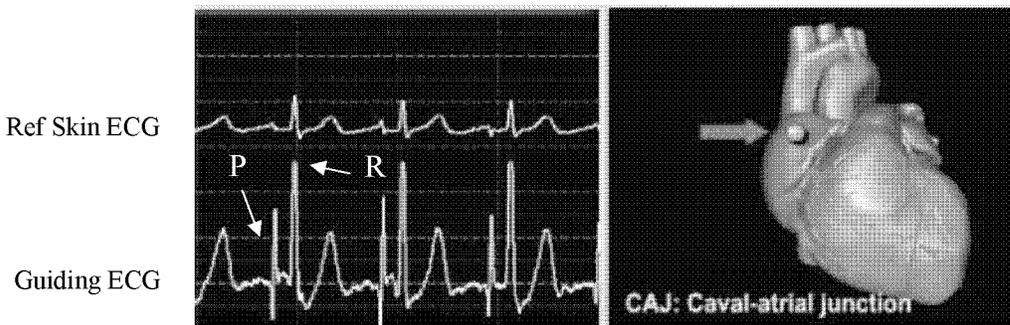


Figure 8: ECG waveform at the tip of the catheter at CAJ right below the SAN

3.5 Right atrium

Figure 9 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the right atrium (RA). The P-wave continues to have a negative component indicating that the catheter tip continues to be below the sino-atrial node. The P-wave amplitude has increased significantly when compared to Figures 7 and 8. This is an

indication that the tip of the catheter is in the middle of the right atrium where the P-wave intensity is maximal due to the right-atrial activity.

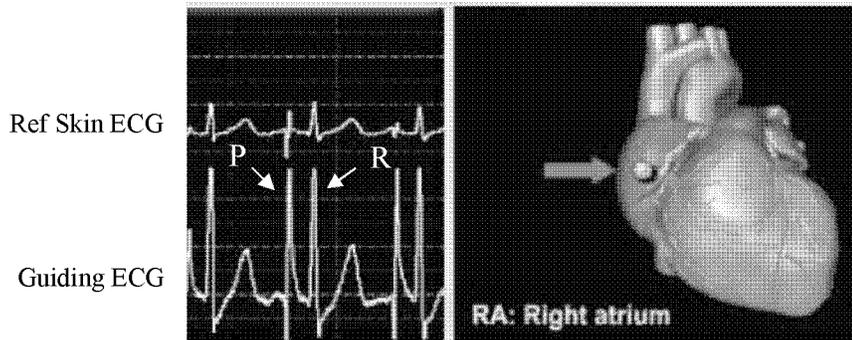


Figure 9: ECG waveform at the tip of the catheter in the RA.

3.6 Inferior Vena Cava

Figure 10 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the inferior vena cava (IVC). The P-wave has changed polarity when compared to Figure 7. In Figure 7 the P-wave is positive whereby in Figure 10 the P-wave is negative. This is an indication that the catheter tip is approaching the inferior vena cava. The relatively high negative amplitude of the P-wave compared to the positive one in Figure 7 is an indication that the tip of the catheter is just entering the inferior vena cava coming from the right atrium.

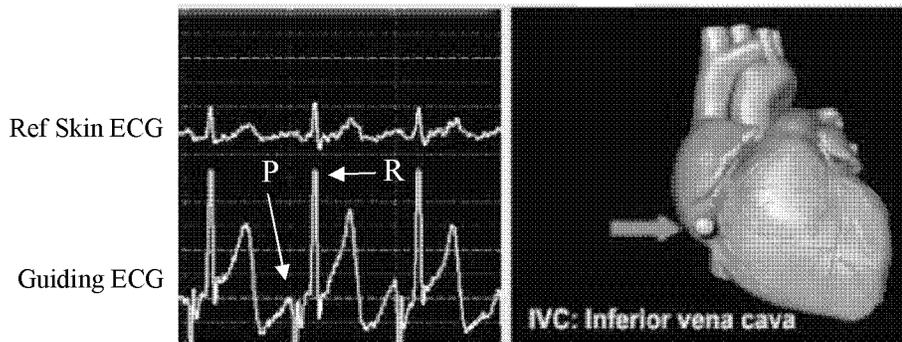


Figure 10: ECG waveform at the tip of the catheter in the IVC.

3.7 Catheter tip placement verification

As described in Section 3 of this Sapiens™ TLS User's Manual, using the Sapiens™ TLS the ECG waveforms can be unambiguously mapped to specific catheter tip locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described in Section 3.1.-3.6, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Per institutional guidelines and in accordance with clinical judgment, in indicated patients, and under the conditions described by this User's Manual, Sapiens™ TLS may be used in conjunction with ultrasound-guided vein puncture or open vein access to replace chest X-ray and fluoroscopy for intra- and post-procedural central venous catheter tip location confirmation.

Using Sapiens™ TLS, central venous catheter tip location can be documented for the patient's chart either on paper or electronically.

Using Sapiens™ TLS, the location of the central venous catheter tip can be determined and documented as required by the different types of central venous catheters and by different institutional guidelines, for example:

1. When the tip of a PICC catheter must be placed in the lower third of the superior vena cava, the ECG waveforms illustrated in Figure 7 must be detected and documented at the tip of the PICC catheter.
2. When during intra-procedural catheter insertion or, at later times, during periodical post-procedural catheter tip verification, the long end of a hemodialysis catheter must be placed in the right atrium while its short end must be placed at the caval-atrial junction, then the ECG waveform in Figure 9 must be detected and documented at the long tip and, respectively, the ECG waveform in Figure 8 must be detected and documented at the short tip of the hemodialysis catheter.
3. When the tip of a central venous catheter (CVC) or of an implantable port must be placed at the caval-atrial junction, then an ECG waveform like the one in Figure 8 must be detected and documented at the tip of the catheter.

4. Error Messages and Troubleshooting

1. Electrodes not connected
If Sapiens™ TLS does not detect any connection of electrodes to the patient, a message is displayed on the status bar (5) in Figure 3. In such a case, verify that the skin electrodes are well attached to the patient's skin, that the ECG cable clips are well attached to the snap nipple on the electrodes and that the Sapiens™ TLS Adaptors are well connected to the red clip of the ECG cable. Verify that the ECG cable is well attached to the ECG module. If the error situation persists, you may replace the ECG skin electrodes with new ones. If the problem persists, contact your Romedex representative.
2. ECG module not connected
If Sapiens™ TLS does not detect the presence of an ECG module, a message is displayed on the status bar (5) in Figure 3. In such a case, verify that the USB cable between the ECG module and the laptop is well connected. Close and reopen the Sapiens™ TLS software. If the problem persists, contact your Romedex representative.
3. Battery status

The battery status is displayed on the task bar of the Windows operating system. To check battery status, close the Sapiens™ TLS software and point the mouse cursor to the battery icon on the Windows task bar. When finished, reopen the Sapiens™ TLS software.

4. Printer error

A printer error message is displayed when printing if the printer is not connected or if it is out of paper. Check the printer connection and paper status and try again. If the problem persists, contact your Romedex representative.

5. Cleaning and Disinfection

To clean the Sapiens™ TLS system:

1. Turn off the system
2. Dampen a nonabrasive cloth with either warm water or rubbing alcohol
3. Gently wipe the dampened cloth over the exterior surfaces of the ECG module and of the laptop.

For a list of disinfectants recommended for use please contact Romedex International.

Warning: Do not submerge the Sapiens™ TLS ECG module or the laptop or allow fluid to enter any of the connectors.

6. Warranty

The manufacturer, Romedex International Srl, warrants this product against defects in material and workmanship for a period of one year from the date of original purchase, and during such period agrees to repair, or at Romedex International's discretion, replace any defective unit free of charge. The warranty on the repaired or replaced unit continues from the purchase date of the original unit. This warranty does not cover damages resulting from misuse, abuse, modification, or alteration of the Sapiens™ TLS.

The following actions void the warranty of the Sapiens™ TLS:

1. Opening or servicing the ECG module or the laptop
2. Removal of system labels by anyone other than by Romedex authorized service personnel
3. Connecting the ECG module to any unauthorized laptop
4. Connecting any unauthorized peripheral to the laptop
5. Installing software on the laptop other than by authorized Romedex personnel or under authorized Romedex personnel guidance.

7. Service and Repair

For servicing information or to return your Sapiens™ TLS for repair, please contact Romedex International's technical support at service@romedex.com.

Warning: Only qualified personnel should attempt to service the Sapiens™ TLS system.

8. Technical Specifications

1. Laptop: ASUS Eee 900HA or better, 100-240V, 50/60 Hz
2. Laptop power consumption: Less than 40W
3. Operating system: Windows XP or later
4. ECG module: 4-lead, full patient isolation, defibrillation protected
5. Dimensions ECG module: 0.8" x 2.4" x 4" (2 cm x 6 cm x 10 cm)
6. Connector type: USB
7. ECG cable: 4-lead, 10 ft (3 m)
8. IEC 60601-1: Type CF Applied Part when used with the Sapiens TLS or Arrow-Johans Adaptors

9. Disposal Information

To return the Sapiens™ TLS for end of life recycling please contact your nearest Romedex sales or distributor office in the country of purchase.

10. Contact Information

For additional information and training materials, please go to the Romedex International web site: www.romedex.com.

If you have any questions or comments regarding the use of this product please contact:

*Romedex International Srl
58 Aleea Arubium Str
Bucharest, 022944 Romania
Tel: +40.743.490.892
Fax: +40.317.107.048
Email: info@romedex.com*

11. References

- a. *Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation*, by Nancy Moureau et al. published in the Journal of the Association for Vascular Access in 2010, JAVA Vol. 15 No. 1 2010, pp. 9-15
- b. *The ECG method for positioning the tip of PICCs: results from two preliminary studies*, by Mauro Pittiruti et al. published in the Journal of the Association for Vascular Access in 2008, JAVA Vol. 13 No. 4 2008, pp. 112-119

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evGuideTM / SapiensTM System
Human Factors / Usability Validation Report

REVISION HISTORY

Section	Description	Author	Date
ALL	Initial Release	Sorin Grunwald	3/10/10

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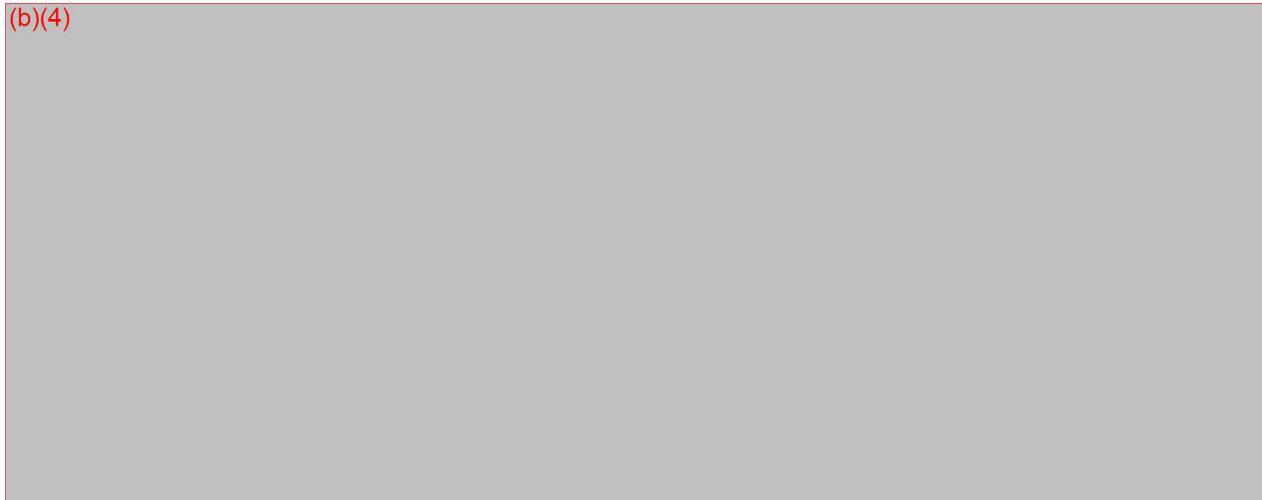
1 Introduction

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2 Goal and Objectives

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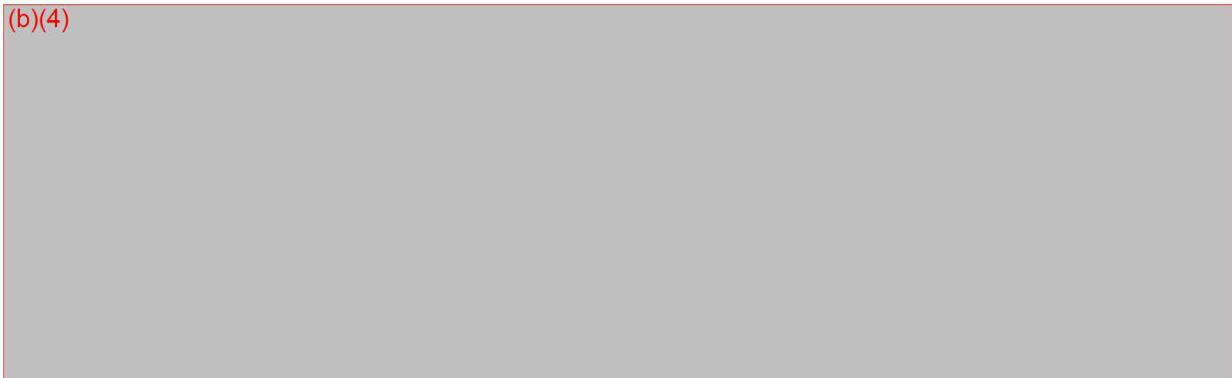
3 References

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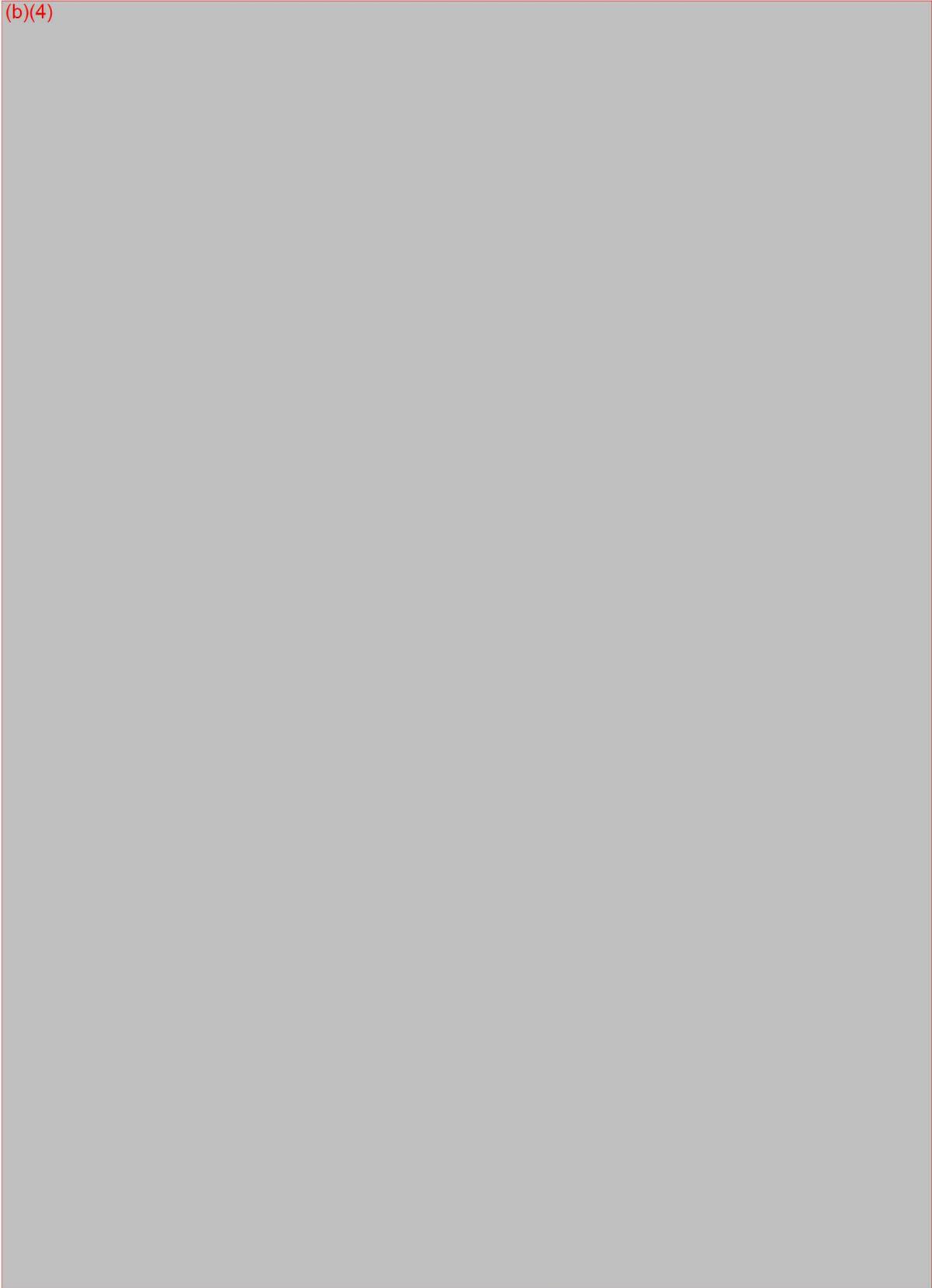
4 Study centers and participants

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5 Use scenarios analysis and task selection

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5.2 Analysis of strengths and weaknesses of similar products

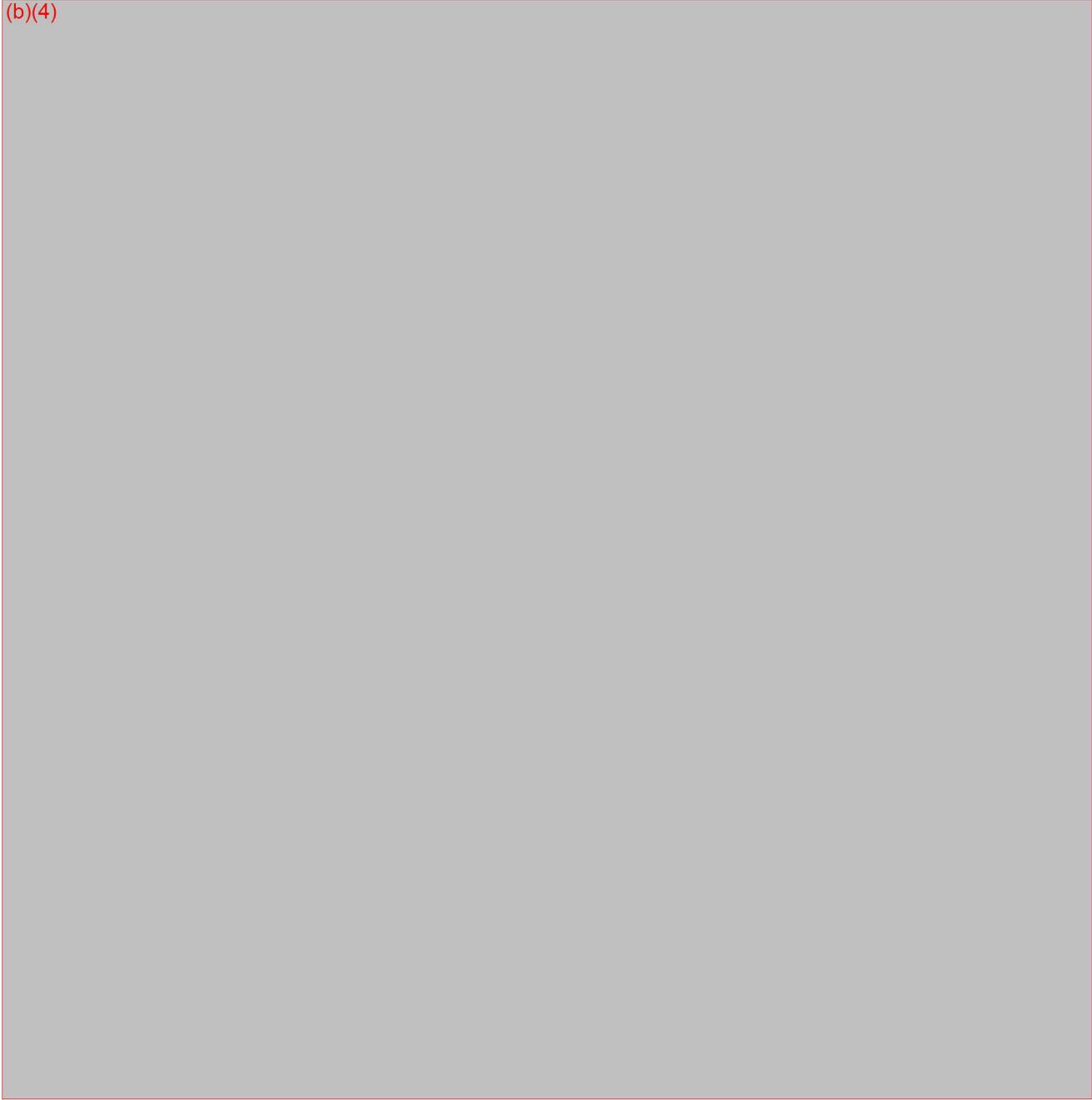
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6 User training

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7 evGuide TLS setup

The evGuide TLS system consists of the following elements (Figure 1):

1. PC/Laptop running Sapiens™ TLS software
2. ECG module
3. USB connection cable to the ECG module
4. ECG cable
5. Sterile Sapiens™ TLS Adaptor connected to the stylet of a PICC catheter
6. Skin ECG electrodes
7. Optional label printer
8. Optional remote control

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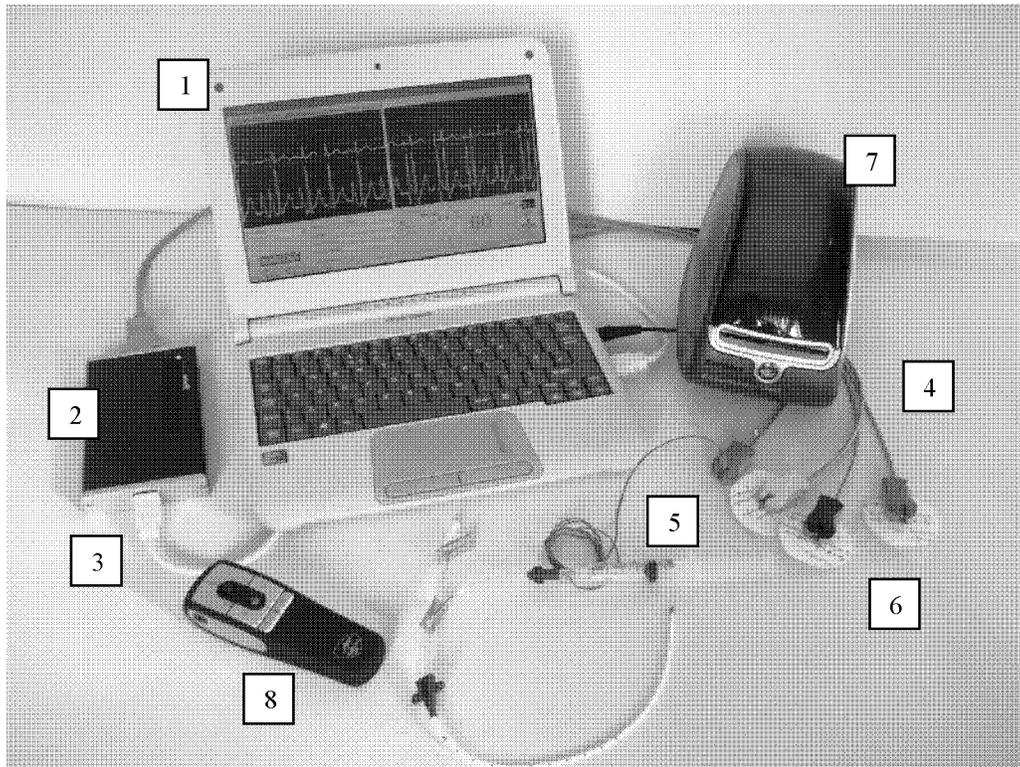


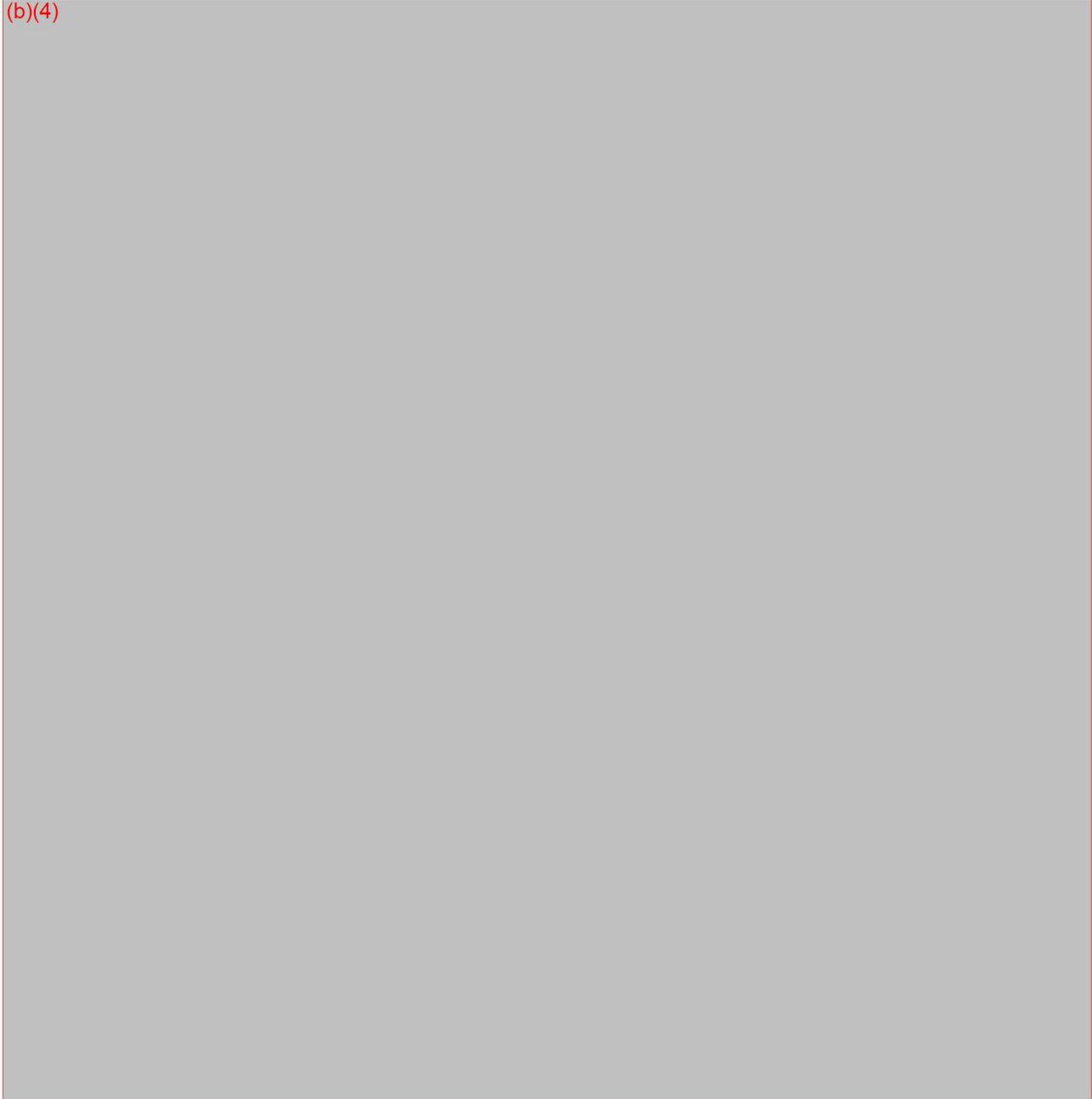
Figure 1: evGuide TLS – system configuration

During the catheter placement procedure, three electrodes are connected to the patient's skin using non-sterile off-the-shelf electrodes the standard ECG cable provided with the evGuide system: yellow clip to the left shoulder, green clip to the lower left abdomen, black clip to the lower right abdomen. The ECG cable is connected to the ECG module outside the sterile field. After a commercially available central venous catheter has been inserted in the central veins per the institution's guidelines, an evGuide TLS adaptor either in the electrical or in the saline configuration is used to connect the proximal end of the venous access device to the red clip (Right Arm) of the ECG cable provided with the system. The sterile evGuide TLS adaptor transitions from the sterile field (connection to the sterile central venous access device) to the non-sterile field (ECG module). The ECG module is connected via a USB cable to the laptop running the evGuide TLS application software. An optional printer can be connected to the laptop in order to document placement procedure results. An optional remote control (360 degrees wireless mouse) can be used to control the evGuide software remotely, potentially from the sterile field. The laptop runs on batteries and, when turned on, automatically starts the evGuide TLS software. The evGuide TLS software displays on the screen endovascular ECG waveforms as acquired by the ECG module from the skin electrode(s) and the evGuide TLS adaptor connected to the venous access device. By looking at the ECG waveform changes the user can estimate the location of the catheter tip as shown in the animation demo included with the evGuide software.

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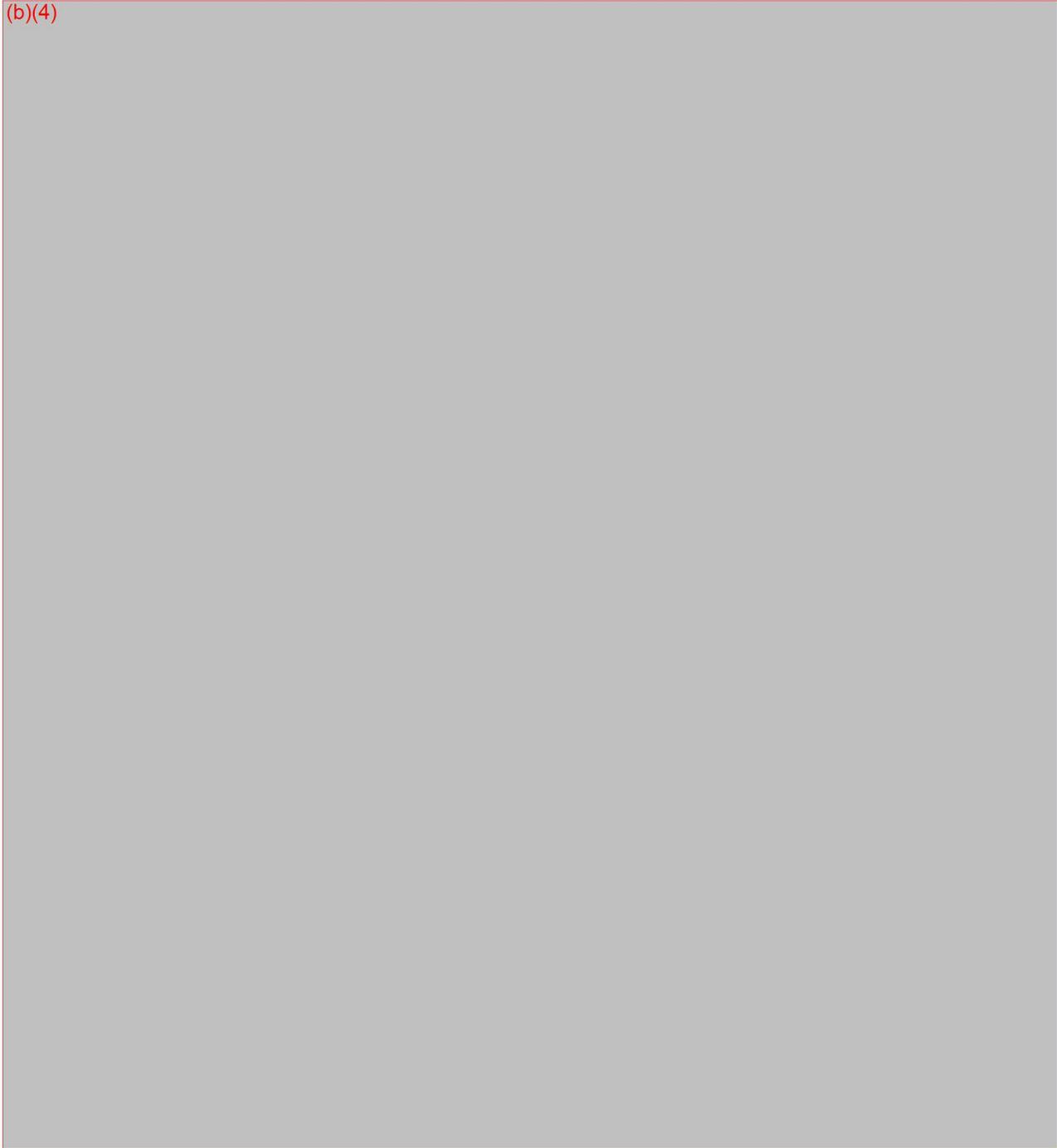
8 Recording of data and of validation test results

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9 Acceptance criteria

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10 Human factors / usability validation – Use Scenarios

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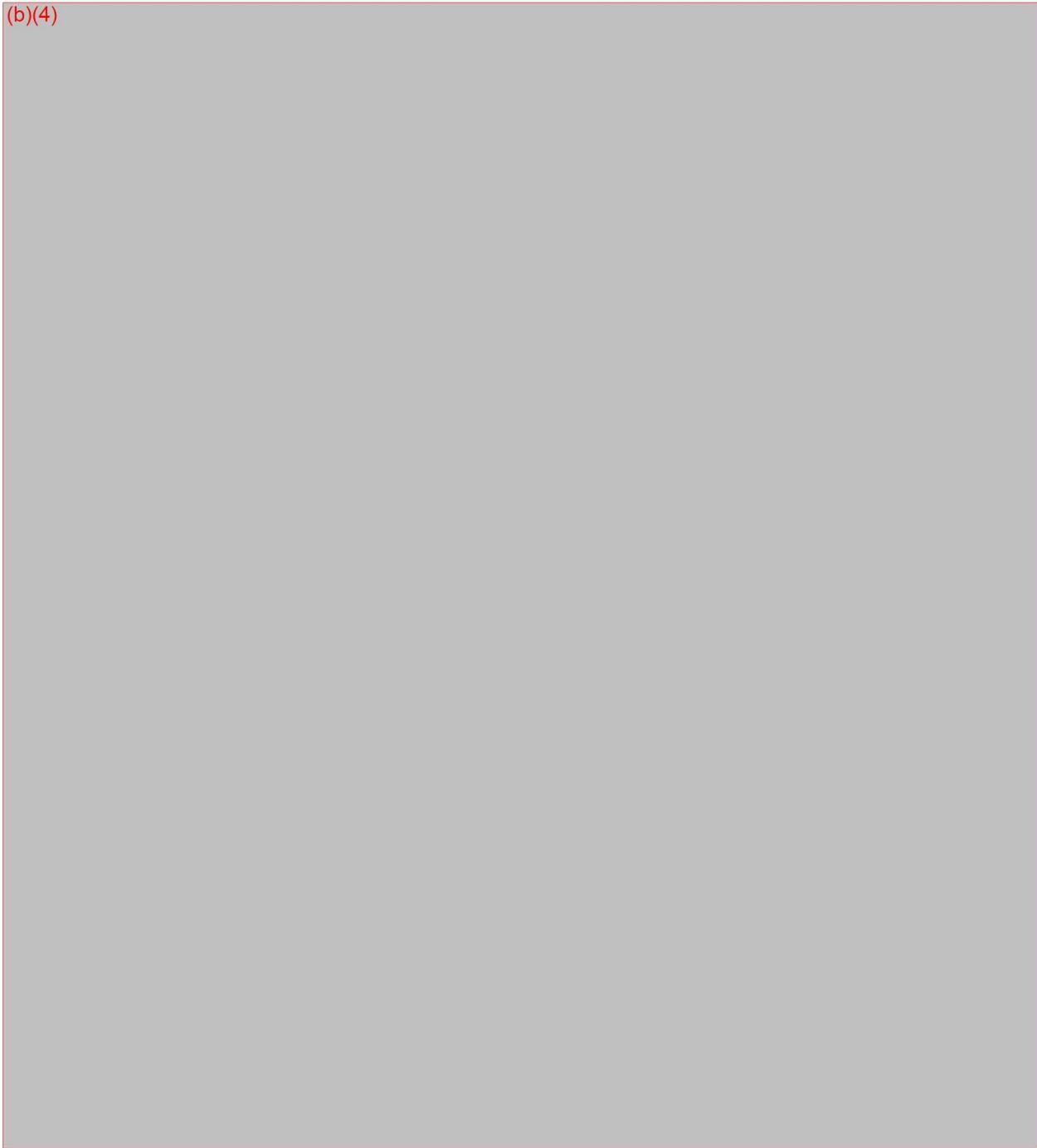
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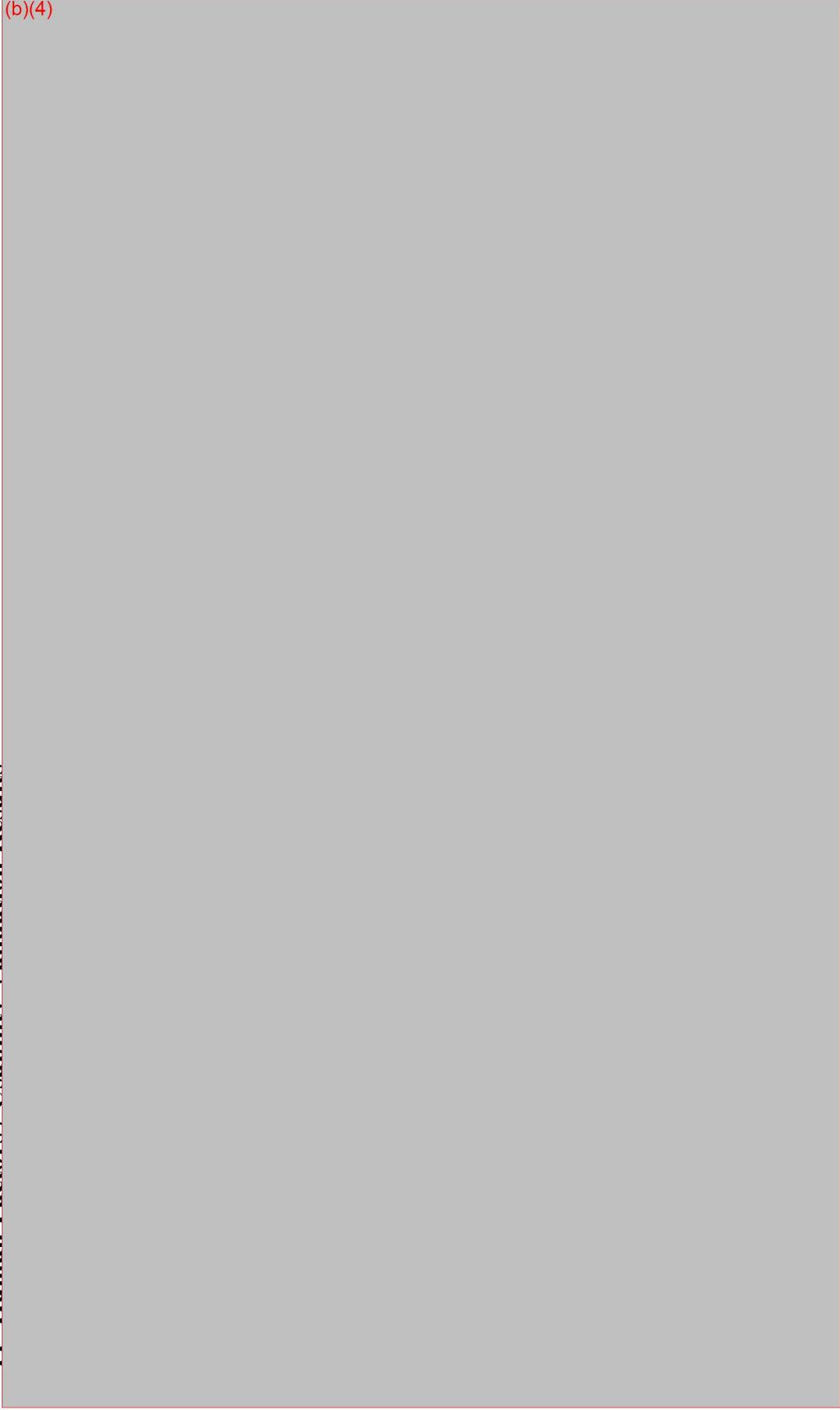
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11 Human Factors / Usability Validation Results



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12 Conclusion

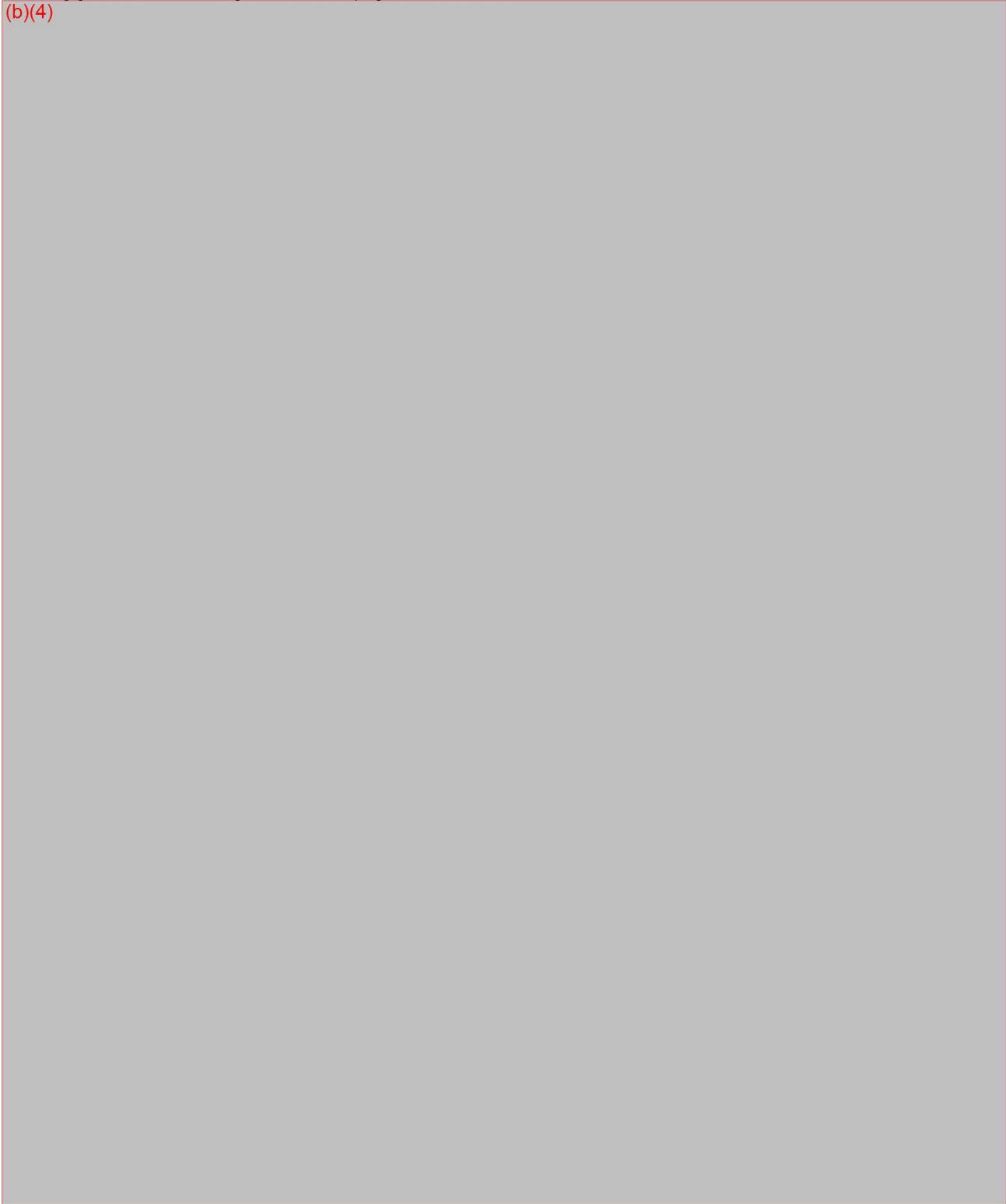
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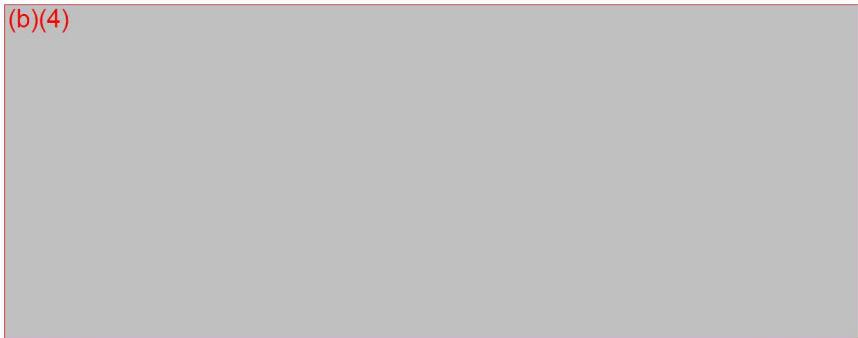
Appendix A: Sample usability questionnaire

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evGuide-Sapiens™ TLS Post-Market Clinical Study Report

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Signature

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REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
S. Grunwald		A	5/28/2010	Initial version
(b)(6)			6/3/2010	Reviewed version

1. Overview and purpose

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2. Study Summary

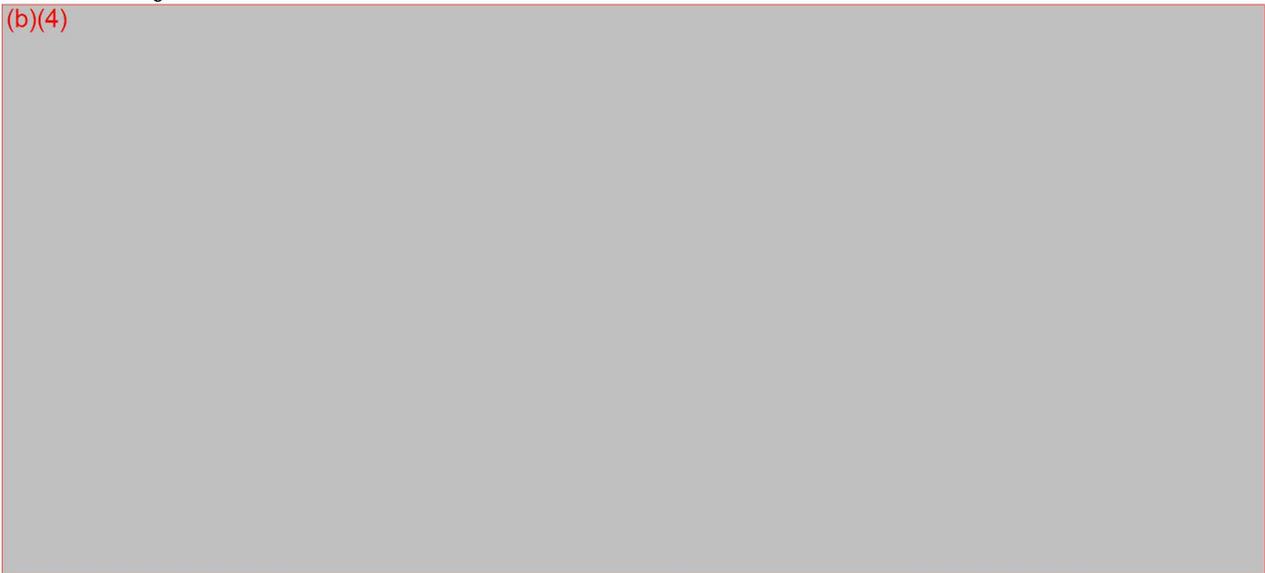
2.1. Indications for Use

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location

2.2. Objective

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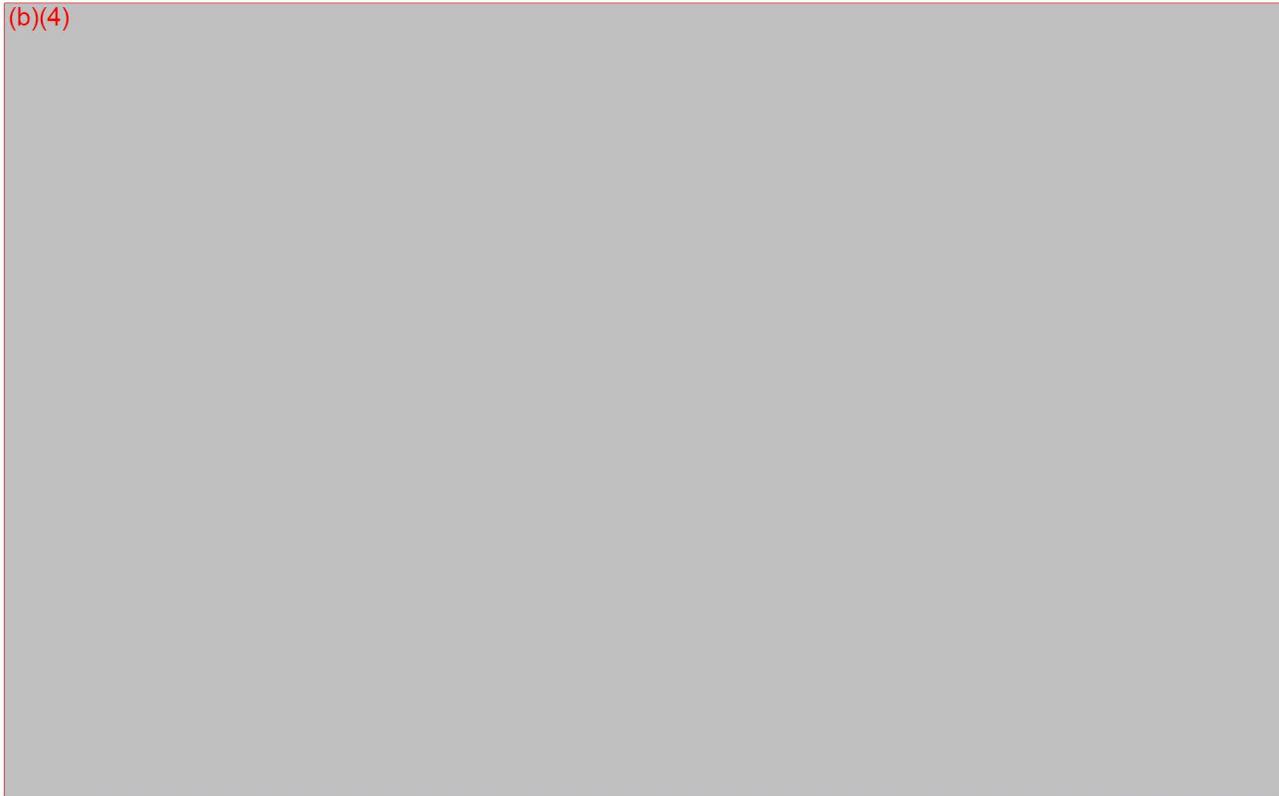
3. Methodology

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4. Patient Selection Criteria

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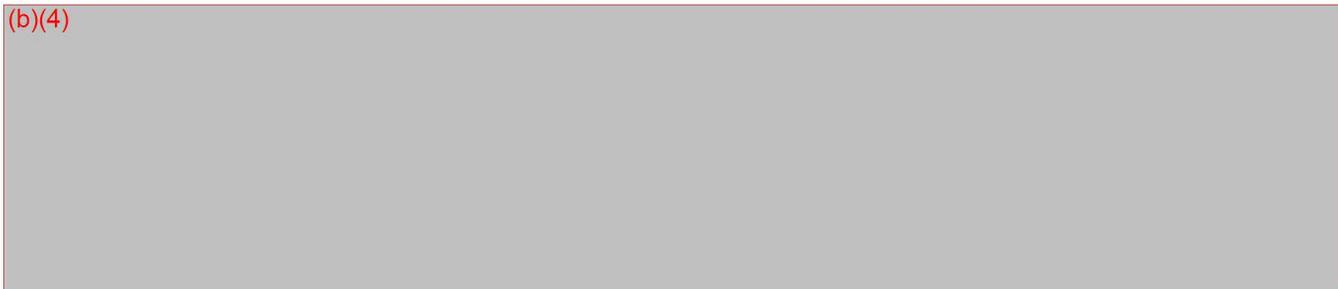
5. Study Results

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6. Conclusion

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CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Date of Submission 12/8/2009	User Fee Payment ID Number MD6046572-956733	FDA Submission Document Number (if known) K093775
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SECTION A TYPE OF SUBMISSION				
PMA <input type="checkbox"/> Original Submission <input type="checkbox"/> Premarket Report <input type="checkbox"/> Modular Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment <input type="checkbox"/> Licensing Agreement	PMA & HDE Supplement <input type="checkbox"/> Regular (180 day) <input type="checkbox"/> Special <input type="checkbox"/> Panel Track (PMA Only) <input type="checkbox"/> 30-day Supplement <input type="checkbox"/> 30-day Notice <input type="checkbox"/> 135-day Supplement <input type="checkbox"/> Real-time Review <input type="checkbox"/> Amendment to PMA & HDE Supplement <input type="checkbox"/> Other	PDP <input type="checkbox"/> Original PDP <input type="checkbox"/> Notice of Completion <input type="checkbox"/> Amendment to PDP	510(k) <input checked="" type="checkbox"/> Original Submission: <input checked="" type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated (Complete section I, Page 5) <input type="checkbox"/> Additional Information <input type="checkbox"/> Third Party	Meeting <input type="checkbox"/> Pre-510(K) Meeting <input type="checkbox"/> Pre-IDE Meeting <input type="checkbox"/> Pre-PMA Meeting <input type="checkbox"/> Pre-PDP Meeting <input type="checkbox"/> Day 100 Meeting <input type="checkbox"/> Agreement Meeting <input type="checkbox"/> Determination Meeting <input type="checkbox"/> Other (specify):
IDE <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	Humanitarian Device Exemption (HDE) <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment	Class II Exemption Petition <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Evaluation of Automatic Class III Designation (De Novo) <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Other Submission <input type="checkbox"/> 513(g) <input type="checkbox"/> Other (describe submission):

Have you used or cited Standards in your submission? Yes No (If Yes, please complete Section I, Page 5)

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name Romedex International Srl		Establishment Registration Number (if known) 3007923075	
Division Name (if applicable)		Phone Number (including area code) 650.209.4838	
Street Address 58 Alcea Arubium		FAX Number (including area code) 650.887.0348	
City Bucharest	State / Province	ZIP/Postal Code 022944	Country ROMANIA
Contact Name Sorin GRUNWALD PhD			
Contact Title Managing Director		Contact E-mail Address sorin@romedex.com	

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Division Name (if applicable)		Phone Number (including area code) 650.209.4838	
Street Address 175 Colorado Av.		FAX Number (including area code) 650.887.0348	
City Palo Alto	State / Province CA	ZIP Code 94303	Country USA
Contact Name Sorin GRUNWALD PhD			
Contact Title US FDA Agent for Romedex International Srl		Contact E-mail Address sorin@romedex.com	

SECTION D1

REASON FOR APPLICATION - PMA, PDP, OR HDE

<input type="checkbox"/> New Device <input type="checkbox"/> Withdrawal <input type="checkbox"/> Additional or Expanded Indications <input type="checkbox"/> Request for Extension <input type="checkbox"/> Post-approval Study Protocol <input type="checkbox"/> Request for Applicant Hold <input type="checkbox"/> Request for Removal of Applicant Hold <input type="checkbox"/> Request to Remove or Add Manufacturing Site	<input type="checkbox"/> Change in design, component, or specification: <input type="checkbox"/> Software / Hardware <input type="checkbox"/> Color Additive <input type="checkbox"/> Material <input type="checkbox"/> Specifications <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Location change: <input type="checkbox"/> Manufacturer <input type="checkbox"/> Sterilizer <input type="checkbox"/> Packager
<input type="checkbox"/> Process change: <input type="checkbox"/> Manufacturing <input type="checkbox"/> Packaging <input type="checkbox"/> Sterilization <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Labeling change: <input type="checkbox"/> Indications <input type="checkbox"/> Instructions <input type="checkbox"/> Performance Characteristics <input type="checkbox"/> Shelf Life <input type="checkbox"/> Trade Name <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Report Submission: <input type="checkbox"/> Annual or Periodic <input type="checkbox"/> Post-approval Study <input type="checkbox"/> Adverse Reaction <input type="checkbox"/> Device Defect <input type="checkbox"/> Amendment
<input type="checkbox"/> Response to FDA correspondence:		<input type="checkbox"/> Change in Ownership <input type="checkbox"/> Change in Correspondent <input type="checkbox"/> Change of Applicant Address
<input type="checkbox"/> Other Reason (specify):		

SECTION D2

REASON FOR APPLICATION - IDE

<input type="checkbox"/> New Device <input type="checkbox"/> New Indication <input type="checkbox"/> Addition of Institution <input type="checkbox"/> Expansion / Extension of Study <input type="checkbox"/> IRB Certification <input type="checkbox"/> Termination of Study <input type="checkbox"/> Withdrawal of Application <input type="checkbox"/> Unanticipated Adverse Effect <input type="checkbox"/> Notification of Emergency Use <input type="checkbox"/> Compassionate Use Request <input type="checkbox"/> Treatment IDE <input type="checkbox"/> Continued Access	<input type="checkbox"/> Change in: <input type="checkbox"/> Correspondent / Applicant <input type="checkbox"/> Design / Device <input type="checkbox"/> Informed Consent <input type="checkbox"/> Manufacturer <input type="checkbox"/> Manufacturing Process <input type="checkbox"/> Protocol - Feasibility <input type="checkbox"/> Protocol - Other <input type="checkbox"/> Sponsor	<input type="checkbox"/> Response to FDA Letter Concerning: <input type="checkbox"/> Conditional Approval <input type="checkbox"/> Deemed Approved <input type="checkbox"/> Deficient Final Report <input type="checkbox"/> Deficient Progress Report <input type="checkbox"/> Deficient Investigator Report <input type="checkbox"/> Disapproval <input type="checkbox"/> Request Extension of Time to Respond to FDA <input type="checkbox"/> Request Meeting <input type="checkbox"/> Request Hearing
	<input type="checkbox"/> Report submission: <input type="checkbox"/> Current Investigator <input type="checkbox"/> Annual Progress Report <input type="checkbox"/> Site Waiver Report <input type="checkbox"/> Final	
<input type="checkbox"/> Other Reason (specify):		

SECTION D3

REASON FOR SUBMISSION - 510(k)

<input checked="" type="checkbox"/> New Device	<input type="checkbox"/> Additional or Expanded Indications	<input type="checkbox"/> Change in Technology
<input type="checkbox"/> Other Reason (specify):		

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	LJS	2	LDF	3	DQY	4	DQY
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

- 510 (k) summary attached
 510 (k) statement

Information on devices to which substantial equivalence is claimed (if known)

	510(k) Number		Trade or Proprietary or Model Name		Manufacturer
1	K091324	1	Sherlock 3CG TPS	1	Bard Access Systems
2	K032613	2	Transvenous Pacemaker Placement Assist Device	2	Peter Rothenberg
3	K973371	3	Conduction Anesthesia Kit - Certodyn	3	B. Braun Medical
4	K843263	4	Arrow-Johans ECG Adaptor	4	Teleflex/Arrow International
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Vascular Access Catheter Accessories

	Trade or Proprietary or Model Name for This Device		Model Number
1	Sapiens Tip Location System (TLS)	1	
2		2	
3		3	
4		4	
5		5	

FDA document numbers of all prior related submissions (regardless of outcome)

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

- Laboratory Testing Animal Trials Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code LJS	C.F.R. Section (if applicable) 880.5970	Device Class <input type="checkbox"/> Class I <input checked="" type="checkbox"/> Class II <input type="checkbox"/> Class III <input type="checkbox"/> Unclassified
Classification Panel General Hospital		

Indications (from labeling)

The Sapiens Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients. Limiting but not contra-indicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm and in central venous catheterization procedures performed through femoral or saphenous veins which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.

FDA Document Number (if known)

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

<input checked="" type="checkbox"/> Original <input checked="" type="checkbox"/> Add <input checked="" type="checkbox"/> Delete	Facility Establishment Identifier (FEI) Number	<input checked="" type="checkbox"/> Manufacturer <input checked="" type="checkbox"/> Contract Manufacturer	<input checked="" type="checkbox"/> Contract Sterilizer <input checked="" type="checkbox"/> Repackager / Relabeler
Company / Institution Name (b)(4)		Establishment Registration Number (b)(4)	
Division Name (if applicable)		Phone Number (including area code) (b)(4)	
Street Address (b)(4)		FAX Number (including area code) (b)(4)	
City (b)(4)	State / Province	ZIP Code	Country (b)(4)
Contact Name (b)(4)	Contact Title (b)(4)	Contact E-mail Address (b)(4)	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	Facility Establishment Identifier (FEI) Number	<input checked="" type="checkbox"/> Manufacturer <input checked="" type="checkbox"/> Contract Manufacturer	<input checked="" type="checkbox"/> Contract Sterilizer <input checked="" type="checkbox"/> Repackager / Relabeler
Company / Institution Name (b)(4)		Establishment Registration Number	
Division Name (if applicable) (b)(4)		Phone Number (including area code) (b)(4)	
Street Address (b)(4)		FAX Number (including area code) (b)(4)	
City (b)(4)	State / Province	ZIP Code	Country (b)(4)
Contact Name (b)(4)	Contact Title (b)(4)	Contact E-mail Address (b)(4)	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	Facility Establishment Identifier (FEI) Number	<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Manufacturer	<input type="checkbox"/> Contract Sterilizer <input type="checkbox"/> Repackager / Relabeler
Company / Institution Name		Establishment Registration Number	
Division Name (if applicable)		Phone Number (including area code)	
Street Address		FAX Number (including area code)	
City	State / Province	ZIP Code	Country
Contact Name	Contact Title	Contact E-mail Address	

SECTION I

UTILIZATION OF STANDARDS

Note: Complete this section if your application or submission cites standards or includes a "Declaration of Conformity to a Recognized Standard" statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
1	13485	ANSI/AAMI/ISO	Medical devices - quality management systems - requirements for regulatory devices	2003	
2	14971	ANSI/AAMI/ISO	Medical devices - application of risk management to medical devices	2007	
3	11135-1	ISO	Sterilization of health care products - ethylene oxide - part 1: Requirements for development, validation, and routing control of a sterilization process for medical devices	2007	
4	10993 -4, -5, -6, -7, -10	ISO	Biological evaluation of medical devices - Part 1: Evaluation and testing	2002, 1999, 1994, 2008, 2002	
5	60601-1-1 60601-1-2	IEC/EN	Safety standards for electrical medical equipment	2000/2001 2003/2006	
6	594-2	ISO	Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment - Part 2: Lock fittings	1998	
7	1041	BS EN	Information supplied by the manufacturer of medical devices	2008	

Please include any additional standards to be cited on a separate page.

Public reporting burden for this collection of information is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of the Chief Information Officer (HFA-710)
5600 Fishers Lane
Rockville, Maryland 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

CDHR PREMARKET REVIEW SUBMISSION COVER SHEET

Romedex International Srl

EvGuide Tip Location System

SECTION I- ADDITIONAL STANDARDS CITED IN THE SUBMISSION

FDA forms 3654 are attached in Appendix L

8	Standards No.	Standards Organization	Standards Title	Version	Date
	980	EN	Graphical symbols for use in labeling of medical devices	2008	
9	Standards No.	Standards Organization	Standards Title	Version	Date
	55011	EN	Industrial, scientific and medical RF equipment – radio disturbances characteristics – limits and methods	2007	
10	Standards No.	Standards Organization	Standards Title	Version	Date
	730	IEEE	Software Quality Assurance	1998	
11	Standards No.	Standards Organization	Standards Title	Version	Date
	829	IEEE	Software test documentation	1998	
12	Standards No.	Standards Organization	Standards Title	Version	Date
	830	IEEE	Recommended practices for software requirements specification	1993	
13	Standards No.	Standards Organization	Standards Title	Version	Date
	1058	IEEE	Software Project management	1998	
14	Standards No.	Standards Organization	Standards Title	Version	Date
	1074	IEEE	Developing software life cycle	1997	
15	Standards No.	Standards Organization	Standards Title	Version	Date
	J-STD-06	IEEE	Software development plan	1995	

CDHR PREMARKET REVIEW SUBMISSION COVER SHEET
Romedex International Srl
EvGuide Tip Location System
SECTION I - ADDITIONAL STANDARDS CITED IN THE SUBMISSION

FDA forms 3654 are attached in Appendix L

8	Standards No.	Standards Organization	Standards Title	Version	Date
	980	EN	Graphical symbols for use in labeling of medical devices	2008	June 2008
9	Standards No.	Standards Organization	Standards Title	Version	Date
	55011	EN	Industrial, scientific and medical RF equipment – radio disturbances characteristics – limits and methods	2007	May 2007
10	Standards No.	Standards Organization	Standards Title	Version	Date
	730	IEEE	Software Quality Assurance	1998	June 1998
11	Standards No.	Standards Organization	Standards Title	Version	Date
	829	IEEE	Software test documentation	1998	1998
12	Standards No.	Standards Organization	Standards Title	Version	Date
	830	IEEE	Recommended practices for software requirements specification	1998	1998
13	Standards No.	Standards Organization	Standards Title	Version	Date
	1058	IEEE	Software Project management	1998	1998
14	Standards No.	Standards Organization	Standards Title	Version	Date
	1074	IEEE	Developing software life cycle	1997	1997
15	Standards No.	Standards Organization	Standards Title	Version	Date
	J-STD-06	IEEE	Software development plan	1995	1995

SECTION 4: INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K093775

Not known at this time _____

Device Name: Sapiens™ TLS

Indications for Use:

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)
Page ___ of ___
(Posted November 13, 2003)

**evGuide ECG Accuracy Comparison
Protocol and Test Report**

REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
S. Grunwald		A	4/2/2010	Initial version

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8. Test Protocol and Results – Clinical Setting.....	13
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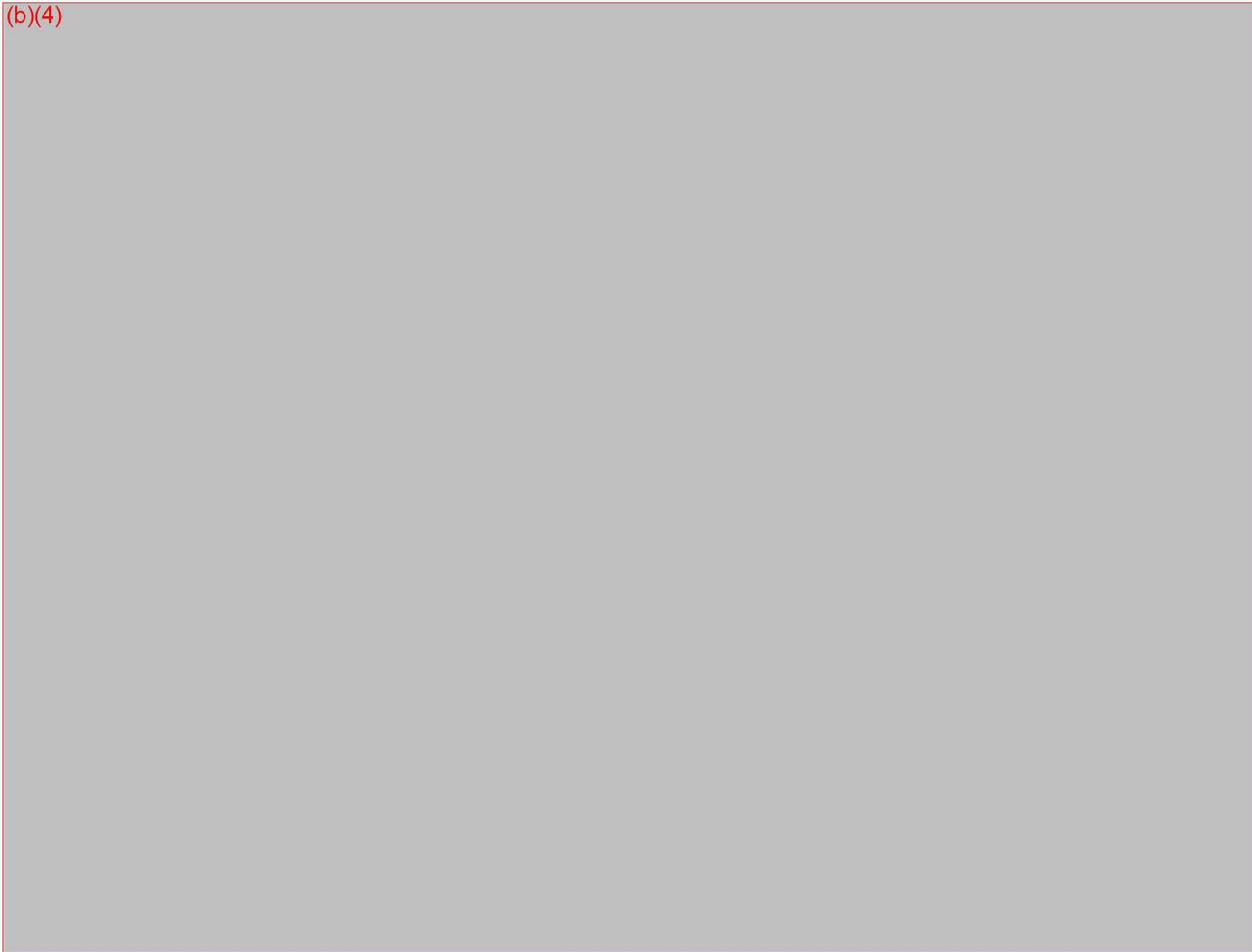
1. Purpose & Scope

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2. Overview of the Test Methods

(b)(4)

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3. Acceptance Criteria

3.1. Bench top testing

(b)(4)

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3.2. Animal Study

(b)(4)

A horizontal rectangular area of the document is redacted with a solid grey fill. The redaction covers the content under section 3.2.

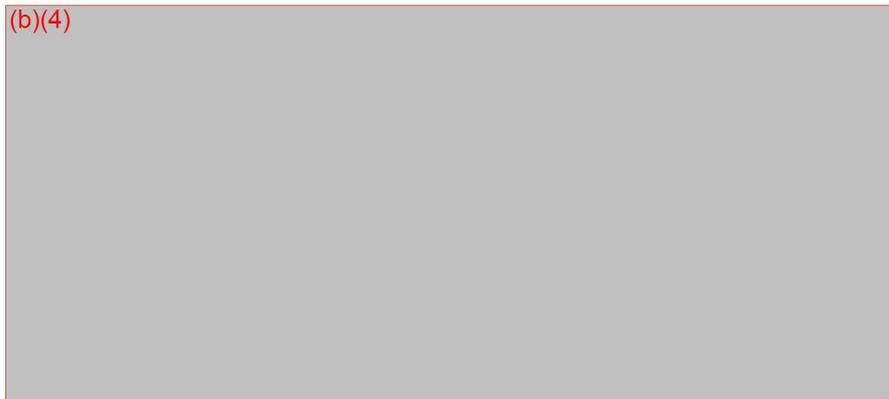
3.3. Clinical Settings

(b)(4)



4. Equipment, Material & Setup

(b)(4)



(b)(4)

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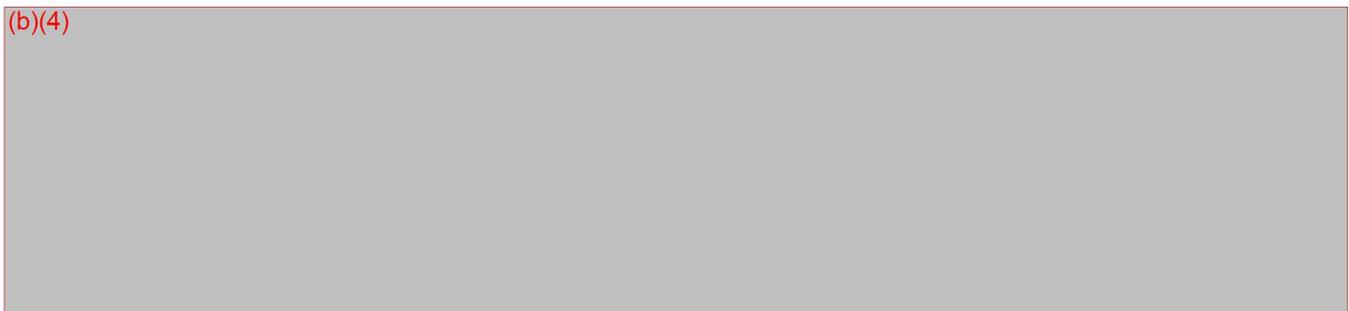
5. References

- (b)(4)
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6. Test Protocol and Results - Bench Top

6.1. Electrical Testing

(b)(4)

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	Test Case Electrical Resistance	Measured Electrical Resistance R [Ohm]	Min – Max Predicate Device Rm - RM [Ohm]	Short circuit [Ohm]	Acceptance Criterion	Pass Fail
1	(b)(4)					
2	(b)(4)					
3	(b)(4)					
4	(b)(4)					
5	(b)(4)					
6	(b)(4)					
7	(b)(4)					
8	(b)(4)					
9	(b)(4)					
10	(b)(4)					

	(Fig. 6)					
11	(b)(4)					
12						

6.2. Waveform Measurement



(b)(4)



(b)(4)



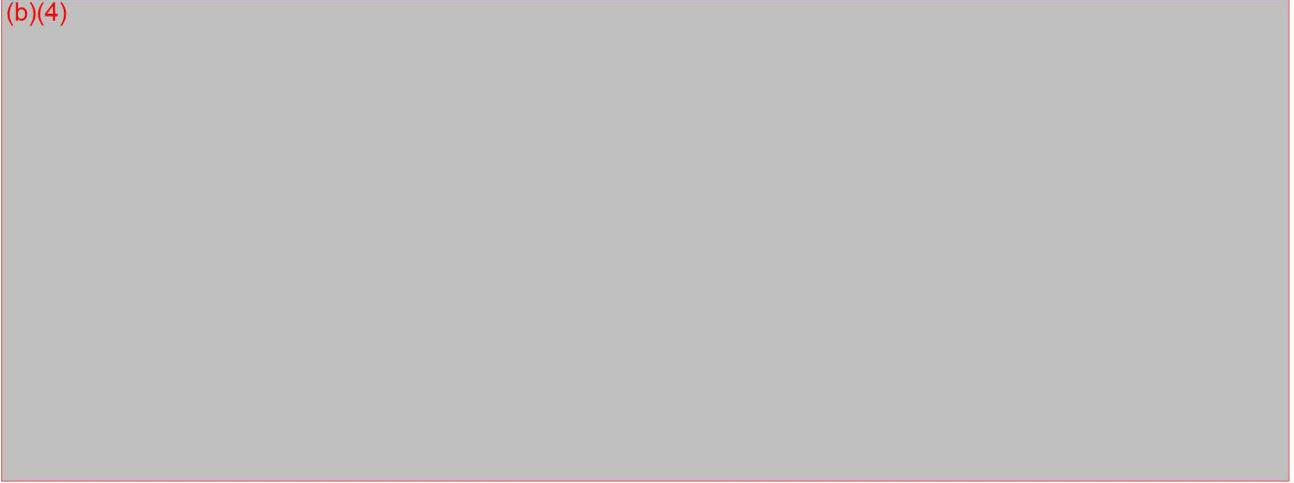
	Test Case Waveform Measurement	(b)(4)	Pass Fail
1	(b)(4)		
2			
3			
4			
5			
6			
7			
8			
9			

		(b)(4)		
10	(b)(4)			
11				
12				
13				

7. Test Protocol and Results – Animal Study

(b)(4)

(b)(4)

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(b)(4)

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	Test Case	(b)(4)	(b)(4)
--	------------------	--------	--------

	Waveform Measurement	(b)(4)
1	(b)(4)	(b)(4)
2	(b)(4)	(b)(4)
3	(b)(4)	(b)(4)

8. Test Protocol and Results – Clinical Setting

8.1. evGuide Electrical Adaptor

(b)(4)



Fig 8.1 (b)(4)



(b)(4)

	Guided device	Date	(b)(4)	Pass Fail
1	(b)(4)			
2				
3				
4				
5				
6				
7				
8				

9	(b)(4)
10	
11	
12	

8.2. evGuide Saline Adaptor

(b)(4)



Figure 8.2.1: (b)(4)



Fig. 8.2.2: (b)(4)

(b)(4)

	Case	Assessment of ECG accuracy evGuide Electrical vs. evGuide Electrical & Arrow-Johans	Pass Fail
1	(b)(4)	[Redacted]	
2			
3			
4			
5			
6			
7			
8			
9			

9. Conclusion

(b)(4)





Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation

Nancy L. Moureau, RN, BSN, CRNI, CPUI, Glenda L. Dennis, RN, CCRN, Elizabeth Ames, RN, CCRN, Robyn Severe, RN, BSN

Abstract

Background: The current standard of care for Peripherally Inserted Central Catheters (PICCs) is radiological confirmation of terminal tip location. Tip location practices in Europe have used electrocardiographic (EKG) guided positioning for central venous catheters for more than twenty years with tip positioning safely confirmed over thousands of insertions (Madias, 2003). The goal of this group was to confirm the findings of a study performed by Pittiruti and his team; and to establish safe function in the use of EKG guidance for verification of terminal tip position with PICCs placed at McKenzie Willamette Medical Center.

Methods: In 2008/2009 McKenzie Willamette Medical Center conducted a study to determine whether or not EKG guidance can be used as a reliable means to accurately place and confirm terminal tip location of PICCs. A group of trained nurses performed PICC placement using EKG guidance followed by radiological confirmation of SVC position. All PICCs placed from October 2008 to December 2009 were included in the study. Tip location was confirmed using either radiological confirmation alone, EKG plus radiological confirmation, or EKG alone.

Results: A total of 417 PICCs were placed during the study period. EKG guidance alone was used in the placement and confirmation of 168 PICCs. Both EKG and chest x-ray confirmation were used in the placement of 82 of the PICCs; 240 of the PICCs were placed with the use of EKG and then position correlated using the traditional chest x-ray procedure.

Discussion: EKG guided PICC placement proved accurate in consistently guiding the terminal tip to the superior vena cava (SVC). The procedure was easily taught and duplicated by members of the PICC team. The study demonstrated a definite correlation between the height (size) of the P-wave and the location of the terminal tip within the SVC. With knowledge of this correlation, transition from placing PICCs using EKG guidance with chest x-ray confirmation to confirmation of tip placement using just EKG guidance without chest x-ray confirmation was attained. Application of EKG placement/confirmation performed during insertion saves time previously spent waiting for x-ray confirmation readings, saves cost of chest x-ray, prevents patient exposure to radiation and saves time required for tip repositioning of malpositioned tips found after the end of the procedure.

Background

While radiographic imaging is the current standard of care for Peripherally Inserted Central Catheter (PICC) tip confirmation (Scott, 1995), electrocardiographic (EKG) guided positioning, which has been widely used throughout the world in conjunction with central venous catheters (CVCs), is applicable for position confirmation of

PICCs (Chu, et al., 2004; Jalaieian, Mottahedi, Ghanad, & Peyvandi, 2005; Pittiruti, et al., 2008). With the number of PICC placements increasing, a more accurate and efficient means of tip confirmation is needed. PICCs are placed primarily through the veins of the arm. One of the primary reasons for chest x-ray (CXR) is to rule out the presence of insertional complications such as malposition (Jalaieian, et al., 2005). Use of EKG guidance for placement of PICCs can speed time to first usage by reducing time required for x-ray interpretation and by reducing repositioning delays (Francis, Picard, Fajardo, & Pizzi, 1992; Tiernay, Katke, & Langer, 2000).

Chest x-rays are used to verify the terminal tip after CVC

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DOI: 10.2309/java.15-1-3

placement as well as to rule out the presence of pneumothorax, a complication occurring with subclavian or internal jugular catheters. While EKG tip location does not address the presence of a pneumothorax, PICCs consistently demonstrate reduced insertional risk without pneumothorax. When patient symptoms demonstrate respiratory complications following CVC placement, a CXR is easily performed to identify the origin of the problem.

The challenge with small diameter PICCs is to locate the terminal tip and have consistent interpretation of where the distal superior vena cava is positioned. Radiographic films taken with portable equipment use the anterior/posterior (A/P) view to verify position of the terminal CVC tip. Radiographic interpretation variations occur with positioning, anatomic aberrations, arterial placement and obesity providing a false sense of security with the A/P view. A corresponding lateral view has been noted by several authors as necessary in determining accurate placement of CVCs and PICCs but is rarely employed in daily practice (Lum, 2004; Madias, 2003; Royer, 2001). Variation is also present in landmarks used to interpret radiographic results and distal SVC position on 2-D radiographic films (Vesely, 2003). A more accurate means of tip position confirmation has been extensively studied throughout the world, primarily with CVCs, but more recently with PICCs (Chu, et al., 2004; Jalaeian, et al., 2005; Pittiruti, et al., 2008). Pittiruti and his team of physicians and nurses performed multiple EKG confirmation studies on open and closed ended PICCs validating accurate distal SVC position. The methods used included guidewire and saline infusion for electrical conductivity represented in the p-wave of an electrocardiogram (EKG) rhythm. When a normal sinus rhythm is visible on an EKG monitor, the p-wave is seen just prior to the QRS complex (QRS). With intracavitary monitoring of electrical activity the p-wave changes and becomes amplified or taller as a catheter is advanced into the SVC. When the p-wave peaks, the tip is at the SVC/right atrial junction (SVC/RA). This study is thought to be the first published nursing-based PICC EKG tip location study performed in the United States (US), confirming the findings of Pittiruti and his team while demonstrating application with US based equipment.

Methods

In 2008/2009 McKenzie Willamette Medical Center conducted a study of EKG guided placement of PICCs followed by radiological confirmation of SVC position to determine if the procedure could be duplicated with accuracy and dependability. Peripherally inserted central catheters used in the study included both closed-ended (Groshong™ Bard Access, SLC Utah) and open-ended (Power PICC™ Bard Access, SLC Utah) catheters. A review of EKG literature available at the time of the study revealed 95-100% accuracy with EKG guided CVC or PICC placement into the superior vena cava (SVC) (Francis, et al., 1992; Hoffman, et al., 1988; Karaaslan, Altinisik, Peker, Nayir, & Ozmen, 2009; W. T. McGee, et al., 1993; Pittiruti, et al., 2008; Schummer, et al., 2004). The desire to recreate this study was based on the level of success reported in the literature.

Following a Critical Care Committee review and approval, patients undergoing PICC placement from October 2008 through December 2009 received verification of tip placement with either radiological confirmation alone, EKG and radiological

confirmation, or EKG alone. The first ten patients involved in the study used the EKG tip location method and a secondary confirmation with chest x-ray method. After the initial ten patients, PICCs were placed using the EKG method only, with verification based on the judgment of the clinician reading the EKG during placement. When chest x-ray was necessary for other reasons, catheter tip location was also reviewed and findings were correlated with results of EKG tip location method.

Criteria for patients' inclusion with EKG tip location study included all of the following: a) any adult 18 years or older; b) with a normal sinus rhythm; c) a clearly visible p-wave; d) who were scheduled to receive a PICC for prescribed treatment. Criteria which excluded patients from the EKG placement study included: a) the presence of an arrhythmia resulting in lack of p-wave or indistinguishable QRS complex, or b) the dependency on a pacemaker for heart function. Initially a conservative approach was applied at this institution for selection of PICC candidates for use of EKG tip location. Placement of catheters was performed by PICC trained experienced radiological nurses using the guidewire and saline EKG location techniques. Radiographic confirmation was verified by interventional cardiologists for consistency with this study. EKG equipment included an EKG adapter (Pacerview, San Clemente, CA) and a cable with alligator clamp (Pacerview, Grabber, San Clemente, CA)

When placing a PICC using the EKG tip location method, a conductor is required within the tip of the catheter. Two methods of creating conductivity within the catheter include: use of a guidewire within the catheter or filling the catheter with a saline solution. Both of these methods are described below and were used as steps in the study.

Steps for placing EKG guided PICC with guidewire technique:

1. Attach 3 or 5 lead monitor to patient (always apply all new leads); determine if the patient is in Normal Sinus Rhythm (NSR), atrial fibrillation or is dependently paced. If the patient is in NSR, proceed with EKG guided PICC insertion.
2. Detach the left leg lead from the patient and attach it (red lead) to the EKG adapter lead button.
3. Select the vein for PICC insertion using ultrasound scanning.
4. Measure selected vein to estimated location of Superior Vena Cava (SVC).
5. Set up sterile field; prep and drape patient.
6. Don personal protective equipment (PPE).
7. Trim the PICC to the desired length making sure guidewire is at the very distal end of the PICC but not extended outside the catheter. Flush PICC with normal saline.
8. Place the EKG cable into sterile cover/sleeve. Remember the cable is unsterile and must be covered.
9. Insert the PICC using ultrasound guided modified Seldinger technique (MST).
10. When the PICC is approximately 50% to its intended goal of the distal SVC/caval atrial junction, attach the EKG Alligator cable to the guide wire in the PICC, carefully punching the tip of the grabber through the sterile sleeve and covering the connection with a sterile 4x4.
11. Flush the PICC again with normal saline.

12. An inverted QRS complex should appear on the monitor. The p-wave is normal size initially, increasing in amplitude as the PICC is advanced. Compare p-wave size from initial normal complex to peak level. (Note: Size may vary with QRS complex comparison with p-wave and be larger than QRS. The determinant is p-wave change measured to peak with biphasic notch.)
13. When the p-wave is about $\frac{3}{4}$ of the full peaked level, approx $\frac{3}{4}$ the size of the QRS, the PICC tip is in the lower or distal SVC (also known as proximal SVC in relation to the heart).
14. When the p-wave is fully peaked or at the highest amplitude, it is at the caval atrial junction (SVC/RA).
15. When a small positive wave spike is seen in the p-wave, the tip is in the right atrium.
16. When the p-wave becomes biphasic (expands beyond the baseline up and down), the PICC tip is in the low right atrium/high right ventricle. This is known as an atrial spike.
17. If no QRS pattern is seen during advancement of the catheter, the PICC has malpositioned in the internal jugular or contra-lateral in the opposite subclavian vein. Attempts to reposition can be made until the inverted QRS is seen on the monitor.
18. Print final strip with P-wave at the same amplitude as QRS to confirm location of the tip. Include this EKG strip as part of the patient's record.

(Note: You may see some respiratory variation in the wave form.)

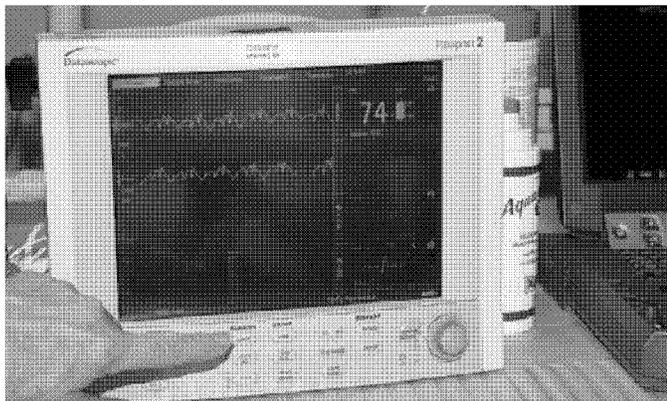


Photo 1. EKG Interpretation of PICC tip location. Note p-wave amplitude near amplitude of inverted QRS. This demonstrates PICC tip location near the Caval Atrial Junction. **G Dennis**

Steps for placing EKG guided PICC with saline filled lumen:

1. Attach 3 or 5 lead monitor to patient (always apply all new leads; do not use any currently in use with other monitors); determine if the patient is in Normal Sinus Rhythm (NSR), atrial fibrillation, or is dependently paced. If the patient is in NSR, proceed with EKG guided PICC insertion.
2. Detach the left leg lead from the patient and attach it (red lead) to the EKG adapter lead button.
3. Select the vein for PICC insertion using ultrasound scanning.

4. Measure selected vein to estimated location of Superior Vena Cava (SVC).
5. Set up sterile field; prep, and drape patient. Drop a sterile injection cap with needle penetration septum onto the sterile field.
6. Don personal protective equipment (PPE).
7. Prefill a 20cc syringe with saline and attach a steel needle.
8. Trim the PICC to the desired length; remove the guidewire and apply the injection cap with needle septum. Flush the PICC with normal saline.
9. Place the EKG cable in sterile cover/sleeve.
10. Insert the PICC using ultrasound guided modified Seldinger technique (MST).

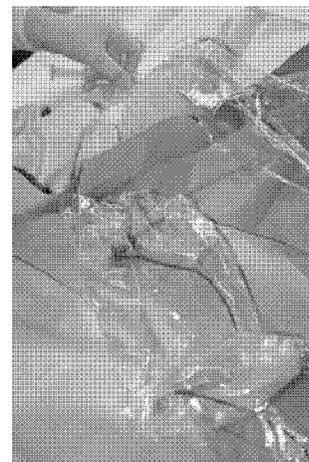


Photo 2. Sterile sleeve covering the EKG alligator cable. **G Dennis**

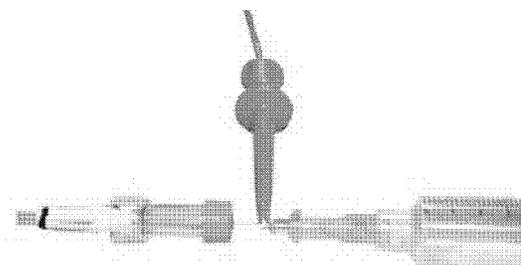
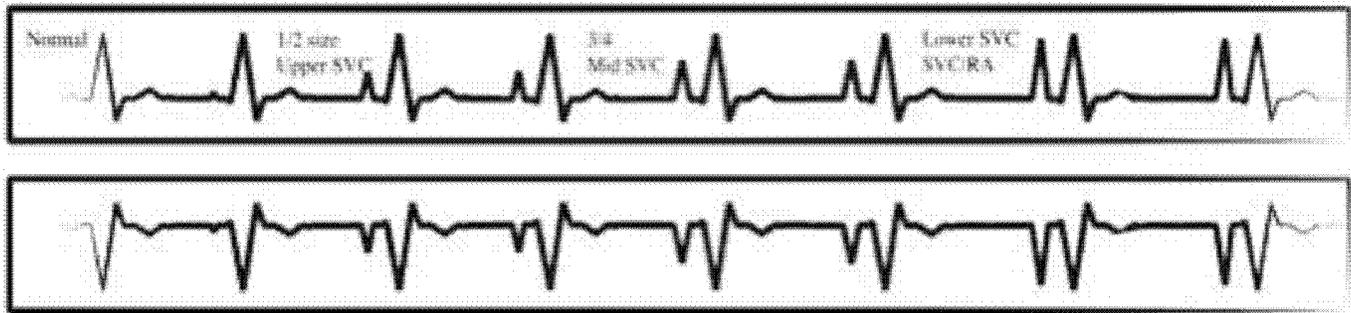


Photo 3. Close up of EKG alligator cable clipped to steel needle shaft for saline-only method of EKG tip placement. **G Dennis**

11. When the PICC is approximately 50% to its intended goal of the distal SVC/caval atrial junction, attach the alligator cable to the needle shaft (the needle is inserted through the injection cap) carefully punching the tip of the grabber through the sterile sleeve, and covering the connection with a sterile 4x4.
12. Flush the PICC again with normal saline 5-10ml.
13. An inverted QRS complex appears on the monitor. The p-wave is normal size initially, increasing in amplitude as the PICC is advanced. Compare p-wave size from initial normal complex to peak level. (Note: Size may vary with QRS complex comparison with p-wave and be larger than QRS. The determinant is p-wave change measured to peak with biphasic notch.)
14. When the p-wave is about $\frac{3}{4}$ the size of the QRS, the PICC tip is in the lower SVC.
15. When the p-wave is the same amplitude as the QRS, it is at the caval atrial junction.
16. When a small positive wave spike is seen in the p-wave,

Figure 1: P-Wave Simulated Interpretation (used with permission PICC Excellence, Inc.)



the tip is in the right atrium.

17. When the p-wave becomes biphasic (expands beyond the baseline), the PICC tip is in the low right atrium/high right ventricle. This is known as an atrial spike.
18. If no QRS pattern is seen during insertion procedure, the PICC has malpositioned in the internal jugular or is contralateral in the opposite subclavian vein. Attempts to reposition can be made until the QRS is seen on the monitor.
19. Print final strip with P-wave at peak amplitude as QRS to confirm location of the tip. Include this EKG strip as part of the patient's record.

(Note: You may see some respiratory variation in the wave form)

Results

A total of 417 PICCs were placed from October 2008 through December 2009 in this 100 bed facility. EKG tip location was used in 250 (60%) of PICC placements. Of those correlated with CXR results by the interventional cardiologist, 240 agreed and 8 disagreed (3%) with optimal position in the SVC. Valved catheters composed the largest PICC group with 399 (96%).

Left-sided placements were in only 76 of the 417 placements (18%) and basilic vein was used in 346 (83%) placements. Position verified as distal/lower SVC or caval/atrial junction with 367 placements (88%). Other placement locations in 50 (12%) placements included SVC 2 (.4%), mid-SVC 18 (4%), axial 4 (.9%) and other 26 (6%).

The most common reasons for the inability to use EKG were:

- a) The presence of atrial fibrillation
- b) Rhythm that prevented or impaired p-wave interpretation
- c) Patient dependence on a pacemaker.

The study confirmed when using the EKG method to place PICCs the terminal tip location could be predicted based on the size of the p-wave, relative to the peak level and QRS complex. These findings were confirmed through correlation with chest x-rays after placement with EKG.

A learning curve was present in gaining proficiency in interpretation and with application of all advantages of EKG PICC tip guidance. Specific details for the learning period in this study were the following:

- Four catheters required repositioning in December 2008. Three PICCs were located in the right atrium, and one looped in the innominant vein extending contralateral. All four locations required retraction or repositioning of the catheter.

- Two catheter placements failed to visualize QRS complex or p-wave changes with one curled in the basilic vein and the other repositioned from azygos vein twice prior to correct positioning with EKG. Both placements were then confirmed using chest x-ray.
- One of the eight PICCs listed as uncorrelated from EKG to CXR had a position in the distal SVC; retraction of 5cm was originally advised by radiologist.

Discussion

Throughout the 15 month period of this study, EKG guidance was used in positioning and confirming placement for PICCs. In the most difficult placements, EKG reduced the number of chest x-rays needed and provided immediate feedback to the clinician to speed placement. Analysis of p-wave amplitude to note peak configuration and biphasic activity during advancement through the SVC and RA junction requires training and experience to reach 100% accuracy in interpretation.

Respiratory variations, ventilator vibration and action, muscle twitching or excessive patient movement caused signal interruptions or inability to interpret tracing of EKG and p-wave. Closed ended catheters require a continuous infusion of saline or flushing of saline to keep the valve open and the signal somewhat consistent. Even with a steady infusion, breaks may occur with valved catheters where signal is lost but should return with continued flow of saline to reopen valve. Application of new leads to each patient resulted in improved signal.

Variables to this study included:

1. Poor initial understanding of biphasic spike and presentation of p-wave in right atrium at the beginning of the study period.
2. Adding 4 new clinicians during the course of the 2008/2009 study may have caused variation and reduction of accuracy in data interpretations.
3. Multiple physicians interpreting PICC tip chest x-rays in different acceptable locations.
4. Use of the data category "other" with failure to specify in 4% of final tip location results. Data collection categories overlapped, (distal SVC, Caval atrial junction, mid SVC, lower SVC, SVC, axial, other) and greater clarity was needed in the study for correct final placement.

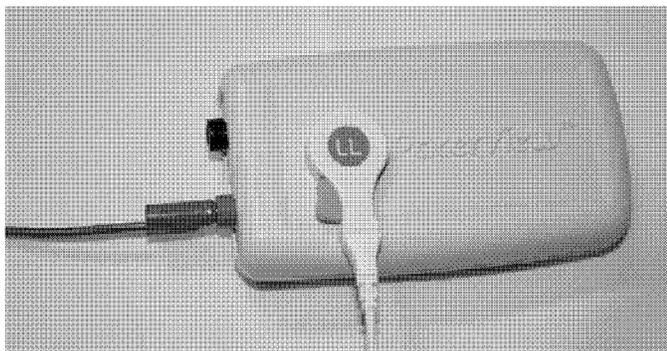


Photo 4. Pacerview device. Note EKG lead LL attached to Pacerview unit. *G Dennis*



Photo 5. Vygon/Advanced Medical Vygocard and cable connection for catheter and EKG monitor. *PICC Excellence, Inc*

Table 1

EKG Device Company	Name of Device	FDA Indication/European CE
Arrow International www.arrowintl-europe.com	Adapter: Arrow-Johans™* JAdapter for Right Atrial Electrocardiography	FDA Clearance: pending CE Mark: Yes
B. Braun www.cvc-partner.com	Certodyn, Alphacard	FDA Clearance: unknown CE Mark: Yes
Pacerview www.pacerview.com	Pacerview device and Grabber	FDA Clearance: Yes No longer available for purchase
Romedex International SRL www.romedex.com	Sapien Tip Location System TLS	FDA Clearance: pending CE Mark: Yes
Vasonova www.vasonova.com also has doppler	Vasonova Visual Positioning System (VPS)	FDA Clearance: Yes CE Mark: unknown
Vygon/Advanced Medical www.vygonusa.com	Vygocard and cable	FDA Clearance: pending CE Mark: Yes



Photo 6. B Braun Alphacard. *PICC Excellence, Inc.*

The current standard of radiographic interpretation of CVC/PICC tip location by chest x-ray is often imprecise and subject

to observer variability. In this study, variation was noted in the tip determinations by different radiologists and in their definition of optimal placement location. Differing anatomic landmarks (carina, right superior heart border) are used to identify optimal location in the SVC with interpretation changing from person to person, some desiring SVC/RA junction and others opting for mid-SVC rather than deeper placement (Vesely, 2003). When viewing a chest x-ray flat film or even a digital film, the exact desired location is difficult to pin-point; typically there is a range of acceptable options and even those can be debated. Manufacturer recommendations for central line placement specify placement in the SVC and not the right atrium. FDA central venous catheter working group identified distal SVC as optimal location for non-dialysis catheters (Scott, 1995). EKG guidance provides a precise SVC position in more than 95% of placements (Francis, et al., 1992; D. McGee & Gould, 2003; W. T. McGee, et al., 1993; Schummer, et al., 2004) also reducing the need to reposition catheters (Gebhard, et al., 2007). In this study accuracy of correlated EKG/CXR position reached 97%. Validation of EKG positioning correlates with the gold standard for positioning when using the transesophageal imaging (Chu, et al, 2004). While it is

prudent to recheck tip position with a chest x-ray when abnormal symptoms arise following CVC or PICC placement, consensus is that EKG virtually eliminates the need to confirm tip position by chest x-ray (Madias, 2003). CXR may be necessary for CVCs other than PICCs and certainly for those patients in which the p-wave is not discernable. EKG guidance has demonstrated superior performance in guiding a catheter to the right location and confirming safe position.

Recommendations

During the process of this study, certain pinpointed actions saved time and improved accuracy of the process. Key points included:

1. Always use new leads that you apply to the patient even if this means you add a second set. It is better not to use leads of a monitored patient since connection to your monitor may cause the telemetry staff to lose their signal.
2. Connect to the same monitor for all patients. Use of a single monitor reduces variation and inaccuracies in interpretation.
3. Do not hold cables or EKG connectors; attach them and move on to other things. If the signal continues to be noisy and difficult to interpret, move the contact point of the alligator connector by sliding it down on the wire or needle confirming firm connection.
4. Understand that the presence of biphasic activity of the p-wave at the opposite side under baseline denotes entry into the right atrium. A negative or biphasic spike with elongation indicates advancement through the right atrium into the ventricular region. Identification and evaluation of biphasic activity is crucial to accurate position of the catheter tip.
5. If no Normal Sinus Rhythm is present, the catheter is not in the area of the SVC or if no p-wave variation occurs, the patient is on a dependent pacer.

EKG guidance provided other time saving benefits. On the average, time to release of the PICC resulted in time reduction of 30 minutes when EKG confirmation was used rather than waiting for chest x-ray confirmation. With an average of 10% repositioned for PICCs in prior months, use of EKG reduced repositioning after placement for time savings of 21 hours (417 x 10% reposition rate x 30 minutes/reposition). Time savings would likely be more significant for larger non-radiology PICC based facilities.

EKG adapter unit and cable used for positioning are available through multiple companies (see Table 1). The device used for this study (Pacerview) is no longer commercially available. Other companies carry CE mark for European usage (similar to FDA clearance) and are pending with the United States with Food and Drug Administration (FDA) submission.

Conclusion

EKG guided PICC placement proved accurate in consistently guiding the terminal tip to the superior vena cava (SVC). The procedure was easily taught and duplicated by members of the PICC team. The study demonstrated a definite correlation between the peak height (size) of the p-wave and the location of the terminal tip within the distal SVC. With knowledge of this correlation, transition from placing PICCs using EKG guidance

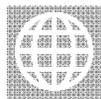
with chest x-ray confirmation to confirmation of tip placement using just EKG guidance without chest x-ray confirmation was easily attained. The incorporation of EKG guidance to current PICC and CVC insertions provides improvements in flow process by reducing delays. Application of EKG placement/confirmation performed during insertion saves time previously spent waiting for x-ray confirmation readings and saves time required for tip repositioning of malpositioned tips found after the end of the procedure by allowing the inserter to guide the terminal tip to the desired location by watching the p-wave activity. Additionally, EKG placement saves the cost of a chest x-ray and saves the patient exposure to radiation by eliminating the need for x-ray confirmation of tip position. The EKG guided PICC placement confirmation used in this study provided precise positioning demonstrating that previous studies are clearly reproducible.

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The EKG method for positioning the tip of PICCs: results from two preliminary studies

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Abstract

Two preliminary studies were conducted to determine feasibility of using the electrocardiography (EKG) method to determine terminal tip location when inserting a peripherally inserted central catheter (PICC). This method uses the guide-wire inside the catheter (or a column of saline contained in the catheter) as an intracavitary electrode. The EKG monitor is then connected to the intracavitary electrode. The reading on the EKG monitor reflects the closeness of the intracavitary electrode (the catheter tip) to the superior vena cava (SVC). The studies revealed that the EKG method was extremely precise; all tips placed using the EKG method and confirmed using x-ray were located in the superior vena cava. In conclusion, the EKG method has clear advantages in terms of accuracy, cost-effectiveness, and feasibility in conditions where x-ray control may be difficult or expensive to obtain. The method is quite simple, easy to learn and to teach, non-invasive, easy to reproduce, safe, and apt to minimize malpositions due to failure of entering the SVC.

Background

The importance of the position of the tip of any central venous access device (VAD) was stressed in 1998 by the Position Statement of the National Association of Vascular Access Network (NAVAN, now AVA). This position states the optimal position of the tip of a central VAD (excluding the VADs designed for hemodialysis) is the lower third of the superior vena cava (NAVAN, 1998; Scott, 1988; Scott, 1995). Though guidelines from other USA and European associations (Royal College of Nurses, Infusion Nursing Society, Society of Interventional Radiology, American Society of Parenteral and Enteral Nutrition, European Society of Parenteral and Enteral Nutrition, etc.) have offered different definitions of the optimal tip position, there is wide agreement that no central VAD should have its tip above the middle third of the superior cava vein or below the mid-portion of the right atrium (McGee and Gould, 2003; Taylor and Palagiri, 2007). In fact, positioning of the tip of a central line in an inappropriate site of the venous system is associated with a significant increase in the risk of malfunction, fibrin sleeve formation and venous thrombosis.

A 'short' catheter - i.e. a catheter whose tip is located in the upper or middle third of the superior vena cava (SVC) or in the innominate veins - has a 10 to 50 percent increased risk of central venous thrombosis (Caers et al., 2005) (Table I). Also, a high position of the tip of the VAD is associated with intimal damage due to mechanic irritation of the endothelium, with erosion and even perforation to the walls of the vein. Formation of a fibrin sleeve around the catheter occurs more frequently with a short catheter; this is typically associated with VAD malfunction (persistent withdrawal occlusion, or ball valve obstruction). In addition to these complications, the presence of a sudden or sustained increase of central venous pressure such as coughing, vomiting, etc. has been known to cause the 'short' catheter to dislocate, also known as 'tip migration' (Puel et al., 1993).

Conversely, a 'long' catheter, a catheter whose tip is in the lower portion of the right atrium or in the right ventricle or beyond, may carry the risk of arrhythmias, tricuspid valve dysfunction, erosion, or atrial thrombosis (Korones et al., 1996).

Finally, the tip of the catheter may be inadvertently positioned in the subclavian vein, in the internal jugular vein, or in other thoracic veins (internal mammary vein, azygos, etc.). This type of malposition is almost constantly associated with pain on infusion, early VAD malfunction and subsequent venous thrombosis.

While correct positioning of the tip of the catheter is of great importance during any central venous cannulation, it plays a crucial role in mid-term and long term VADs such as peripher-

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ally inserted central catheters (PICC), tunneled catheters and ports, which are frequently inserted in patients requiring chemotherapy with vesicant drugs or hyper-osmolar nutritional solutions. Standard of Care for central venous catheters (CVC) dictates in the United States that the position of the tip must be confirmed by x-ray prior to use (INS 2006; NAVAN 1998). When the tip location cannot be confirmed in the superior vena cava, the catheter must be repositioned. Tip verification techniques have focused primarily on the x-ray. Other forms of tip verification have been used throughout Europe, with or without x-ray, incorporating electrocardiogram interpretation.

Methods for Preventing Malpositions

At present, the 'gold standard' for preventing malpositions and verifying the tip of the catheter is through radiology, either as intra-procedural fluoroscopy or as a post-procedural chest x-ray. On the fluoroscopic monitor or on the radiological film, the tip must be seen in the area correspondent to the lower third of the superior vena cava, i.e. no more than 2 cm below the image of the main right bronchus.

While confirmation of tip placement in the superior vena cava is mandatory, the radiological assessment of the tip position does have a few limitations and disadvantages:

- any type of radiological assessment is associated with x-ray exposure for the patient and/or for the health operator; such exposure can be relevant for intra-operative fluoroscopy or with repeated chest x-rays;
- the radiological landmarks used to determine catheter tip location may be unclear or significantly affected by physiological or pathological anatomic variations, false perspectives, or errors of interpretation (this is particularly true for intra-procedural fluoroscopy). In the case of post-procedural control, greater accuracy can be achieved by studying the chest in both the anterior-posterior view and in the lateral view. The use of dual views, while it increases accuracy, requires longer x-ray exposure and higher costs.
- In most cases, the radiological assessment requires the availability of an expensive and logistically cumbersome machine plus a radiology technician and/or a radiologist all adding to the procedural cost. This gives us an inappropriate cost-effectiveness ratio. Radiological assessment a problem with a PICC insertion which, in the United States, is most frequently performed by nurses at bedside. In this situation, the intra-procedural fluoroscopy may be difficult or impossible to adopt while the post-procedural chest x-ray carries a significant burden in terms of costs, organization and time delay. Also, in most cases the nurse who has inserted the PICC must rely on the intervention of the radiologist to interpret tip location.*

**This aspect might be overcome in some countries such as UK or USA, where there is a growing tendency to authorize nurses, if specifically trained, to interpret the x-ray. In April 2008, the Association for Vascular Access (AVA) published a Position statement on this subject. (AVA, 2008).*

Tip confirmation by chest x-ray is less expensive, safer and more commonly used than fluoroscopy, though, in some cases the catheter has to be repositioned. Catheter tip repositioning

Table 1: Incidence of catheter-related thrombosis and catheter dysfunction, depending on tip position (modified from Caers et al., 2005)

Tip position	# cases	Thrombosis	Dysfunction
Brachiocephalic vein	31	45.2%	6.5%
Cranial 1/3 SVC	42	19%	16.7%
Middle 1/3 SVC	142	4.2%	1.4%
Caudal 1/3 SVC	66	1.5%	0%
RA or IVC	18	5.6%	5.6%

requires a new procedure, a second radiological assessment, major discomfort for the patient and for the nurse or physician who has implanted the device, a significant time delay, repeated x-ray exposure, and increased costs.

Some non-radiological methods which can be useful in reducing the risk of malposition of the tip of the catheter include establishing the proper choice for venous access, using ultrasound for guidance, establishing baseline anthropometric estimates from landmarks, and using electromagnetic tools to detect direction of insertion.

1) Proper choice of the venous approach

In centrally inserted VADs, the supraclavicular approach to the right internal jugular vein, to the right subclavian vein or to the right innominate vein (by ultrasound guidance) is characterized by a lower incidence of malposition since the catheter almost invariably enters the superior vena cava vein. Nonetheless, the risk of malpositioning with a 'short' or 'long' catheter still persists.

2) Ultrasound Guidance

The use of ultrasound for needle guidance with CVC placement is known to increase success and reduce complications. Soon after PICC insertion, while the stylet is still inside the PICC, ultrasound examination of the internal jugular veins is a simple and reliable method to rule out a gross malposition, though it cannot give information about the correct length of the catheter. Post-procedural ultrasound control of tip position can be done by surface or trans-esophageal echocardiography, but the cost is high and requires specially trained operators.

3) Anthropometric estimates and surface landmarks.

There are several landmark methods for estimating the desired length of a central venous catheter or a PICC; usually, they are based on the assumption that the atrio-caval junction is located at the level of the third intercostal space, on the right parasternal border. The anthropometric methods utilized for central venous catheters apply formulas which are derived from large population studies. These measurements estimate the desired length of the catheter knowing the site of venipuncture and the height of the patient (Peres, 1990). Both anthropometry and surface landmark methods are quite precise in estimat-

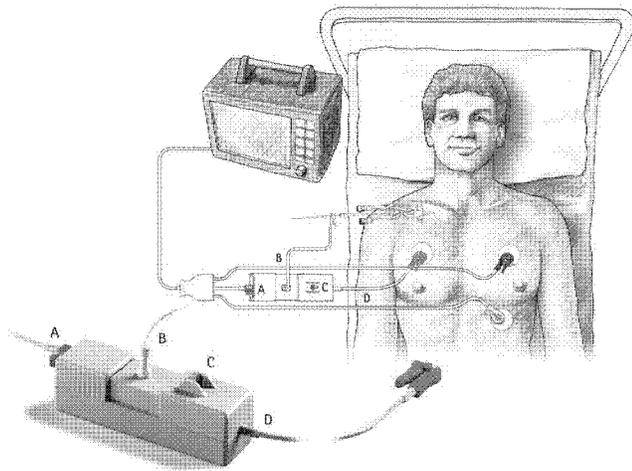


Fig. 1 – Diagram showing how the intracavitary electrode replaces the ‘red’ or ‘right shoulder’ electrode of the standard surface EKG (Figure reproduced by courtesy of BBraun. A = electrode connected with EKG monitor; B = cable connecting to intracavitary electrode; C = switch to shift from surface electrode to intracavitary electrode; D = surface electrode to the right shoulder of the patient)

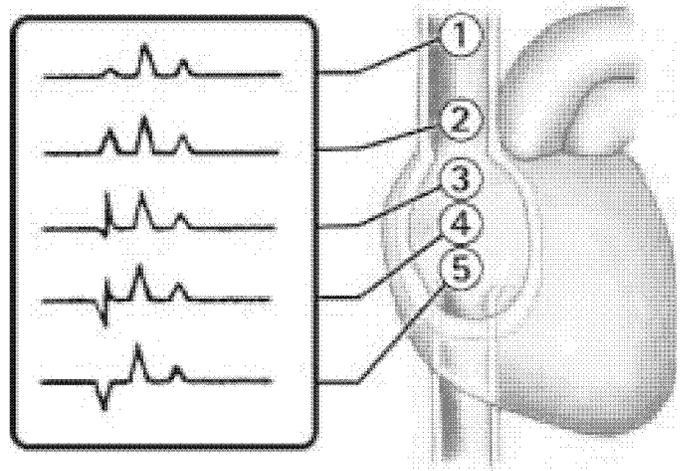


Fig. 2 – Changes of the P wave as a function of the tip of the intracavitary electrode (Figure reproduced by courtesy of BBraun)

ing the length of the catheter in the adult patients, but not in children. Measurements provide a possible length for catheter placement in the SVC without adjustment for anatomical variations, directional or functional malpositioning.

4) Electromagnetic tracking methods.

These usually consist of an electromagnetic signal from a wire installed in the catheter by means of a surface apparatus connected to a monitor (Navigator, manufactured by Viasys; Sherlock, manufactured by Bard; Cath-Finder, manufactured by Pharmacia Deltec). They are primarily used with PICCs and need a specific technological design of the catheter and/or of its stylet. Some authors have demonstrated a significant reduction in the incidence of malposition, from 13.4% down to 2.5%, using such devices (Naylor, 2007). Their main limitation is that, while they do ascertain that the PICC is in the right direction, they do not give information about the correct location of the catheter (Royer and Earhart, 2007).

The Electro-cardiographic Method for Positioning the tip of Central Lines

The “ideal” method for checking the position of the tip should have the following features:

1. It should provide a way to check the position of the tip both during the procedure (to avoid repositioning manoeuvres) as well as after the procedure (to confirm tip position of the VAD);
2. The method should be easily and autonomously performed by the inserter of the VAD, either a nurse or a physician;
3. The method should be accurate enough to ascertain that the catheter has gone in the *right direction* (straight along the axis internal jugular vein – innominate vein – SVC) and to

the *right depth* (not too long, not too short, but exactly at the atrio-caval junction);

4. It should be inexpensive, non-invasive, and easy to repeat with reproducible results;
5. It should be easy to learn and easy to teach;
6. It should provide a way to print and record the results to allow for documentation in the patient’s records.

Correct determination of catheter terminal location, in addition to identification and correction of malpositioning are all necessary components of PICC or CVC placement. Finding a method to perform these processes with ease during the insertion procedure will reduce time, speed usage, and save the patient from additional exposure and cost. We suggest the method that most closely meets all of these requirements is the location of terminal tip by use of the electrocardiographic (EKG) method. This method interprets the location of the catheter tip by using EKG with an intracavitary electrode (Corsten et al., 1994; Francis et al., 1992; Cavatorta et al., 1999; Gebhard et al., 2007; Antonaglia et al., 2008; David et al., 2005; Schummer et al. 2005; Cavatorta et al., 2001; Dionisio et al., 2001).

The basic principle of the EKG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an intracavitary electrode which replaces the ‘red’ or ‘right shoulder’ electrode of the standard surface EKG (Figure 1). When the EKG monitor is connected to the intracavitary electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the intracavitary electrode (i.e. the tip) to the seno-atrial nodus. A ‘giant’ P wave – as high as the QRS – indicates that the tip is inside the right atrium; when the P wave is as small as in the surface EKG, the

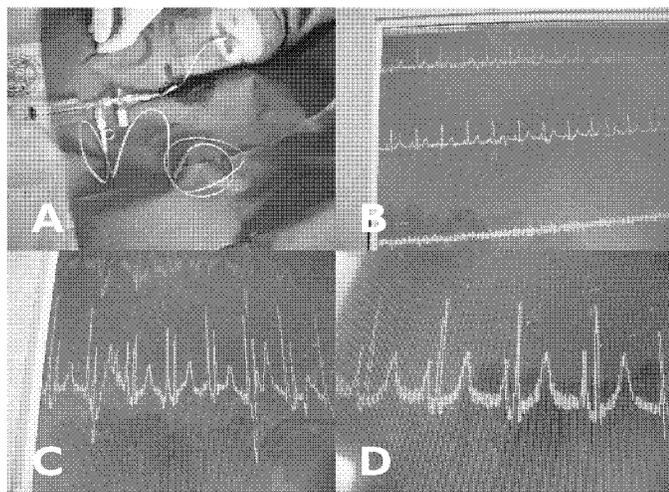


Fig. 3 – EKG method for positioning the tip of an open-ended PICC:

a – the PICC is inserted for the estimated length (previous anthropometric measurement), filled with normal saline and connected to the EKG monitor through the VygoCard, so to work as intracavitary electrode

b – standard EKG reading

c – tip in right atrium (giant P wave)

d – tip at atrio-caval junction (P wave half of QRS)

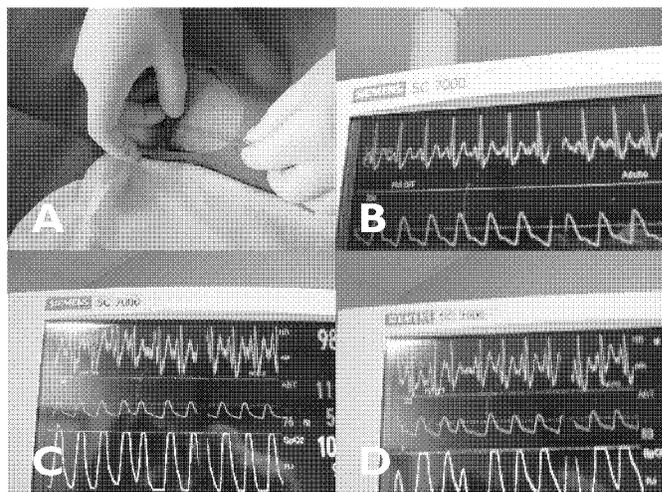


Fig. 4 – EKG method for positioning the tip of a closed-ended PICC:

a – the PICC is inserted for the estimated length, filled with normal saline and connected to the EKG monitor through the VygoCard; to make the catheter work as intracavitary electrode, it must be flushed continuously with saline so keep the valve open

b – standard EKG reading

c – tip in right atrium (giant P wave)

d – tip at atrio-caval junction (P wave half of QRS)

tip of the electrode is in the superior cava vein or above; a P wave whose height is half of the QRS is considered indicative of the atrio-caval junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava) (Figure 2). Thus, simply by monitoring the height of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium.

Limiting factors for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. The EKG method was first introduced in 1949 (Von Hellerstein et al., 1949) and has been successfully used for central venous catheter placement in Europe (especially Germany) since the '90s (Schummer et al., 2004).

During the last two decades, many clinical papers have demonstrated – with a few exceptions (Schummer et al., 2003; Schummer et al., 2004) – the accuracy of the EKG method, compared to the standard radiological assessment. Quite recently, other Authors (Gebhard et al., 2007) provided substantial research that has proven the EKG method is more specific and more precise when compared to conventional methods (i.e.: methods based on anthropometric measurements or standard formulas for estimating depth of catheter insertion, as available in the literature). In this clinical randomized study, all tips checked with the EKG method were in the superior vena cava or above, in contrast with other methods which showed 16% of those tips in the right atrium or in the right ventricle; also, only 3% of the tips checked by the EKG method were located above the superior vena cava (axillary, subclavian, internal jugular vein, innominate vein) versus

15% of the tips positioned with other methods.

This same clinical trial has shown that the EKG method did not significantly increase the length of time required to perform the procedure, and actually saved time by avoiding the need to reposition the catheter and get a second chest x-ray.

Many clinical trials have shown that the EKG method has clear advantages in terms of accuracy, cost-effectiveness and feasibility in conditions where X-ray control can be difficult or expensive to obtain (Corsten et al., 1994; Francis et al., 1992; Gebhard et al., 2007; Antonaglia et al., 2008; David et al., 2005). The method is quite simple, easy to learn and to teach, non-invasive, easy to reproduce, safe, and apt to minimize both malpositions due to failure of entering the superior vena cava (tip in internal jugular or subclavian or innominate vein) as well as malpositions due to error in the length of the catheter (catheter too short or too long). Though a thorough computation of the actual costs may differ, depending on the choice of technique and clinical setting, overall costs of the EKG method are consistently lower if compared to the standard check of the tip position by post-procedural X-ray. In fact, (a) the technique is inexpensive (the additional materials needed for the manoeuvre cost less than twenty dollars), (b) it can be performed at bedside, (c) the costs related to performing and interpreting chest X-ray are avoided, and (d) intra-procedural check of the tip position protects from expensive and timely repositioning manoeuvres sometimes needed after chest x-ray.

The trials concerning testing EKG have taken into consideration short term and long term central venous access devices inserted by puncture of the subclavian or the internal jugular vein (Chu et al., 2004; Cheng et al., 2002); in a few cases, the method

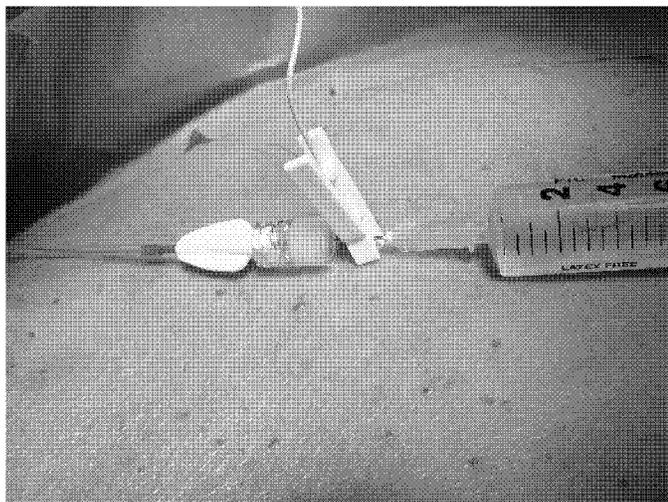


Fig. 5 – Alternative method for using the PICC as intracavitary electrode: electrode with alligator clip attached to a needle inserted in an injectable cap

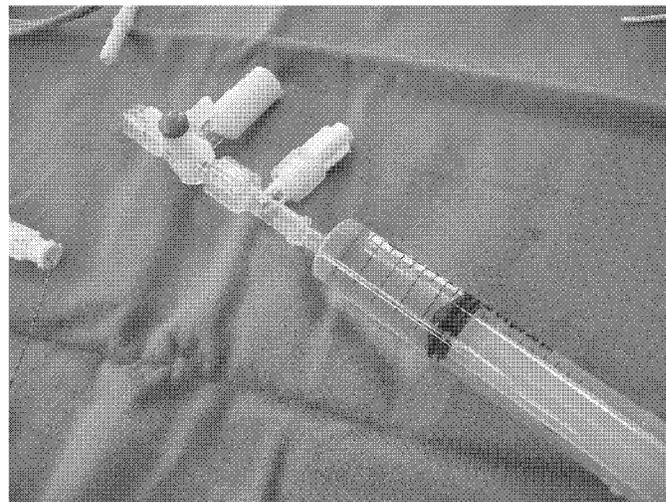


Fig. 6 – VygoCard (manufactured by Vygon)

has also been tested in neonates (Biban et al., 2000; Tierney et al., 2000), with umbilical catheters and epicutaneo-caval catheters.

Considering demonstration of safety and cost-effectiveness of the EKG trial results carried out with central venous catheters within the past few years, we decided to apply this method, which appears so safe and cost-effective, to PICC placement.

The EKG Method for Positioning PICCs

In our 1200 bed University Hospital, PICCs are inserted by members of a dedicated team. The team consists of four physicians (two surgeons, two infectious disease practitioners) and ten nurses. Our team inserts approximately 1000 PICCs and 700 long term central venous access devices per year, and is committed to several clinical tasks, including monitoring VAD related complications, counselling in VAD indications and maintenance, education and training of nurses in our institution, and, most importantly, teaching on a national level. We provided more than 40 courses in 19 different Italian hospitals training clinicians to use ultrasound guided placement of PICCs.

Our experience with the EKG method for standard short term and long term central venous access devices began many years ago. In our hands, the method has proven to be safe and cost-effective, and it has dramatically reduced the number of chest x-rays necessary to check the position of the tip.

Recently, we began a project for verifying the feasibility of applying this method to PICC. Until 2006, our standard protocol for PICC positioning consisted (Pittiruti et al., 2005) of (a) anthropometric estimate of the desired length of the PICC by anatomical landmarks (from the site of puncture to the third intercostal space on the right sternal border); (b) ruling out the presence of the catheter in the internal jugular vein by direct ultrasound examination during the procedure; and (c) postoperative, chest x-ray.

After a few preliminary clinical experiments carried out in 2007, whose goal was to define the technical aspects of the meth-

od, in the first months of 2008 we performed two pilot studies, one on open ended PICCs and one on closed ended (Groshong) PICCs. The details of these studies are listed below.

First study: Open Ended PICCs*

The aim of the first study was to verify the feasibility of the EKG method to open-ended PICCs. After approval of the Ethical Committee of our University, twelve consecutive patients requiring PICC lines were enrolled in this study. Exclusion criteria were: atrial fibrillation or other supra-ventricular arrhythmias; presence of a pace-maker. Desired catheter length was pre-operatively estimated by means of anthropometric parameters. We used the VygoCard device (Vygon) as the electrical transducer between the catheter (filled with standard 0.9% saline solution) and the EKG cable. The VygoCard transducer is part of a 3-way stopcock connected with the catheter and with a cable going to lead III of a standard EKG monitor. The catheter acts as an intracavitary electrode which replaces the traditional 'red' electrode on the right shoulder. The PICCs were inserted in the basilic (first choice) or brachial (second choice) vein at mid-arm under direct ultrasound guidance. Then, the catheter was slowly advanced in the venous system while observing the morphological intracavitary EKG changes until the P wave reached the desired shape and amplitude (one-half of the QRS complex), corresponding to the atrio-caval junction (Fig. 3). The catheter was then secured to the skin by means of a sutureless device. All patients underwent a post-operative chest x-ray (postero-anterior and lateral views). X-ray films were evaluated by an independent radiologist not involved in the insertion procedure; the atrio-caval junction was radiologically identified as 2 cm below the carina.

In this study, all twelve PICCs were successfully inserted. The "atrio-caval junction p-wave" was observed in all cases, in one patient after withdrawing and re-introducing the catheter. Final position at the atrio-caval junction was confirmed by postoperative intracavitary EKG control and chest x-ray in all



Fig. 7 – AlphaCard (manufactured by BBraun)

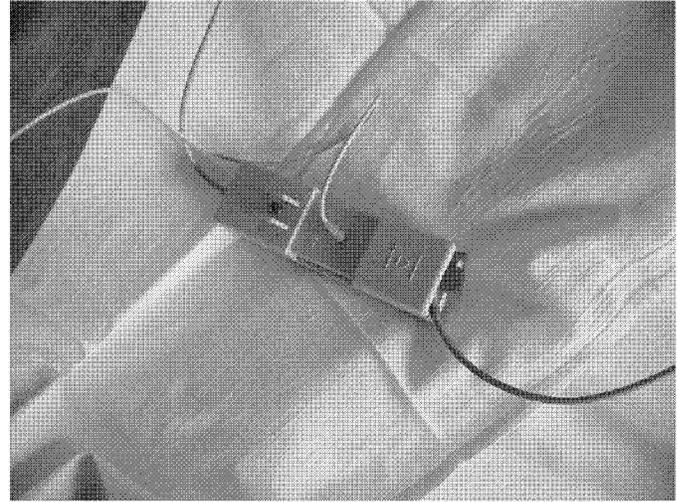


Fig. 8 – Certodyn (manufactured by BBraun)

patients. Consistently, no primary malpositions were observed on chest X-ray and all catheter tips appeared to be at the atrio-caval junction on X-ray films. In 3 cases the catheter length, as preoperatively estimated by anthropometric measurement, was significantly different (> 2 cm) from the length measured by the atrio-caval junction P wave; though, the final tip position was chosen according to the EKG measurement, and chest X-ray films were consistent with the EKG data.

***This study has been presented at the 2008 Meeting of the Infusion Nursing Society (Pittiruti, LaGreca, Scoppettuolo et al., 2008).*

Second study: Groshong PICCs**

In the second pilot study, six consecutive ICU patients requiring PICC lines were studied. The aim of this study was to verify the feasibility of the EKG method during the insertion of closed ended PICCs. Exclusion criteria were atrial fibrillation or other supra-ventricular arrhythmias, and/or the presence of a pace-maker. We used the VygoCard device (Vygon) as the electrical transducer between the catheter (filled with standard 0.9% saline solution) and the EKG cable. After ultrasound guided insertion in the basilic (first choice) or brachial (second choice) vein at mid-arm, each catheter was connected to an infusion line and a continuous saline infusion was started to keep the distal valve open. Baseline EKG rhythm was visualized. Then the catheter was slowly advanced in the venous system while observing the morphological changes of the P wave until the P wave reached the desired amplitude (one-half of the QRS complex), corresponding to the atrio-caval junction (Fig. 4). All patients underwent a post-operative chest x-ray (posterior-anterior and lateral views): the atrio-caval junction was radiologically identified as 2 cm below the carina. All x-rays confirmed EKG results of atrio-caval placement.

In this study, all six Groshong PICCs were successfully inserted. The “atrio-caval junction P wave” was observed in 5 patients.

In one case, the baseline cardiac signal was disturbed by electrical artefacts and the patient was excluded from the protocol. No primary malpositions were observed on chest x-ray and all catheter tips appeared to be at the atrio-caval junction on x-ray films.

**This study has been presented at the 2008 Meeting of the European Society of Intensive Care Medicine (Pittiruti, LaGreca, Brutti et al., 2008)*

Discussion

At present, the most common technique utilized for checking the position of the tip of CVCs by the EKG method employs the use of a guidewire inserted in the catheter as an intracavitary electrode, with the tip of the guidewire free in the bloodstream.

To adapt the EKG method to PICC insertion, we chose the alternative technique (already described for dialysis catheters and umbilical catheters), where the intracavitary electrode is the column of saline contained in the catheter itself (Pawlik et al., 2004; Madias, 2003; Madias, 2004). This is made possible by two different options: (a) With the first option, the PICC is closed proximally with a needle-injectable cap; a blunt needle or blunt ended connector is partially inserted in the cap, and an extension cable is connected to the access (Fig. 5); (b) The second option is more simply done with the proximal end of the PICC connected to a special device consisting of a 3-way stopcock with a transducer (VygoCard, Vygon, Fig. 6) or in a transducer directly attached to a syringe (AlphaCard, BBraun, Fig. 7); the transducer has an extension cable which connects to the EKG monitor.

The manoeuvre is further simplified by utilizing a specific commutator (Certodyn, BBraun, Fig. 8) connected to both the standard ‘red’ surface electrode on the right shoulder of the patient and to the intracavitary electrode. Changing the position of the switch, it is possible to read the EKG either as standard surface EKG or as intracavitary EKG. The changing morphology of the P wave is best appreciated reading D II.

Before reading the P wave change but after removal of the internal stylet, the PICC is filled with normal saline. If the PICC has a closed end, in order to maintain a column of fluid which may act as continuous intracavitary electrode, it is necessary to have a continuous infusion of saline through the system. Open ended PICCs have not additional requirements other than connection and saline flushing.

The best way to precisely locate the atrio-caval junction is to advance the PICC inside the venous system downward to the superior vena cava and beyond, until the typical 'giant' P wave (as high as the QRS) appears. This full sized P wave indicates that the right atrium has been reached. Once the P wave reaches full height, the PICC is slowly drawn backward until the P wave progressively reduces its height to ½ of the QRS: this corresponds to the atrio-caval junction. The PICC can then be secured to the skin in this position with the knowledge that the terminal end is at the caval-atrial junction.

Disadvantages of this method for checking the position of the tip of PICCs are:

- The method assumes the presence of a P wave on the standard EKG; in situations where the P wave is not present or not readable (atrial fibrillation, atrial flutter, marked tachycardia, pacemaker-driven rhythm), the method cannot be used;
- In some cases of closed ended PICCs, the Groshong valve may not open easily or continuously; intermittent flow across the valve may be consistent with a good infusion, but it causes intermittent EKG reading because the column of saline is interrupted.

Advantages of the EKG method:

- The method is accurate, safe, simple, non-invasive, easy to perform, easy to learn and easy to teach;
- It is inexpensive since it only requires an EKG monitor and a disposable sterile transducer (either Vygocard or Alphacard) with the extension cable;
- The manoeuvre can be performed at bedside, like most PICC insertions, and can easily be carried out by a nurse after minimal training;
- The method gives definitive information about the position of the tip directly during the procedure, thus saving time and resources;
- The costs as well the x-ray exposure associated with the radiological assessment are avoided in most cases;
- The correct position of the tip can be documented in the medical chart by appropriate printing of the EKG track.

Conclusion

The EKG method for determining caval-atrial junction terminal tip location is well documented in Europe and, through this study, has demonstrated accurate and safe use with PICCs. Though more studies are needed to standardize the procedure and to evaluate the accuracy of the method in different clinical situations and for different types of PICCs, we think these two pilot studies are very promising. This research suggests that the EKG method may strongly improve both the cost-effectiveness and the safety of the procedure for terminal tip interpretation on insertion and potentially, any time evaluation is desired.

Acknowledgments

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evGuide-Sapiens™ TLS ADAPTOR

INSTRUCTIONS FOR USE

DESCRIPTION:

- Sapiens™ TLS Adaptor is a family of sterile adaptors made of medical grade materials to facilitate placement of central venous access devices. Sapiens™ TLS adaptors are packaged in sterile individual pouches. Alternatively, the Sapiens™ TLS adaptors can be included in venous access device kits by the corresponding manufacturer of market available devices, e.g., PICC, CVC, hemodialysis catheters, implantable ports, and other central lines.
- The Sapiens™ TLS Adaptor must be used with the Sapiens™ Tip Location System. The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients. Limiting but not contraindicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous veins which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location. Please refer to the Sapiens™ TLS system User's Manual.
- The Sapiens™ TLS Electrical Adaptor, the adaptor is a sterile 39" long isolated stainless steel wire with a plug connector at one end and an alligator clip at the other end. The alligator clip is used to attach the Sapiens™ TLS adaptor to any commercially available stylet or guidewire used for central venous catheter placement. The plug connector is used to connect the adaptor to the ECG cable provided with the Sapiens™ TLS system.
- The Sapiens™ TLS Electrical Adaptor can also be used in combination with the Arrow-Johans Adaptor (Teleflex). In such a situation, the alligator clip of the Electrical Adaptor must be connected to the snap connector of the Arrow-

Johans Adaptor.

CONTRAINDICATIONS:

- All contraindications of central venous catheters apply as specified by the central venous catheter manufacturer.
- There are no contraindications specific to the Sapiens™ TLS Adaptor

POSSIBLE COMPLICATIONS:

- All complications indicated by the manufacturer of the central venous catheter should be considered when using the Sapiens™ TLS adaptor.
- There are no complications specific to the Sapiens™ TLS Adaptor.

WARNINGS:

- Refer to the Sapiens™ TLS User's Manual, its warnings and precautions when considering using Sapiens™ TLS for catheter tip placement confirmation.
- Monitor catheter tip placement per institutional policy.
- Release the central venous catheter after insertion according to your institution's guidelines.
- Do not release the central venous catheter based on Sapiens™ TLS information if the signal on the screen is unstable or does not show the ECG waveforms as illustrated in Figures 4 through 9 and according to the Sapiens™ TLS User's Manual. In such a case, use a different method for guiding the placement of your central line as indicated by the institutional guidelines and clinical judgement, e.g., chest X-ray or fluoroscopy.
- If the Sapiens™ TLS Adaptor becomes damaged, remove the adaptor with caution as to not change the position of the catheter.
- The Sapiens™ TLS Adaptor is for Single Use Only.
- Sapiens™ TLS Adaptor is sterilized by ethylene oxide (ETO).
- Do not re-sterilize the adaptor or accessories by any method.
- The manufacturer shall not be liable for any damages caused by reuse or re-sterilization of this adaptor or accessories.
- Contents are sterile in an unopened, undamaged package.
- Do not use adaptor or accessories if package is opened or damaged.

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- The Sapiens™ TLS Adaptor is not intended to diagnose or treat disease.

PRECAUTIONS:

- Do not use sharp instruments near the adaptor.
- Adaptor may be damaged if clamps other than what is provided are used.
- Examine adaptor before each insertion for damage.
- Read instructions carefully before using this device. The adaptor should be manipulated by a qualified, licensed physician or other qualified health care professional.
- The medical techniques and procedures described in these instructions for use do not represent all medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgment in treating any specific patient.
- Use standard hospital protocols when applicable.
- Discard gloves and change to a new pair of sterile gloves after connecting the Adaptor to the Sapiens™ TLS System and completing the setup of the Sapiens™ TLS System per User's Manual.
- Beware of the adaptor wire. Tripping over the adaptor might cause malfunction of the adaptor, detachment of the adaptor connectors from the system or injuries for the user.

Note: After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations

Note: For detailed central venous catheter preparation and insertion information, follow the instructions stated in the catheter's Instruction for Use provided by the catheter manufacturer.

ELECTRICAL VS. SALINE ADAPTORS

The choice between using the Sapiens™ TLS Electrical Adaptor or the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor is a matter of user preference and workflow optimization and is potentially subject to institutional guidelines. Please refer also to the Instructions for Use of the respective adaptors.

Typical situations for using the Sapiens™ TLS Electrical Adaptor are:

1. Placement of open-ended PICCs with pre-inserted stylets and luer-locks which allow for stylet position control
2. Implantable ports using open vein access with over-the-guidewire catheter placement
3. Any central venous catheter inserted over a guidewire with centimeter markings

Typical situations for using the combination between the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor are:

1. Any post-procedural tip location verification of any central venous catheter type
2. Placement of closed-end PICCs
3. Placement of central venous catheters using the modified Seldinger technique (MST) which do not have pre-inserted stylets, e.g., tunneled catheters like Broviac catheters.
4. Any central venous catheter inserted over a guidewire without centimeter markings, e.g., CVCs.
5. Hemodialysis catheters which may require tip location verification for both ends: the long distal end in the right atrium and the short distal end at the caval-atrial junction.

WORKFLOW

1. Attach ECG skin electrodes as indicated by the Sapiens™ TLS User's Manual.
2. Prepare patient and insert the central venous access device according to institutional protocols and the device instructions for use.
3. When using the Sapiens™ TLS Electrical Adaptor, Figure 1, expose the stylet pre-inserted in the catheter at the distal end close to the touyh borst. Open the Adaptor package and take out the Sapiens™ TLS Adaptor wire. Attach the mini-grabber connector to the exposed stylet close to the touyh borst. Follow the catheter manufacturer's instructions regarding the use of the stylet during procedure. Place the catheter onto the patient where sterile field is established. Clip the Sapiens™ TLS Adaptor wire to the sterile drape to ensure the catheter stays in the sterile field.
4. When using the Sapiens™ TLS Electrical Adaptor in combination with the Arrow-Johans Adaptor, Figure 3, attach the alligator clip of the Electrical Adaptor to the snap clip of the Arrow-Johans Adaptor.
5. In either configuration, attach the plug connector of the Sapiens™ TLS Adaptor wire to the red lead of the ECG cable provided with the Sapiens™ TLS System according to

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User's Manual.

6. The ECG patterns provided by the Sapiens™ TLS Adaptor and System, Figures 4 through 9, may be considered in assessing catheter tip location. Please refer to the Sapiens™ TLS User's Manual for detail information, warnings and precautions regarding tip location confirmation.

WARNING: Failure to verify catheter placement may result in serious trauma or fatal complications.

7. When using the Electrical Adaptor, disconnect the alligator clip from the stylet or guidewire. Remove stylet according to the manufacturer's instructions.
8. Record catheter length, catheter lot number, adaptor's lot number and tip position on patient's chart.
9. Record patient name, catheter length on the Sapiens™ TLS graphical user interface
10. Document tip location by printing using Sapiens™ TLS.

CATHETER TIP PLACEMENT VERIFICATION

As described herein and in the Sapiens™ TLS User's Manual, using the Sapiens™ TLS the ECG waveforms can be unambiguously mapped to specific catheter tip locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment. Per institutional guidelines and in accordance with clinical judgment, in indicated patients, and under the conditions described by this User's Manual, Sapiens™ TLS may be used in conjunction with ultrasound-guided vein puncture or open vein access to replace chest X-ray and fluoroscopy for intra- and post-procedural central venous catheter tip location confirmation.

Using Sapiens™ TLS, central venous catheter tip location can be documented for the patient's chart either on paper or electronically.

Using Sapiens™ TLS, the location of the central venous catheter tip can be determined and documented as required by the different types of central venous catheters and by different institutional guidelines, for example:

1. When the tip of a PICC catheter must be placed in the lower third of the superior vena cava, the ECG waveforms illustrated in Figure 7 must be

detected and documented at the tip of the PICC catheter.

2. When during intra-procedural catheter insertion or, at later times, during periodical post-procedural catheter tip verification, the long end of a hemodialysis catheter must be placed in the right atrium while its short end must be placed at the caval-atrial junction, then the ECG waveform in Figure 9 must be detected and documented at the long tip and, respectively, the ECG waveform in Figure 8 must be detected and documented at the short tip of the hemodialysis catheter.
3. When the tip of a central venous catheter (CVC) or of an implantable port must be placed at the caval-atrial junction, then an ECG waveform like the one in Figure 8 must be detected and documented at the tip of the catheter.

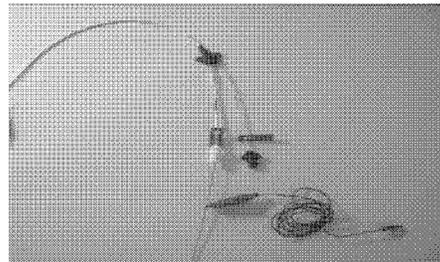


Figure 1: SAPIENS™ TLS Electrical Adaptor

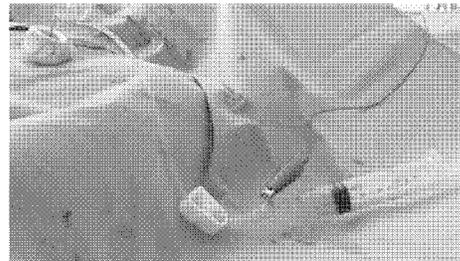


Figure 3: Sapiens™ TLS Electrical Adaptor in combination with Arrow-Johans Adaptor

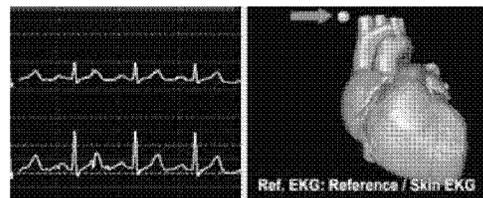


Figure 4: Tip outside thoracic cavity

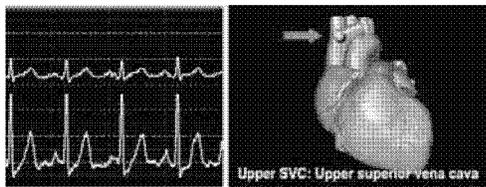


Figure 5: Tip in upper SVC

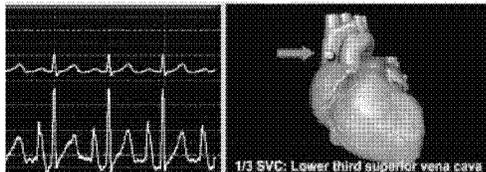


Figure 6: Tip in lower third of SVC

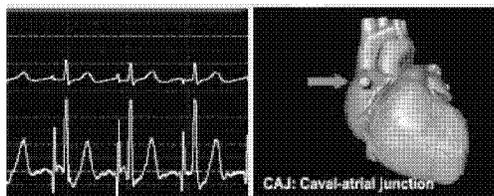


Figure 7: Tip at caval-atrial junction

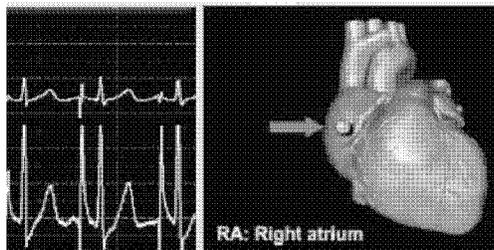


Figure 8: Tip in the right atrium

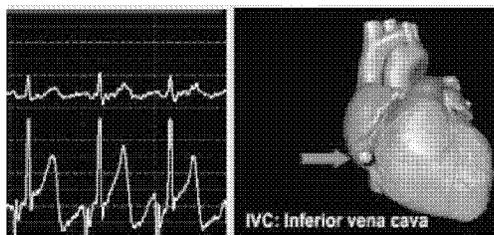


Figure 9: Tip in the inferior vena cava

If you have any questions or comments regarding this product, contact

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Email: info@romedex.com

CONTACT INFORMATION

For additional information, please go to the Romedex International web site:
www.romedex.com.

evGuide Shelf Life Test Protocol

Originator: Sorin Grunwald

Date: 3/25/10

Protocol Approval:

Name	Title	Signature	Date
Sorin Grunwald			

1.0 PURPOSE

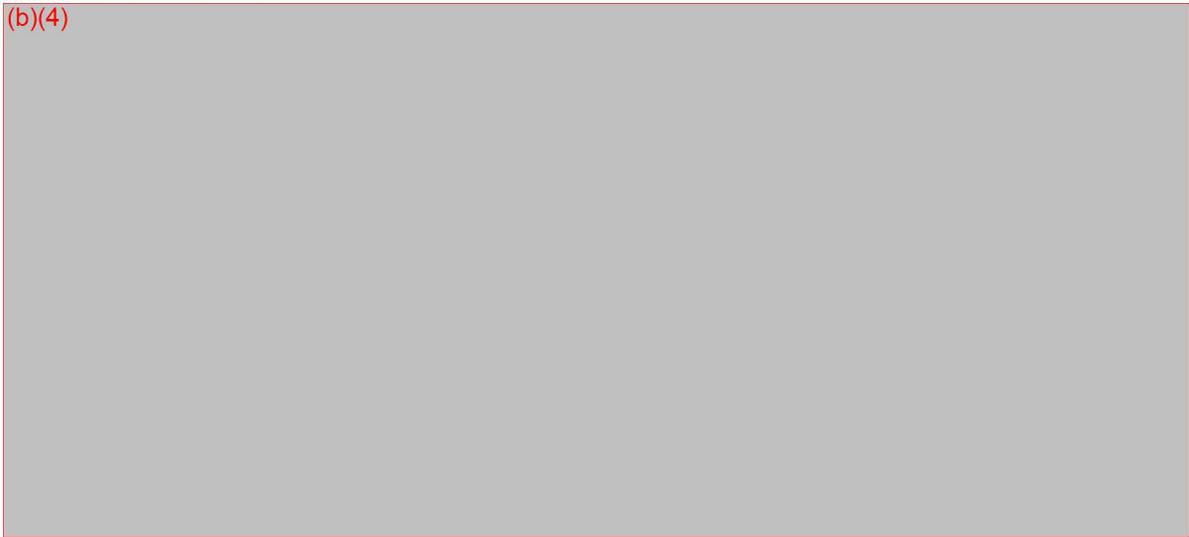
- 1.1. The purpose of this document is to provide an overall protocol for evaluating the packaging and shelf life of the Romedex International evGuide™ / Sapiens™ TLS Electrical Adaptor. The integrity of packaging of the evGuide™ / Sapiens™ TLS Electrical Adaptor will be challenged. The evGuide™ / Sapiens™ TLS Electrical Adaptor will seek for 1-year shelf life after sterilization and accelerated ageing by completing testing as described in this document.

2.0 SCOPE

- 2.1. This protocol applies to the evGuide™ / Sapiens™ TLS Electrical Adaptor and is a required test in the verification process.

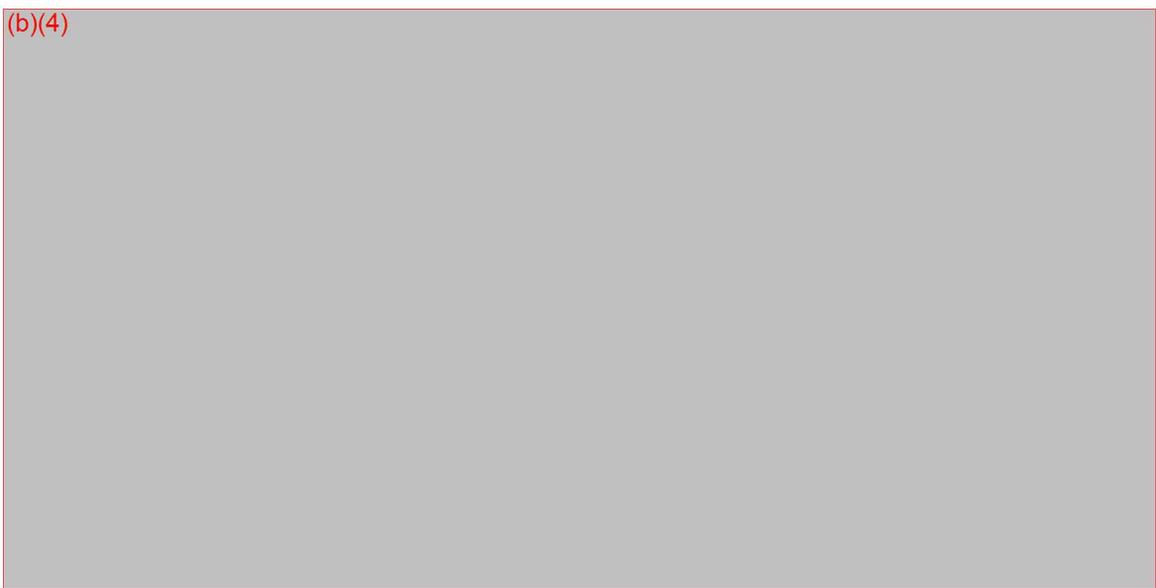
3.0 REFERENCES

(b)(4)



4.0 EQUIPMENT

(b)(4)



(b)(4)



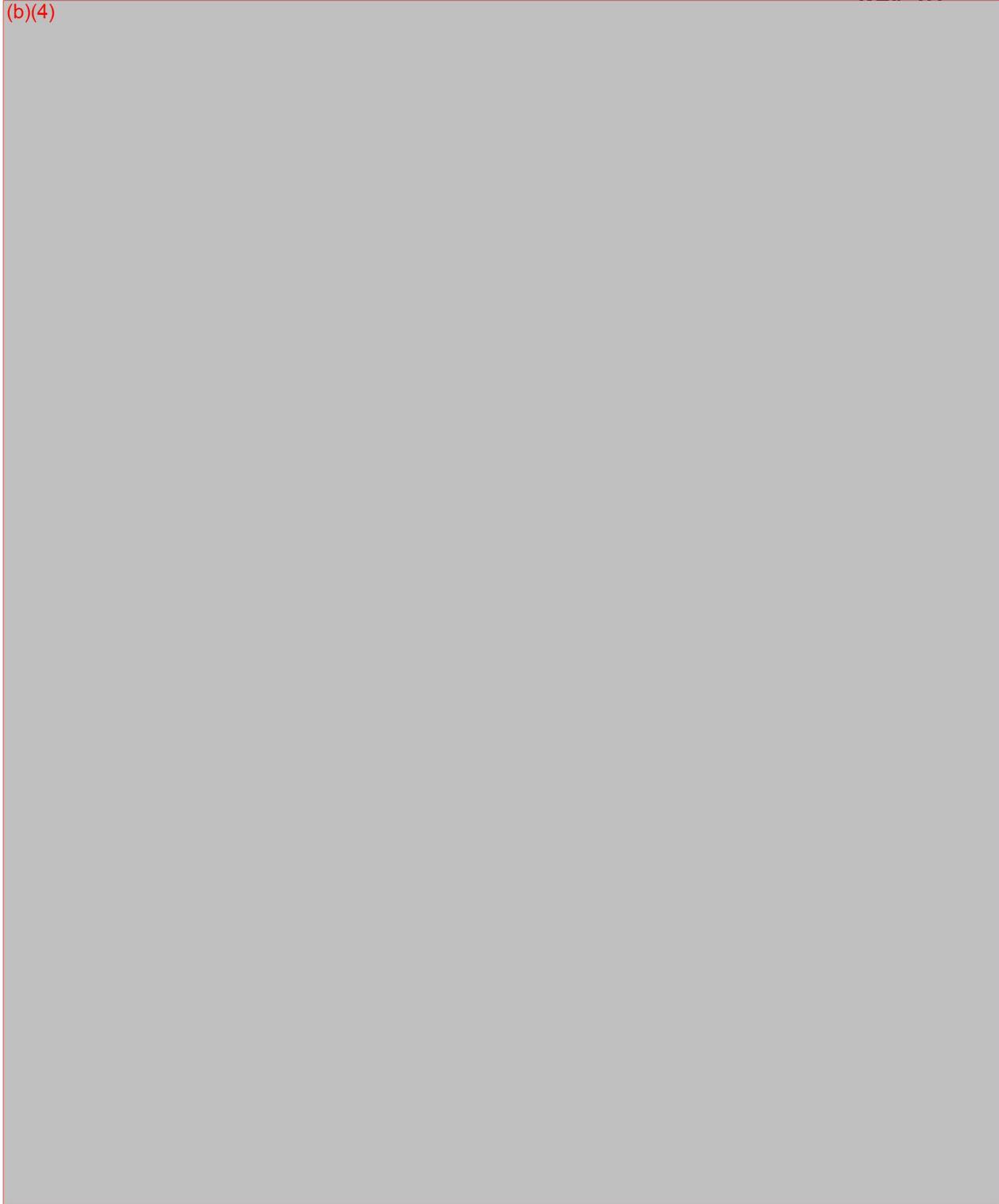
5.0 METHODS AND STRATEGY

(b)(4)



Figure 1. Study flow chart.

(b)(4)



6.0 SUMMARY OF TESTING AND SAMPLING PLANS

(b)(4)



(b)(4)



Table 4: Sample plan for product performance testing.

(b)(4)

7.0 ACCEPTANCE CRITERIA

(b)(4)

8.0 EXISTING PROTOCOLS and DEVIATIONS

(b)(4)

9.0 RESULTS

(b)(4)

10.0 REVISION HISTORY

Section	Description	Author/Date

APPENDIX A
Deviation Records Log Sheet

Name / Date	Section	Deviated Action

**APPENDIX B
Data Sheets**

Date:	Location:	Tester (s):	Report:
-------	-----------	-------------	---------

T=0 group visual inspection

Sample	Label is Legible P/F	Label is affixed P/F	Seal is not peeling P/F	Comments
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				

Test Operator: _____

Reviewed: _____

Date: _____

Date: _____

APPENDIX B: Data Summaries

Date:	Location:	Tester (s):	Report:
-------	-----------	-------------	---------

Sample	Pouch Dye Penetration	Pouch Seal Peel
	Pass/Fail	Pass/Fail
1		
2		
3		
4		
5		
6	(b)(4)	
7		
8		

Reviewed: _____ Date: _____

Technician: see specific test data

APPENDIX B: Data Summaries

Date:	Location:	Tester (s):	Report:
-------	-----------	-------------	---------

Sample #	Pouch Dye Penetration	Pouch Seal Peel
9	Pass/Fail	Pass/Fail
10	(b)(4)	
11		
12		
13		
14		
15		
16		

Reviewed: _____ Date: _____

Technician: see specific test data

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June 5, 2010

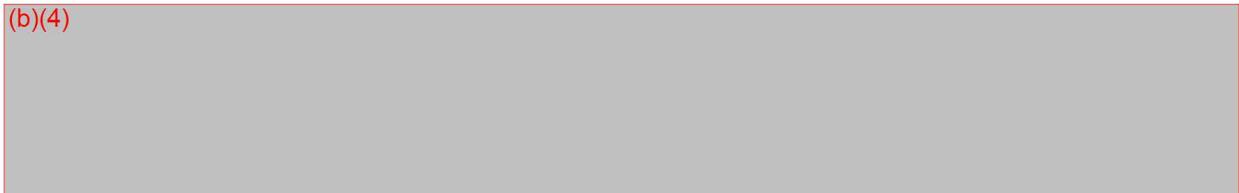
Nikhil Thakur, Reviewer
U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Subject: K093775
Response to your request for additional information from 3/4/2010

Dear Mr. Thakur:

Romedex International Srl is submitting this response to your March 4, 2010 request for additional information for the 510(k) submission referenced above. Your requests (*italics*) and our responses follow. Please note that on March 29, 2010 Romedex applied for and since received a 90 day extension to respond to the request for additional information.

(b)(4)



An updated CDRH Premarket Review Submission Cover Sheet is provided in Attachment 12.

Sorin Grunwald, Ph.D.
Managing Director
Romedex International Srl

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- 16.

510(k) Summary / 510(k) Statement

1. *FDA conducts a comprehensive review of the 510(k) Summary in accordance with 21 CFR 807.92 and the Required Elements for 510(k) Statements in accordance with 21 CFR 807.93. Based on our assessment of your 510(k) Summary in Section 5 of your submission, FDA believes that your Summary does not meet the regulation. Please address the following concerns regarding your 510(k) summary:*
 - a. *Please include a summary comparing the technological modifications made to your device as it relates to your predicate devices.*
 - b. *Please include a summary of the non-clinical testing data that was submitted, referenced or relied on to demonstrate that the Subject Device is safe and effective, and whose performance meets the requirements of its pre-defined acceptance criteria and intended uses.*
 - c. *Please include a summary of the clinical data that was submitted, referenced or relied on, including:*
 - i. *Description upon whom the device was tested*
 - ii. *Data obtained from the tests and especially*
 - iii. *Adverse events and complications*
 - iv. *Other information for SE determination*

Please see the below updates to the 510(k) summary.

510(k) Summary

Proprietary Name: Sapiens™ Tip Location System also known as evGuide™ Tip Location System

Device Trade name: Sapiens™ Tip Location System (TLS)

Product Classification: Class II, 21 CFR §880.5970

LJS - Accessory to Percutaneous, Implanted, Long-Term Intravascular Catheters
General Hospital

Applicant name: Romedex International Srl 58 Aleea Arubium, Bucharest, 022944 Romania,
+1.650.209.4838, info@romedex.com, www.romedex.com

Contact person: Sorin Grunwald Ph.D., MBA, 175 Colorado Ave, Palo Alto, CA 94303,
sorin@romedex.com, Tel: +1.650.209.4838, Fax: +1.650.887.0348

Preparation Date: June 4, 2010

Predicate Devices: K091324 - Sherlock 3CG Tip Positioning System
K032613 - Transvenous Pacemaker Placement Assist Device
K973371 - Conduction Anesthesia Kit
K843263 - Arrow-Johans ECG Adaptor

Indications for Use: The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Device Description: The Sapiens™ TLS consists of the following elements: sterile electrical adaptor, ECG module and cable, laptop running Sapiens™ TLS software, label printer (optional), and remote control (optional). A stylet or a guidewire inserted in a central venous catheter can be connected to the Sapiens™ TLS system via the Sapiens™ TLS Electrical Adaptor establishing a direct electrical connection to the catheter distal tip for ECG signal measurement. A different ECG signal measurement method – the column of saline method – can be used by connecting the Sapiens™ TLS Electrical Adaptor to the Arrow-Johans Adaptor, by connecting the Arrow-Johans Adaptor to any central venous catheter and by injecting saline solution into the catheter lumen through the Arrow-Johans Adaptor, thus establishing electrical conductivity to the distal tip of the catheter. When the central venous catheter or its associated stylet or guidewire is connected to Sapiens™ TLS, the Sapiens™ TLS laptop screen displays skin ECG signals and endovascular electrograms acquired at the location of the distal tip of the catheter. The waveforms provided by Sapiens™ TLS can be used for guiding and positioning of the central venous catheter. These ECG waveforms can be printed using an optional label printer to document the catheter tip location for the patient's file.

Bench Top Safety & Performance Tests: Verification and validation tests have been performed in accordance with Design Controls per 21 CFR §820.30.

Bench top testing has been performed side-by-side with available predicate devices which has demonstrated substantial equivalence of Sapiens™ TLS to the respective predicate devices. The following tests were performed: a) electrical impedance testing and b) ECG waveform accuracy tests.

**Summary of
Non-clinical Data:**

Non-clinical studies were performed which have demonstrated safety and efficacy of Sapiens™ TLS using Electrical Adaptor, good correlation between bench top and in-vivo data, and substantial equivalence with predicate devices. The following tests were performed: a) ECG waveform accuracy comparison with a commercially available ECG monitor, b) ECG waveform accuracy comparison with the Conduction Anesthesia Kit (K973371) and c) system usability and validation testing.

**Summary of
Clinical Data:**

To date, Sapiens™ TLS has been used in Europe for central venous catheter guidance and positioning in five major hospital centers on more than 350 adult patients (ages 19-96) of both genders for placing several types of central venous catheters: PICCs, CVCs, implantable ports, hemodialysis catheters, and tunneled catheters. Several types of users including nurses and physicians have used Sapiens™ TLS for different clinical procedures, e.g., oncology, anesthesia, patient monitoring in the ICU, hemodialysis in different clinical settings: in the operating room, in outpatient clinics and at the bedside.

Side-by-side comparisons with available predicate devices were performed which demonstrated substantial equivalence of Sapiens™ TLS to the respective predicate devices.

In the two analyzed subsets of 362 patients (332 patients from a prospective, multicenter, non-controlled study and 30 patients from a human factors/ usability study), the catheter tip placement using Sapiens™ TLS at the desired location was confirmed with chest X-ray or fluoroscopy in 97% of the cases. No adverse events or complications have occurred.

**Summary of
Technological
Characteristics
Compared to
Predicate Devices**

The subject Sapiens™ TLS Electrical Adaptor combines design features, materials and technological characteristics of marketed predicate devices including the Transvenous Pacemaker Placement Assist Device (K032613) and Conduction Anesthesia Kit (K973371) such as: a) a sterile, insulated, electrically conductive wire of very low electrical resistance; b) a distal end alligator clip to connect to stylets and guidewires; c) a proximal end connector which can be connected to an ECG cable or to an ECG connection switch. When compared to the Conduction Anesthesia Kit, the Sapiens™ TLS Electrical Adaptor has simplified the design of the device by removing the switch box. When compared to Transvenous Pacemaker Placement Assist Device, the Sapiens™ TLS Electrical Adaptor has simplified the design of the device by removing the connection box.

The Sapiens™ TLS Electrical Adaptor may be connected to the ECG pin of the predicate Arrow-Johans Adaptor (K843263) using an ECG cable which allows for the saline conduction method of ECG measurement. Use of the Sapiens™ TLS Electrical Adaptor with the Arrow-Johans Adaptor does not require any modifications of design features, materials, or technological characteristics of the marketed predicate device.

Additionally, the subject Sapiens™ TLS System combines design features, components and technological characteristics of the predicate device Sherlock 3CG Tip Positioning System (K091324) but uses only cardiac electrical signal detection to provide real-time catheter tip location information. The subject Sapiens™ System does not use a passive magnet like the predicate device.

Any differences between technological features of the subject and predicate devices do not raise new questions of safety or efficacy of the subject Sapiens™ TLS device.

**Summary of
Substantial
Equivalence:**

The Sapiens™ TLS has the same intended use and similar indications for use as the commercially available Sherlock 3CG Tip Positioning System (K091324), Transvenous Pacemaker Placement Assist Device (K032613), Conduction Anesthesia Kit (K973371), and Arrow-Johans ECG Adaptor (K843263). Additionally, clinical and non-clinical performance testing has demonstrated that any differences in technological characteristics do not raise new issues of safety or effectiveness when compared to the aforementioned predicate devices. Therefore, the Sapiens™ TLS meets the requirements for substantial equivalence to the referenced predicate devices.

Labeling

2. On page 2 of the Subject Device User Manual, under the heading “Background”, there is a statement regarding the limitation of use for the device. Specifically, the User Manual states, “Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.” However, there is no reference to this cautionary statement under the “Contraindications”, “Warnings”, “Precautions” or “Safety Information” sections of the manual. The statement describes a scenario where the Subject Device’s ability to successfully determine a catheter position is impaired by an underlying medical condition in the patient. Please modify your labeling to specifically identify this concern under “Warnings” or “Precautions.” Additionally, please modify the labeling to reflect the additional steps that a clinician would have to take when using this device with a patient who might have an altered cardiac rhythm due to an underlying disease or medical condition.

The following wording has been added to the User’s Manual in Section 1.4 “Warnings and Precautions” (Attachment 1: evGuide-Sapiens TLS User’s Manual).

- Warning:** *In patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*
- Warning:** *The Sapiens™ TLS User’s Manual provides information about ECG waveforms and their correspondence with specific locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the user must stop using Sapiens™ TLS and use of an additional and/or different method for catheter tip location confirmation, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

3. The labeling for your device contains some symbology that is not accompanied by a description of that symbol in English. For example, the labeling contains a symbol that has the number "2" with a "slash" through it, the terms "Sterile" and "EO" with boxes around them, and an exclamation point (i.e. "!") surrounded by a triangle.. According to 21 CFR, 801.15(c)(1), any symbol on a medical device distributed within the United States, must be accompanied with a description of the symbology in English. Please edit the labeling to comply with this requirement.

It is noteworthy that FDA's Guidance "Use of Symbols on Labels and in Labeling of In Vitro Diagnostic Devices Intended for Professional Use" (November 30, 2004) is only recognized by CDRH's Office of In Vitro Diagnostics, and does not apply to your device.

Please see below for the revised labeling that complies with 21 CFR, 801.15(c)(1):

**ROMEDEX INTERNATIONAL SRL
SAPIENS™ TLS ELECTRICAL ADAPTOR**

 XXXX-XXXXXX  Date of manufacture: XXXX-XX
QTY: 1  Use By: XXXX-XX

 Attention, See Instructions for Use

 Single Use – Do not resterilize

 Sterilized by ethylene oxide

 Sterile unless package is damaged or open



This product does not contain natural rubber latex

U.S. and other patents pending

After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations.





**Manufactured by SC Incerplast SA For:
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022944 Bucharest, Romania
Tel: +1.650.209.4838, Fax: +1.650.887-0348
www.romedex.com**

**ROMEDEX INTERNATIONAL SRL
SAPIENS™ TLS ECG MODULE**



Serial Number: xxxx-xxxxxx



Date of manufacture: xxxx-xx



Attention, See User's Manual



U.S. and other patents pending



**Manufactured by SC Incerplast SA For:
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58 Aleea Arubium
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Fax: +1.650.887-0348
www.romedex.com**

4. Regarding electromagnetic compatibility, the evGuide TLS User Manual states that “Although the evGuide TLS System conforms to certain international safety and electromagnetic compatibility standards, the evGuide TLS System is intended for use by medical personnel who have received evGuide TLS System training.” FDA’s review of electromagnetic compatibility and electrical safety testing performed on the Subject Device shows that the evGuide TLS was only partially tested for electrical safety. Please modify the labeling to specifically identify precautions that the end user should take when operating your device in the presence of electromagnetic radiation (i.e. MRI, CT Scan, X-rays).

The following wording has been added to the User’s Manual in Section 1.4 “Warnings and Precautions” (Attachment 1: evGuide-Sapiens TLS User’s Manual).

Warning: *Do not place and/or use the Sapiens™ TLS system in the presence of strong magnetic fields such as Magnetic Resonance Imaging (MRI) devices. The high magnetic fields created by an MRI device will attract the equipment with a force sufficient to cause death or serious personal injury to persons between the equipment and the MRI device. This magnetic attraction may also damage the equipment. The magnetic and the RF fields associated with the MRI environment may interfere with the display of ECG waveforms. Consult the MRI manufacturer for more information.*

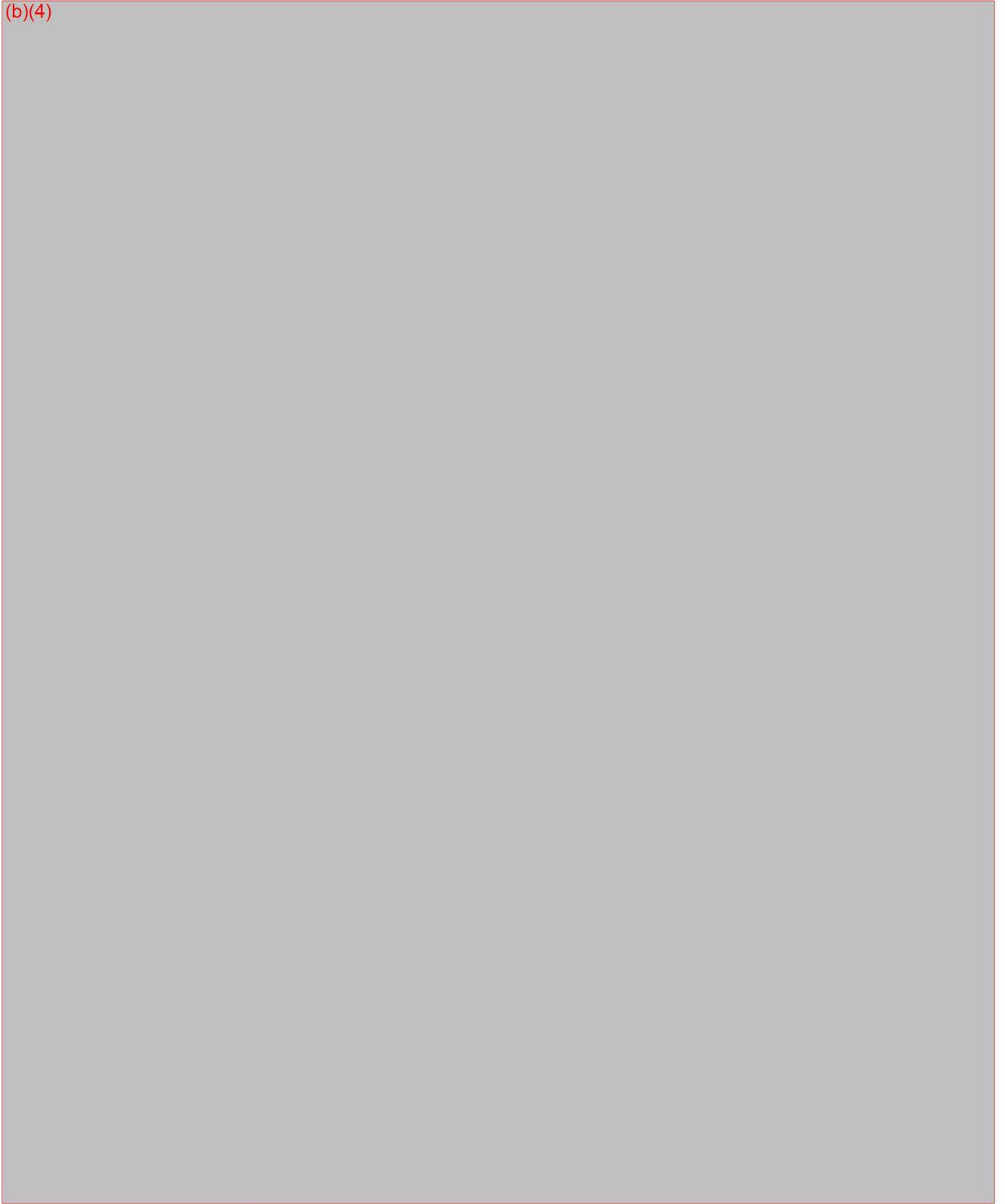
Caution: *Active electric motor driven equipment, such as pumps may interfere with the display of the ECG waveforms. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Caution: *Equipment such as CT scanners, X-rays and fluoroscopy systems, cauterizers and diathermy equipment, operating in close proximity may emit strong electromagnetic or radio frequency interference (RFI) which could interfere with the display of ECG waveforms by Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Caution: *Electric equipment which requires direct contact with the patient may interfere with the display of ECG waveforms by Sapiens™ TLS. Do not use electric cauterization, electric scalpels, and ablation equipment while using Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Sterilization/Shelf Life/Reuse

(b)(4)



(b)(4)



Acceptance criteria and summary of test methodology

(b)(4)



Sample size

(b)(4)



Summary of performance data

(b)(4)



(b)(4)

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Summary of test methodology for the Shelf Life Testing

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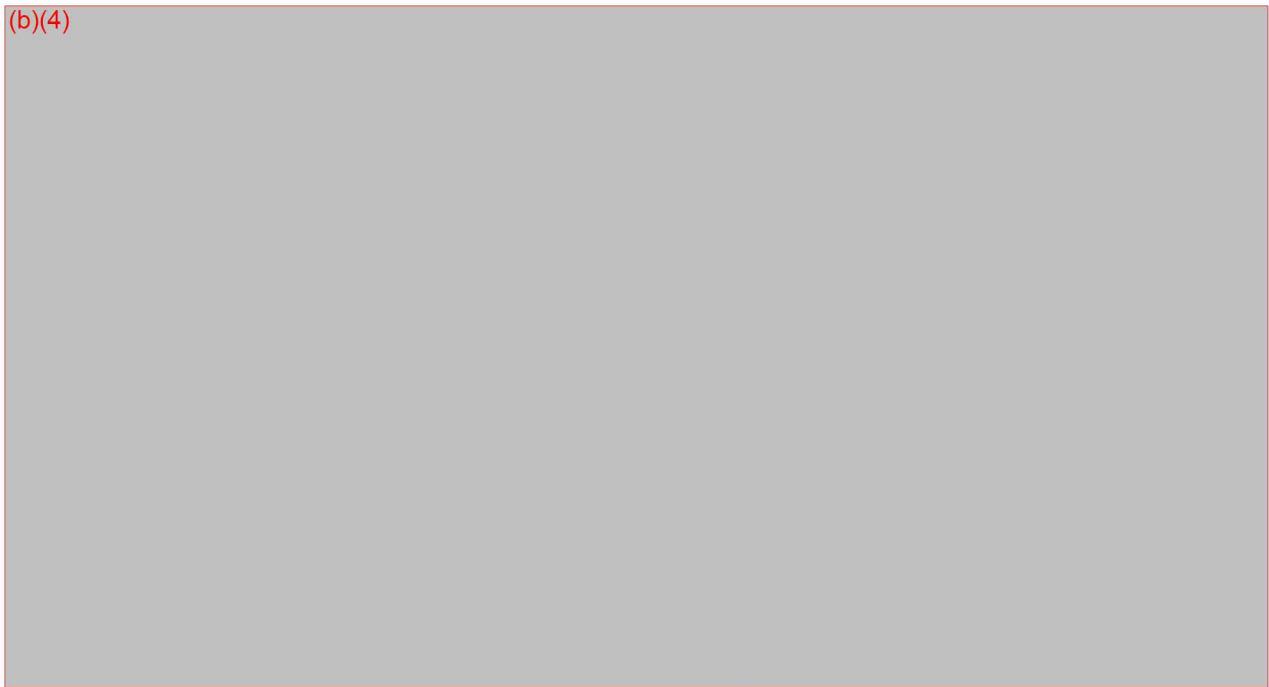
Sample size

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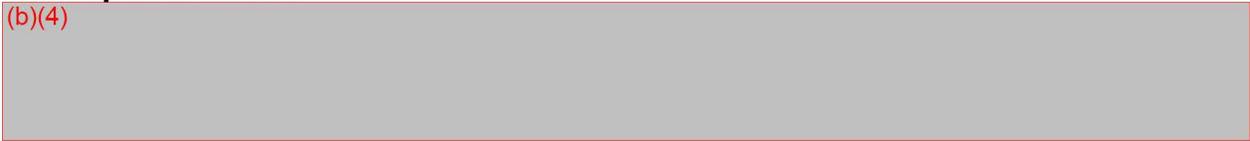
Summary of performance data

(b)(4)

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Acceptance criteria

(b)(4)

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Summary of test methodology

(b)(4)

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Sample size

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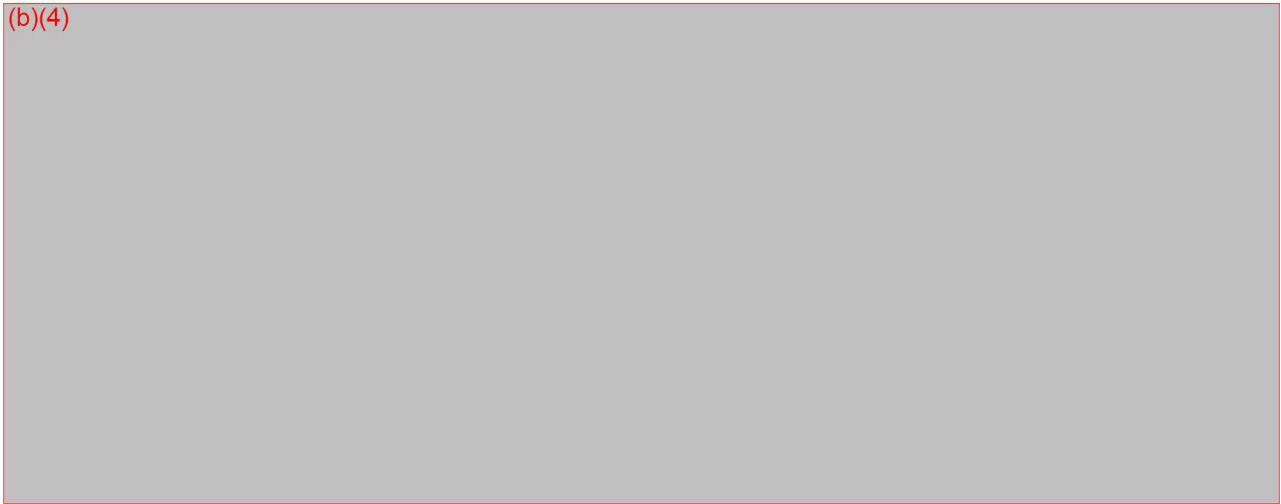
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Summary of acceptance criteria and performance data

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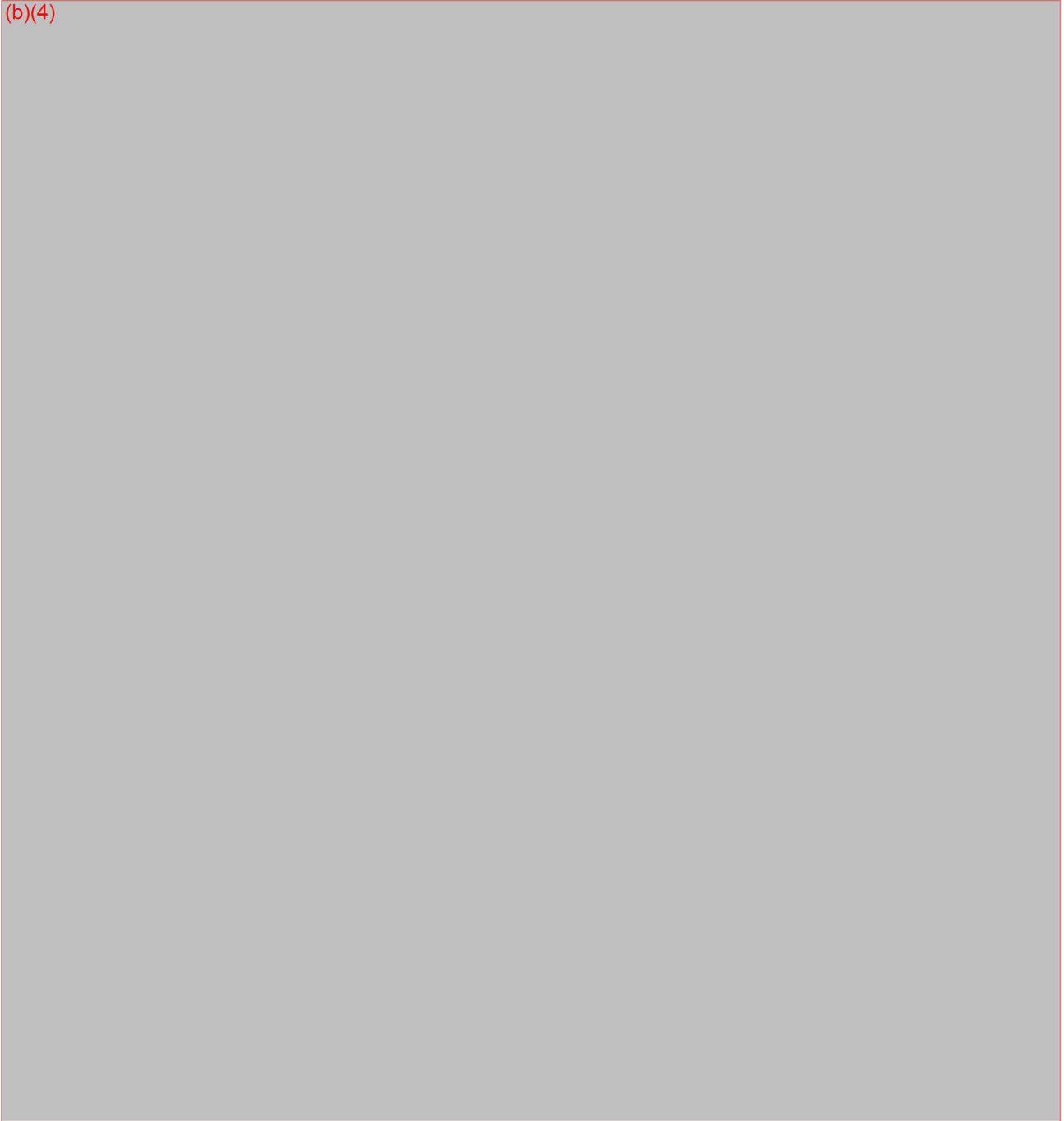
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(b)(4)



Biocompatibility

(b)(4)



(b)(4)



(b)(4)



(b)(4)



Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

(b)(4)



Section of standard	Description	Acceptance criteria	Results	Pass Fail	Report #
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(b)(4)

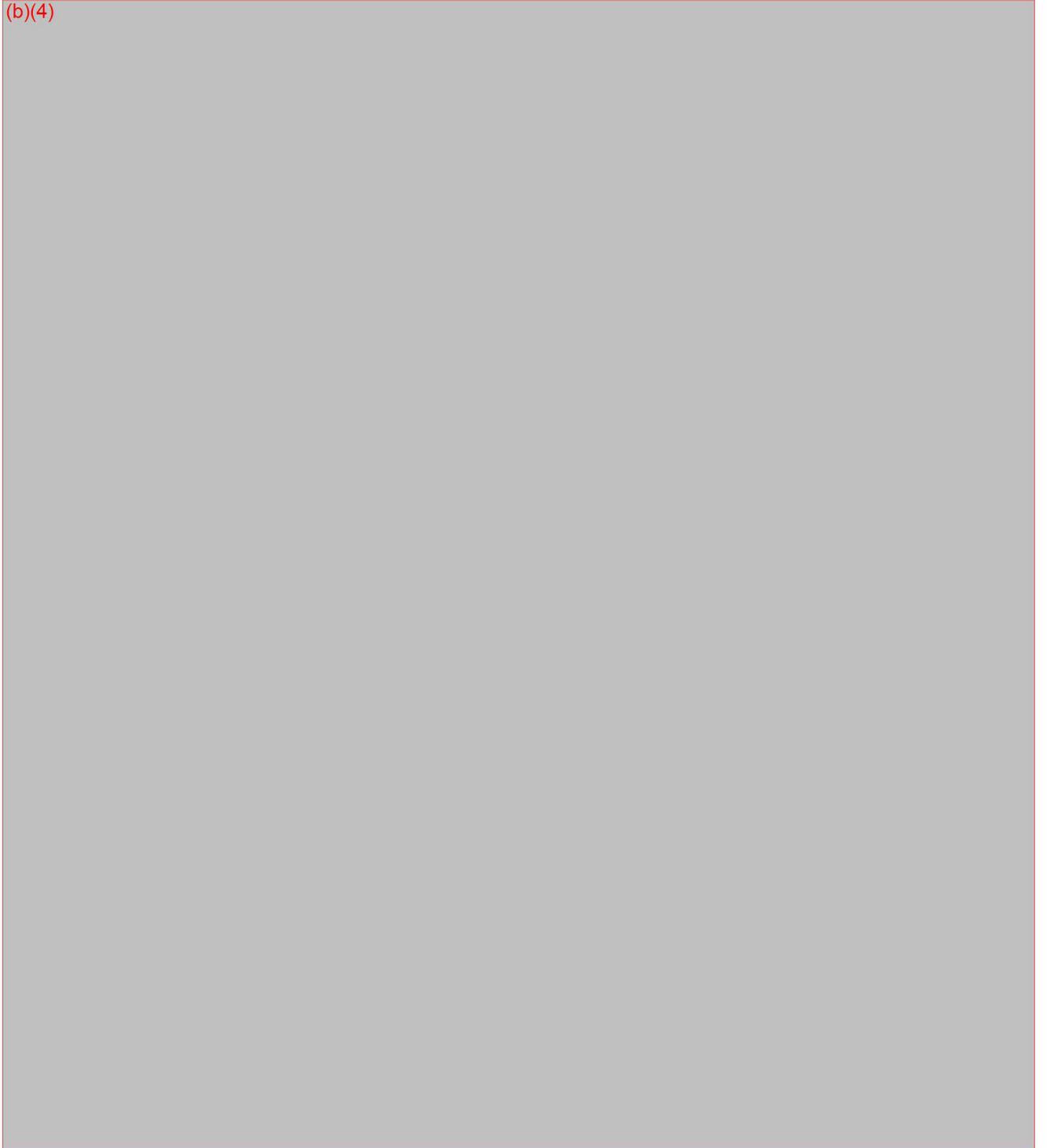


Section of standard	Description	Acceptance criteria	Results	Pass Fail	Report #
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(b)(4)

Performance Testing – Bench

(b)(4)



(b)(4)



Table 1: evGuide TLS Electrical Adaptor

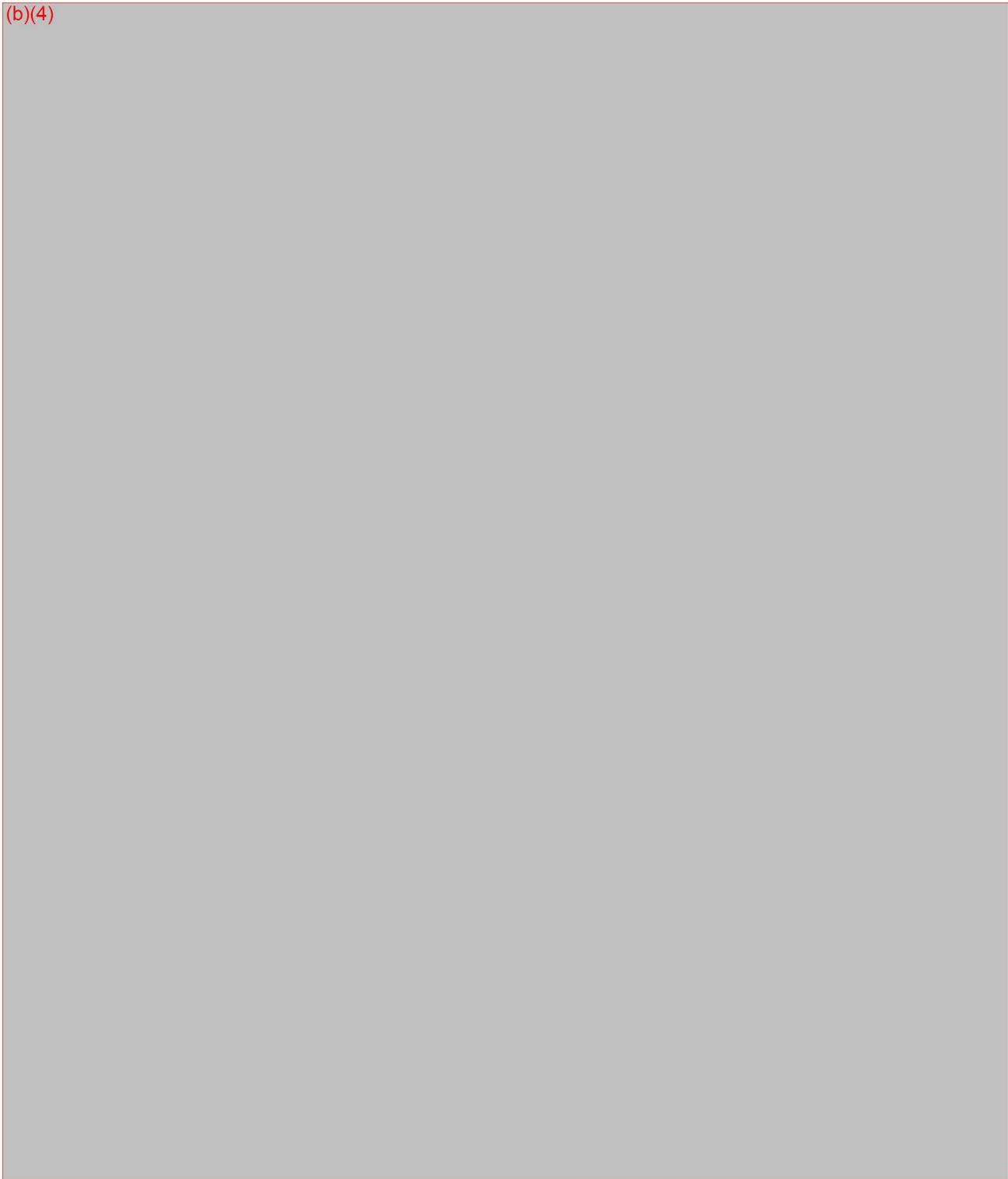
Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
(b)(4)				

Table 2: evGuide TLS Electrical Adaptor and Arrow-Johans Adaptor (connected via alligator-snap connector)

Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
(b)(4)				

Performance Testing – Human Factors

(b)(4)



Results Summary / Conclusion

(b)(4)



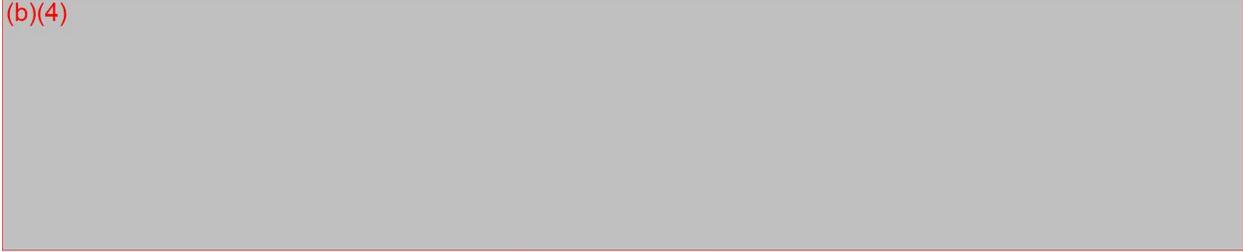
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(b)(4)



Performance Testing – Animal & Clinical

(b)(4)

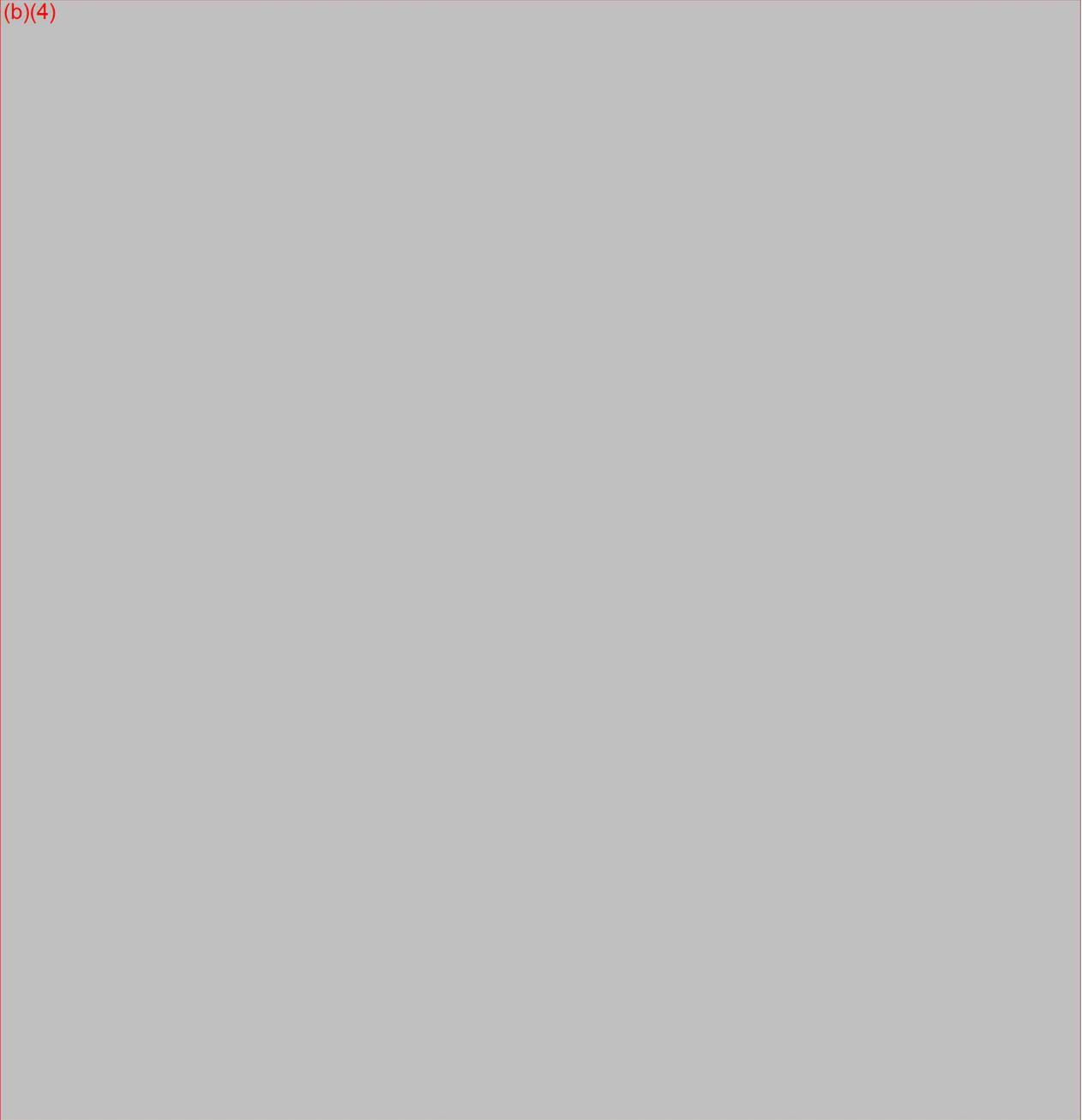
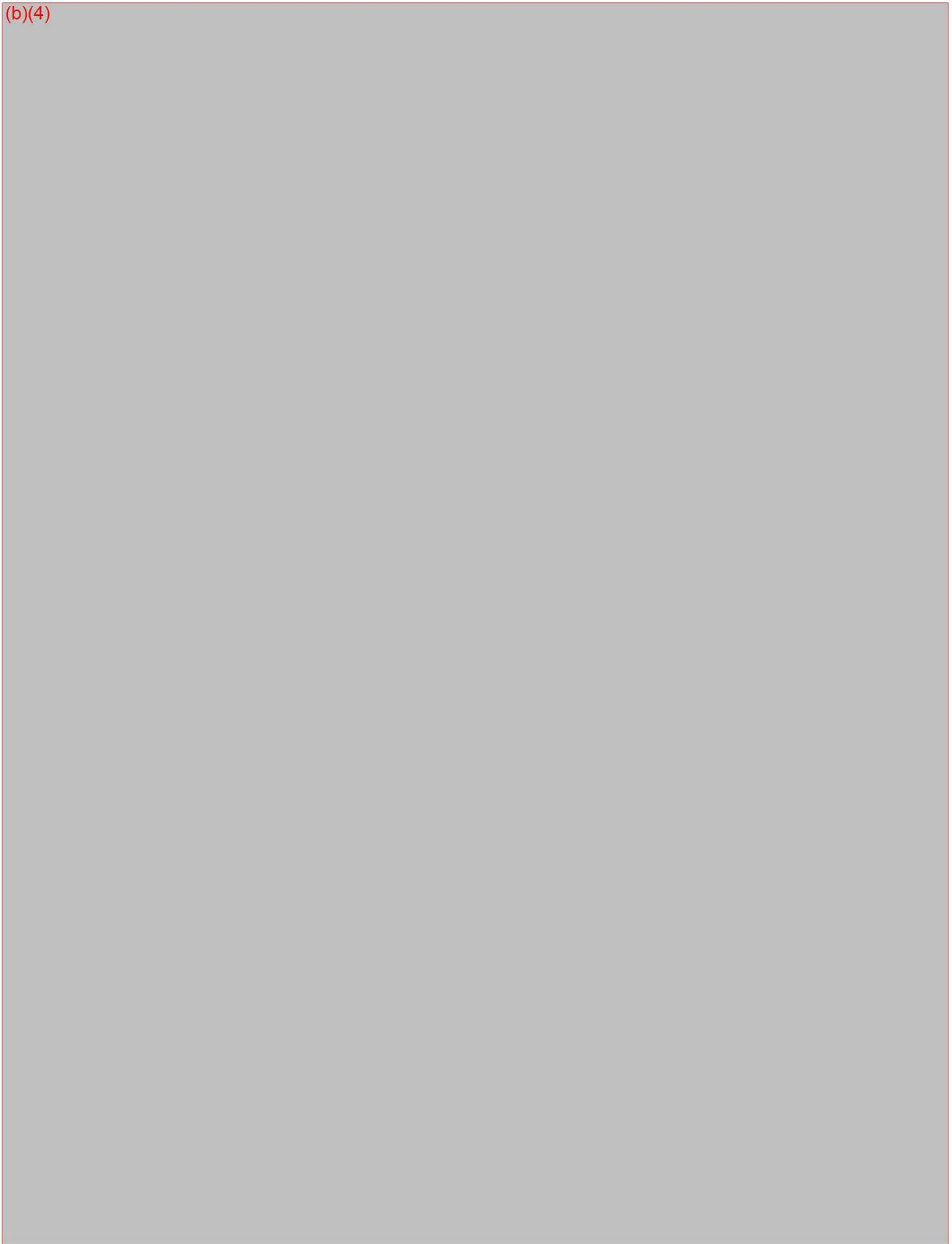


Table 16: Summary of evGuide/Sapiens TLS studies demographics

Patient demographics	Post Market (b)(4)	Human Factors/Usability (b)(4)	Total (b)(4)
(b)(4)			

(b)(4)



(b)(4)

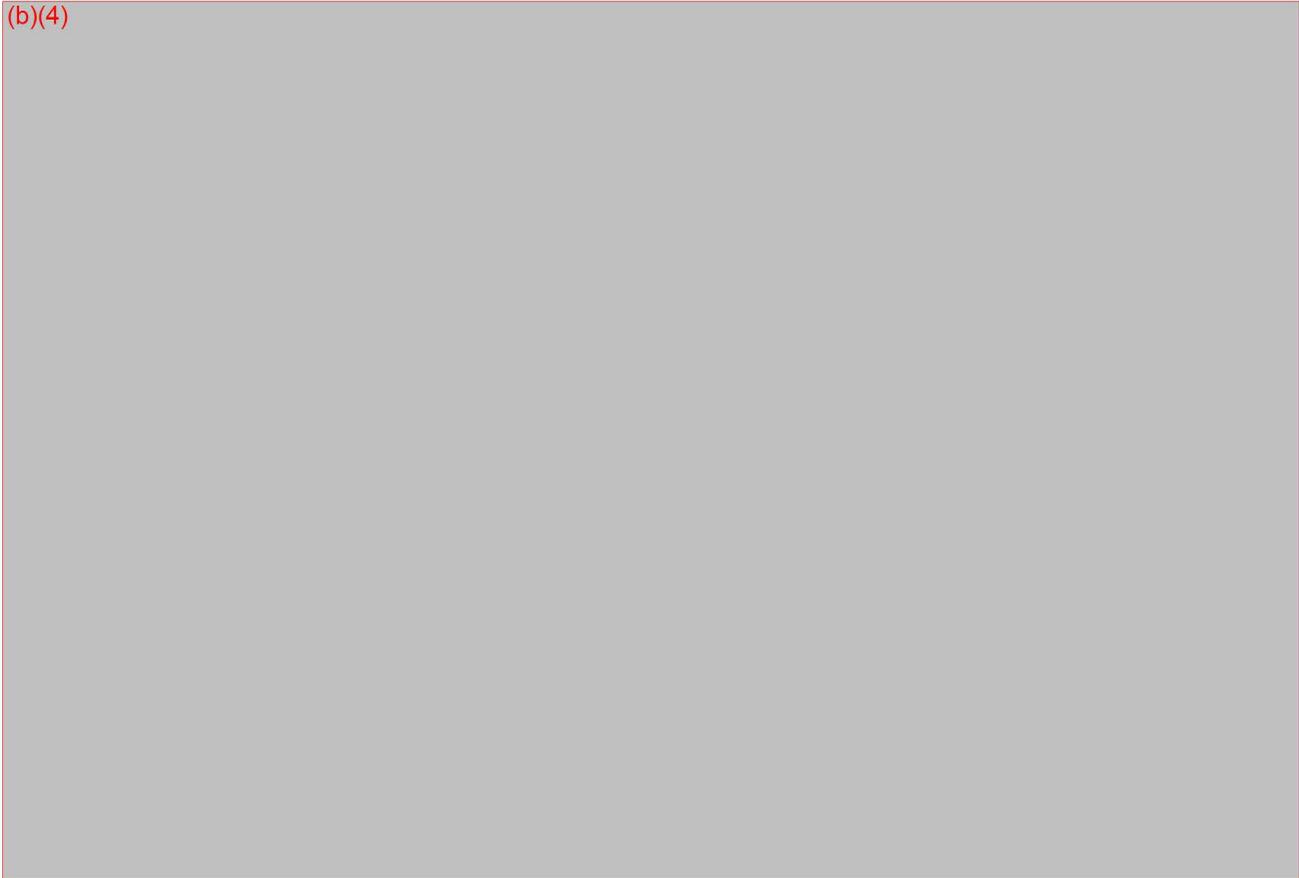


(b)(4)



Device type	Number of devices	Device brands
(b)(4)	(b)(4)	

(b)(4)



Non-clinical Testing Summary:

Electrical impedance measurement	Acceptance Criteria	Result
(b)(4)		

ECG waveform measurements	Acceptance Criteria	Result
(b)(4)		

(b)(4)

Clinical Evaluation Summary

(b)(4)

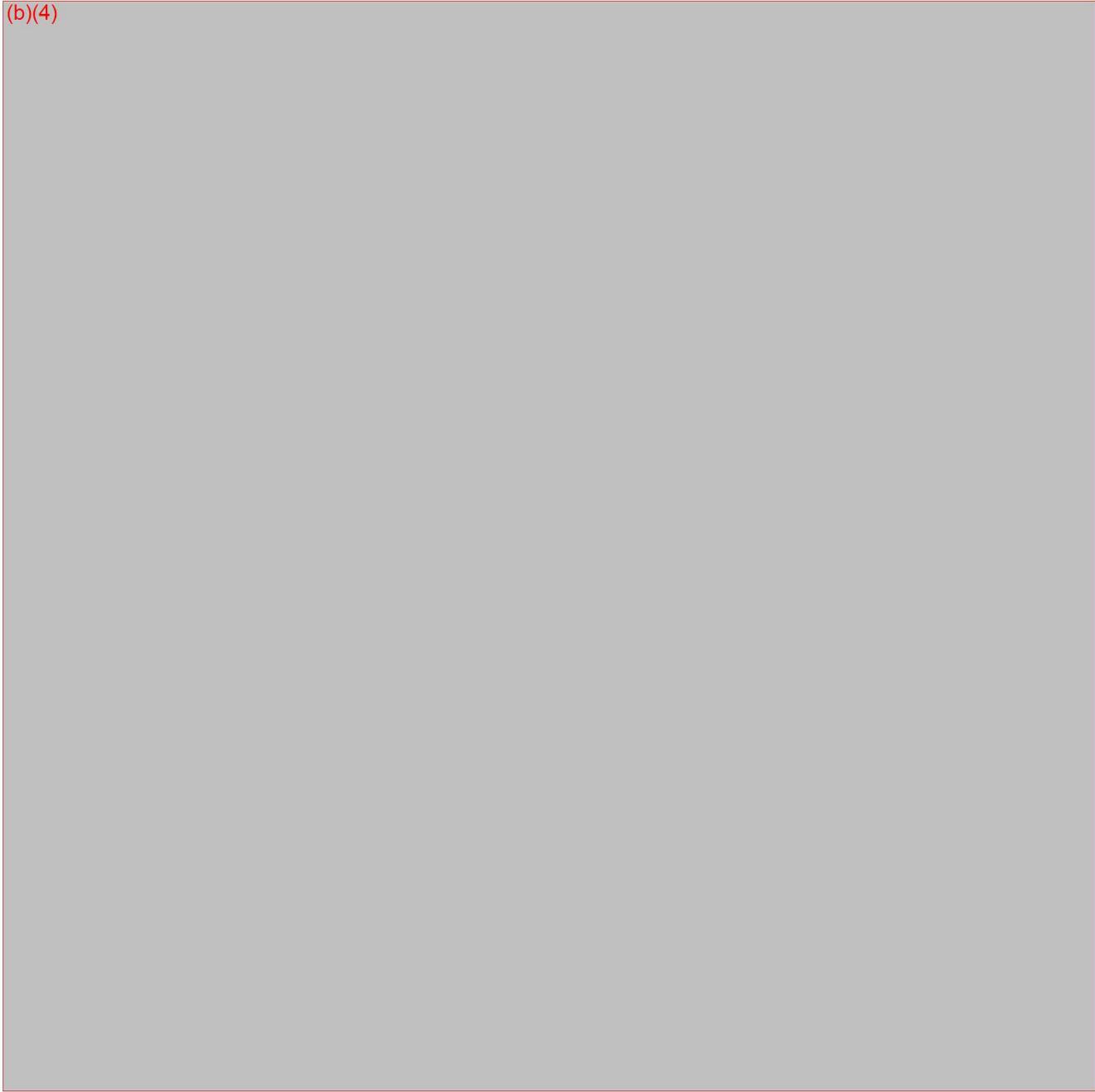
	Case	Physician assessment
1	(b)(4)	
2		
3		
4		
5		
6		
7		
8		
9		

(b)(4)

(b)(4)



(b)(4)



B2: BENCH TOP TEST – WAVEFORM EQUIVALENCE

(b)(4)



	Test Case Waveform Measurement	Equivalent: Pass / Fail
1	(b)(4)	
2		
3		
4		
5		
6		
7		
8		
9		
10		

B3: NON-CLINICAL STUDY – WAVEFORM EQUIVALENCE

(b)(4)

ECG waveform measurements	Acceptance Criteria	Result
(b)(4)		
	(b)(4)	

B4: CLINICAL STUDY – WAVEFORM EQUIVALENCE

(b)(4)



	Guided device	Date	Physician ECG waveform accuracy assessment:	Pass Fail
1	(b)(4)		(b)(4)	
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				



U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

June 08, 2010

ROMEDEX INTERNATIONAL SRL
C/O SORIN GRUNWALD
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PALO ALTO, CALIFORNIA 94303
UNITED STATES
ATTN: SORIN GRUNWALD

510k Number: K093775

Product: EVGUIDE TIP LOCATION SYSTEM

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission **MUST** be sent to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely,

510(k) Staff

1/2093775 /s/ K093775

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sorin@romedex.com

June 5, 2010

Nikhil Thakur, Reviewer
U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

FDA CDRH DMC

JUN 07 2010

Received

14-27

Subject: K093775
Response to your request for additional information from 3/4/2010

Dear Mr. Thakur:

Romedex International Srl is submitting this response to your March 4, 2010 request for additional information for the 510(k) submission referenced above. Your requests (*italics*) and our responses follow. Please note that on March 29, 2010 Romedex applied for and since received a 90 day extension to respond to the request for additional information.

(b)(4)

An updated CDRH Premarket Review Submission Cover Sheet is provided in Attachment 12.

(b)(6)

Sorin Grunwald, Ph.D.
Managing Director
Romedex International Srl

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- 16.

510(k) Summary / 510(k) Statement

1. *FDA conducts a comprehensive review of the 510(k) Summary in accordance with 21 CFR 807.92 and the Required Elements for 510(k) Statements in accordance with 21 CFR 807.93. Based on our assessment of your 510(k) Summary in Section 5 of your submission, FDA believes that your Summary does not meet the regulation. Please address the following concerns regarding your 510(k) summary:*
 - a. *Please include a summary comparing the technological modifications made to your device as it relates to your predicate devices.*
 - b. *Please include a summary of the non-clinical testing data that was submitted, referenced or relied on to demonstrate that the Subject Device is safe and effective, and whose performance meets the requirements of its pre-defined acceptance criteria and intended uses.*
 - c. *Please include a summary of the clinical data that was submitted, referenced or relied on, including:*
 - i. *Description upon whom the device was tested*
 - ii. *Data obtained from the tests and especially*
 - iii. *Adverse events and complications*
 - iv. *Other information for SE determination*

Please see the below updates to the 510(k) summary.

510(k) Summary

- Proprietary Name:** Sapiens™ Tip Location System also known as evGuide™ Tip Location System
- Device Trade name:** Sapiens™ Tip Location System (TLS)
- Product Classification:** Class II, 21 CFR §880.5970
LJS - Accessory to Percutaneous, Implanted, Long-Term Intravascular Catheters General Hospital
- Applicant name:** Romedex International Srl 58 Aleea Arubium, Bucharest, 022944 Romania, +1.650.209.4838, info@romedex.com, www.romedex.com
- Contact person:** Sorin Grunwald Ph.D., MBA, 175 Colorado Ave, Palo Alto, CA 94303, sorin@romedex.com, Tel: +1.650.209.4838, Fax: +1.650.887.0348
- Preparation Date:** June 4, 2010
- Predicate Devices:** K091324 - Sherlock 3CG Tip Positioning System
K032613 - Transvenous Pacemaker Placement Assist Device
K973371 - Conduction Anesthesia Kit
K843263 - Arrow-Johans ECG Adaptor
- Indications for Use:** The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.
- Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.
- Device Description:** The Sapiens™ TLS consists of the following elements: sterile electrical adaptor, ECG module and cable, laptop running Sapiens™ TLS software, label printer (optional), and remote control (optional). A stylet or a guidewire inserted in a central venous catheter can be connected to the Sapiens™ TLS system via the Sapiens™ TLS Electrical Adaptor establishing a direct electrical connection to the catheter distal tip for ECG signal measurement. A different ECG signal measurement method – the column of saline method – can be used by connecting the Sapiens™ TLS Electrical Adaptor to the Arrow-Johans Adaptor, by connecting the Arrow-Johans Adaptor to any central venous catheter and by injecting saline solution into the catheter lumen through the Arrow-Johans Adaptor, thus establishing electrical conductivity to the distal tip of the catheter. When the central venous catheter or its associated stylet or guidewire is connected to Sapiens™ TLS, the Sapiens™ TLS laptop screen displays skin ECG signals and endovascular electrograms acquired at the location of the distal tip of the catheter. The waveforms provided by Sapiens™ TLS can be used for guiding and positioning of the central venous catheter. These ECG waveforms can be printed using an optional label printer to document the catheter tip location for the patient's file.
- Bench Top Safety & Performance Tests:** Verification and validation tests have been performed in accordance with Design Controls per 21 CFR §820.30.

Bench top testing has been performed side-by-side with available predicate devices which has demonstrated substantial equivalence of Sapiens™ TLS to the respective predicate devices. The following tests were performed: a) electrical impedance testing and b) ECG waveform accuracy tests.

**Summary of
Non-clinical Data:**

Non-clinical studies were performed which have demonstrated safety and efficacy of Sapiens™ TLS using Electrical Adaptor, good correlation between bench top and in-vivo data, and substantial equivalence with predicate devices. The following tests were performed: a) ECG waveform accuracy comparison with a commercially available ECG monitor, b) ECG waveform accuracy comparison with the Conduction Anesthesia Kit (K973371) and c) system usability and validation testing.

**Summary of
Clinical Data:**

To date, Sapiens™ TLS has been used in Europe for central venous catheter guidance and positioning in five major hospital centers on more than 350 adult patients (ages 19-96) of both genders for placing several types of central venous catheters: PICCs, CVCs, implantable ports, hemodialysis catheters, and tunneled catheters. Several types of users including nurses and physicians have used Sapiens™ TLS for different clinical procedures, e.g., oncology, anesthesia, patient monitoring in the ICU, hemodialysis in different clinical settings: in the operating room, in outpatient clinics and at the bedside.

Side-by-side comparisons with available predicate devices were performed which demonstrated substantial equivalence of Sapiens™ TLS to the respective predicate devices.

In the two analyzed subsets of 362 patients (332 patients from a prospective, multicenter, non-controlled study and 30 patients from a human factors/ usability study), the catheter tip placement using Sapiens™ TLS at the desired location was confirmed with chest X-ray or fluoroscopy in 97% of the cases. No adverse events or complications have occurred.

**Summary of
Technological
Characteristics
Compared to
Predicate Devices**

The subject Sapiens™ TLS Electrical Adaptor combines design features, materials and technological characteristics of marketed predicate devices including the Transvenous Pacemaker Placement Assist Device (K032613) and Conduction Anesthesia Kit (K973371) such as: a) a sterile, insulated, electrically conductive wire of very low electrical resistance; b) a distal end alligator clip to connect to stylets and guidewires; c) a proximal end connector which can be connected to an ECG cable or to an ECG connection switch. When compared to the Conduction Anesthesia Kit, the Sapiens™ TLS Electrical Adaptor has simplified the design of the device by removing the switch box. When compared to Transvenous Pacemaker Placement Assist Device, the Sapiens™ TLS Electrical Adaptor has simplified the design of the device by removing the connection box.

The Sapiens™ TLS Electrical Adaptor may be connected to the ECG pin of the predicate Arrow-Johans Adaptor (K843263) using an ECG cable which allows for the saline conduction method of ECG measurement. Use of the Sapiens™ TLS Electrical Adaptor with the Arrow-Johans Adaptor does not require any modifications of design features, materials, or technological characteristics of the marketed predicate device.

Additionally, the subject Sapiens™ TLS System combines design features, components and technological characteristics of the predicate device Sherlock 3CG Tip Positioning System (K091324) but uses only cardiac electrical signal detection to provide real-time catheter tip location information. The subject Sapiens™ System does not use a passive magnet like the predicate device.

Any differences between technological features of the subject and predicate devices do not raise new questions of safety or efficacy of the subject Sapiens™ TLS device.

**Summary of
Substantial
Equivalence:**

The Sapiens™ TLS has the same intended use and similar indications for use as the commercially available Sherlock 3CG Tip Positioning System (K091324), Transvenous Pacemaker Placement Assist Device (K032613), Conduction Anesthesia Kit (K973371), and Arrow-Johans ECG Adaptor (K843263). Additionally, clinical and non-clinical performance testing has demonstrated that any differences in technological characteristics do not raise new issues of safety or effectiveness when compared to the aforementioned predicate devices. Therefore, the Sapiens™ TLS meets the requirements for substantial equivalence to the referenced predicate devices.

Labeling

2. On page 2 of the Subject Device User Manual, under the heading "Background", there is a statement regarding the limitation of use for the device. Specifically, the User Manual states, "Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location." However, there is no reference to this cautionary statement under the "Contraindications", "Warnings", "Precautions" or "Safety Information" sections of the manual. The statement describes a scenario where the Subject Device's ability to successfully determine a catheter position is impaired by an underlying medical condition in the patient. Please modify your labeling to specifically identify this concern under "Warnings" or "Precautions." Additionally, please modify the labeling to reflect the additional steps that a clinician would have to take when using this device with a patient who might have an altered cardiac rhythm due to an underlying disease or medical condition.

The following wording has been added to the User's Manual in Section 1.4 "Warnings and Precautions" (Attachment 1: evGuide-Sapiens TLS User's Manual).

- Warning:** *In patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*
- Warning:** *The SapiensTM TLS User's Manual provides information about ECG waveforms and their correspondence with specific locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the user must stop using SapiensTM TLS and use of an additional and/or different method for catheter tip location confirmation, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

3. The labeling for your device contains some symbology that is not accompanied by a description of that symbol in English. For example, the labeling contains a symbol that has the number "2" with a "slash" through it, the terms "Sterile" and "EO" with boxes around them, and an exclamation point (i.e. "!") surrounded by a triangle. According to 21 CFR, 801.15(c)(1), any symbol on a medical device distributed within the United States, must be accompanied with a description of the symbology in English. Please edit the labeling to comply with this requirement.

It is noteworthy that FDA's Guidance "Use of Symbols on Labels and in Labeling of In Vitro Diagnostic Devices Intended for Professional Use" (November 30, 2004) is only recognized by CDRH's Office of In Vitro Diagnostics, and does not apply to your device.

Please see below for the revised labeling that complies with 21 CFR, 801.15(c)(1):

**ROMEDEX INTERNATIONAL SRL
SAPIENS™ TLS ELECTRICAL ADAPTOR**

LOT xxxx-xxxxxx  Date of manufacture: xxxx-xx
QTY: 1  Use By: xxxx-xx

 Attention, See Instructions for Use

 Single Use – Do not resterilize

STERILE EO Sterilized by ethylene oxide

 Sterile unless package is damaged or open

R_x only

This product does not contain natural rubber latex

U.S. and other patents pending

After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations.

CE₁₈₆₈



**Manufactured by SC Incerplast SA For:
Romedex International Srl
58 Aleea Arubium
022944 Bucharest, Romania
Tel: +1.650.209.4838, Fax: +1.650.887-0348
www.romedex.com**

**ROMEDEX INTERNATIONAL SRL
SAPIENS™ TLS ECG MODULE**



Serial Number: xxxx-xxxxxx



Date of manufacture: xxxx-xx



Attention, See User's Manual



U.S. and other patents pending



**Manufactured by SC Incerplast SA For:
Romedex International Srl
58 Aleea Arubium
022944 Bucharest, Romania
Tel: +1.650.209.4838
Fax: +1.650.887-0348
www.romedex.com**

4. Regarding electromagnetic compatibility, the evGuide TLS User Manual states that “Although the evGuide TLS System conforms to certain international safety and electromagnetic compatibility standards, the evGuide TLS System is intended for use by medical personnel who have received evGuide TLS System training.” FDA’s review of electromagnetic compatibility and electrical safety testing performed on the Subject Device shows that the evGuide TLS was only partially tested for electrical safety. Please modify the labeling to specifically identify precautions that the end user should take when operating your device in the presence of electromagnetic radiation (i.e. MRI, CT Scan, X-rays).

The following wording has been added to the User’s Manual in Section 1.4 “Warnings and Precautions” (Attachment 1: evGuide-Sapiens TLS User’s Manual).

Warning: *Do not place and/or use the Sapiens™ TLS system in the presence of strong magnetic fields such as Magnetic Resonance Imaging (MRI) devices. The high magnetic fields created by an MRI device will attract the equipment with a force sufficient to cause death or serious personal injury to persons between the equipment and the MRI device. This magnetic attraction may also damage the equipment. The magnetic and the RF fields associated with the MRI environment may interfere with the display of ECG waveforms. Consult the MRI manufacturer for more information.*

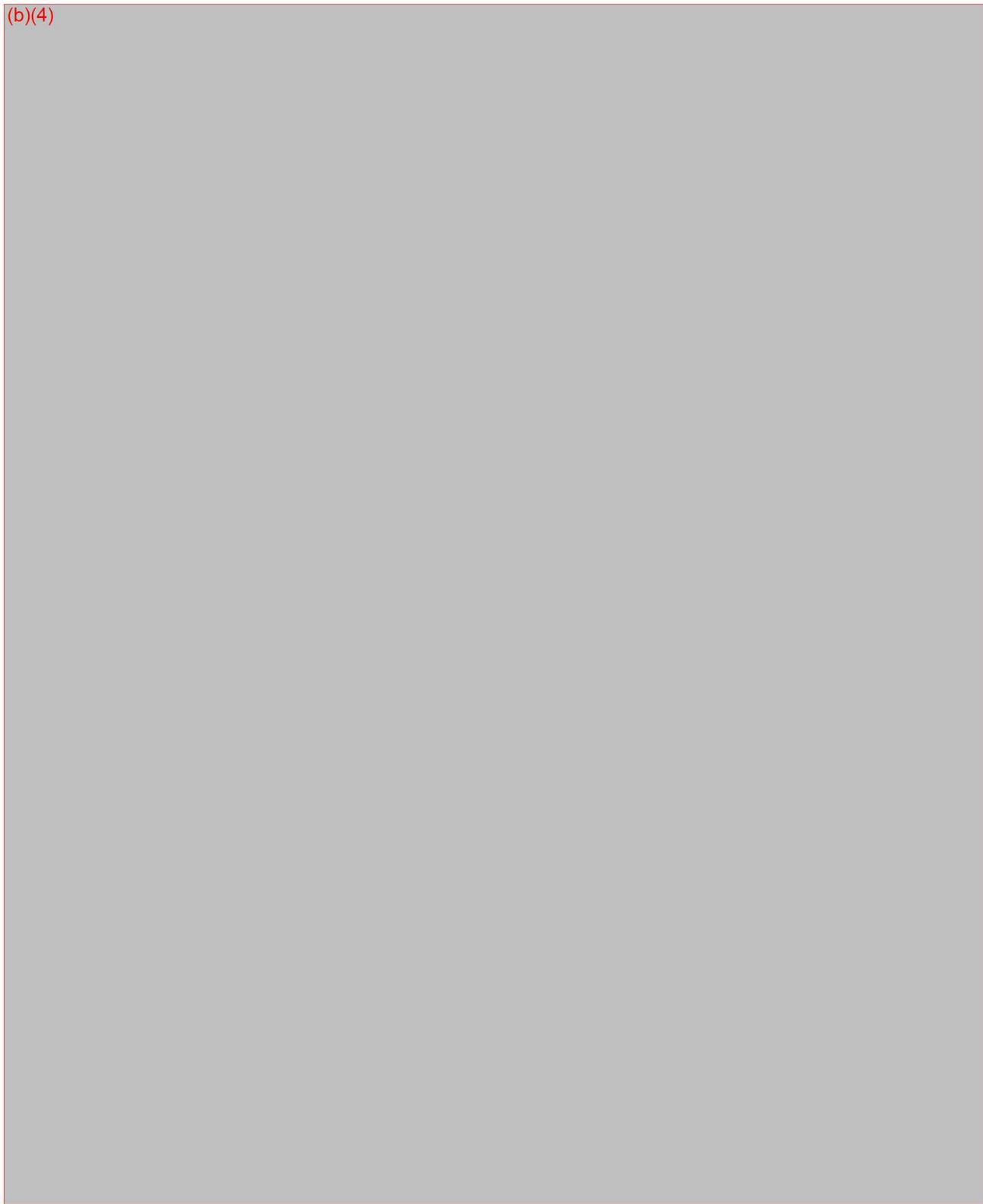
Caution: *Active electric motor driven equipment, such as pumps may interfere with the display of the ECG waveforms. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Caution: *Equipment such as CT scanners, X-rays and fluoroscopy systems, cauterizers and diathermy equipment, operating in close proximity may emit strong electromagnetic or radio frequency interference (RFI) which could interfere with the display of ECG waveforms by Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Caution: *Electric equipment which requires direct contact with the patient may interfere with the display of ECG waveforms by Sapiens™ TLS. Do not use electric cauterization, electric scalpels, and ablation equipment while using Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Sterilization/Shelf Life/Reuse

(b)(4)



(b)(4)



Acceptance criteria and summary of test methodology

(b)(4)



Sample size

(b)(4)



Summary of performance data

(b)(4)



Process conditions	Analyte	Run	(b)(4)
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(b)(4)



(b)(4)



Summary of test methodology for the Shelf Life Testing

(b)(4)



Sample size

(b)(4)



Summary of performance data

(b)(4)



Acceptance criteria

(b)(4)

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Summary of test methodology

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Sample size

(b)(4)

A rectangular area of the page is redacted with a light gray background, covering the content under the 'Sample size' section.

Summary of acceptance criteria and performance data

(b)(4)

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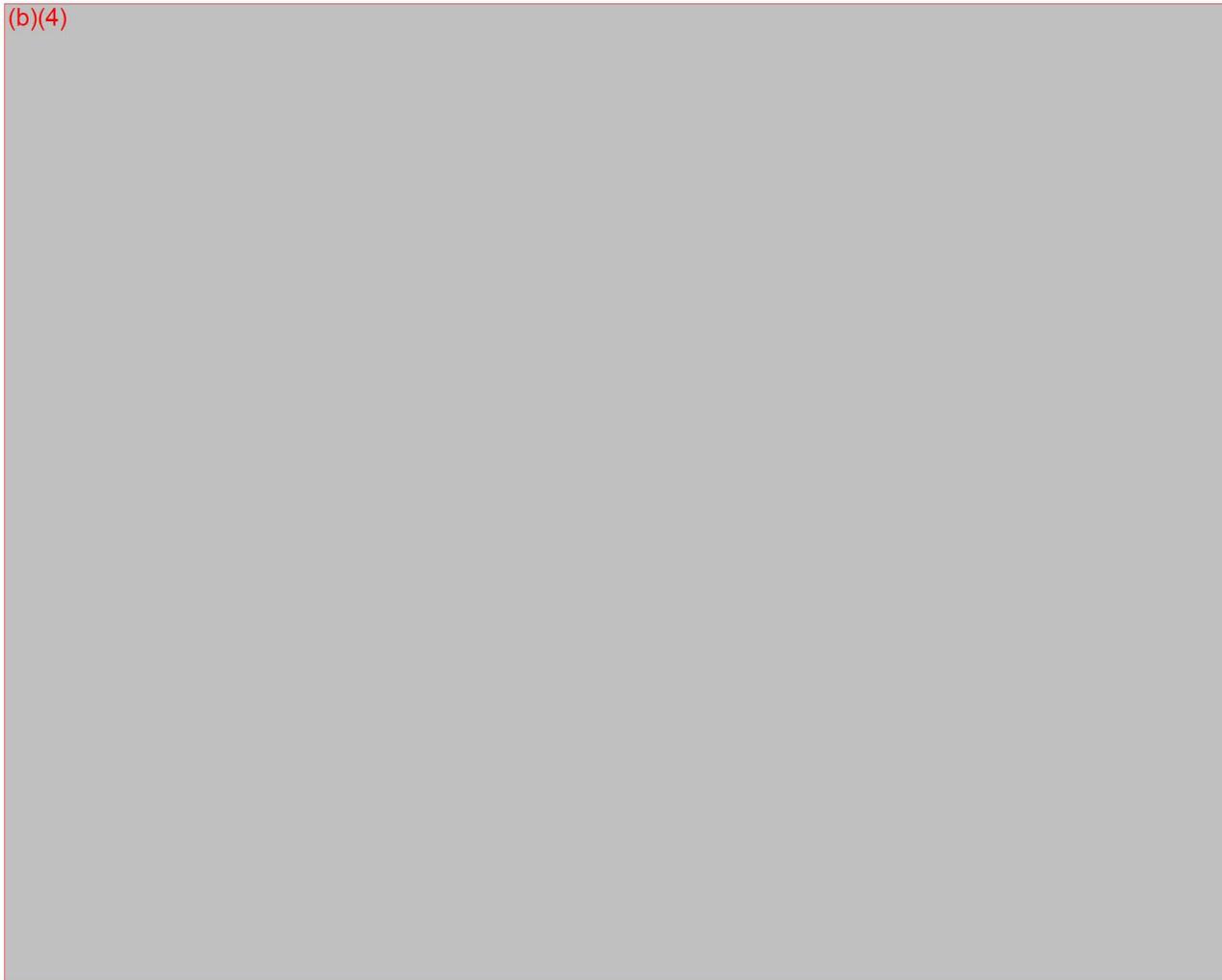


Biocompatibility

(b)(4)



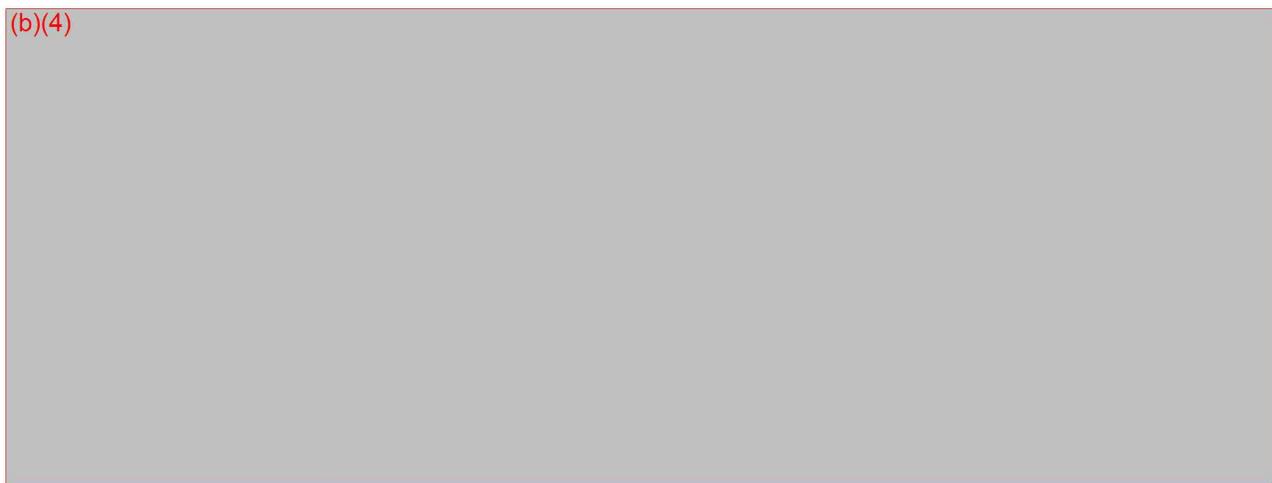
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Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

(b)(4)

Section of standard	Description	Acceptance criteria	Results	Pass Fail	Report #
---------------------	-------------	---------------------	---------	-----------	----------

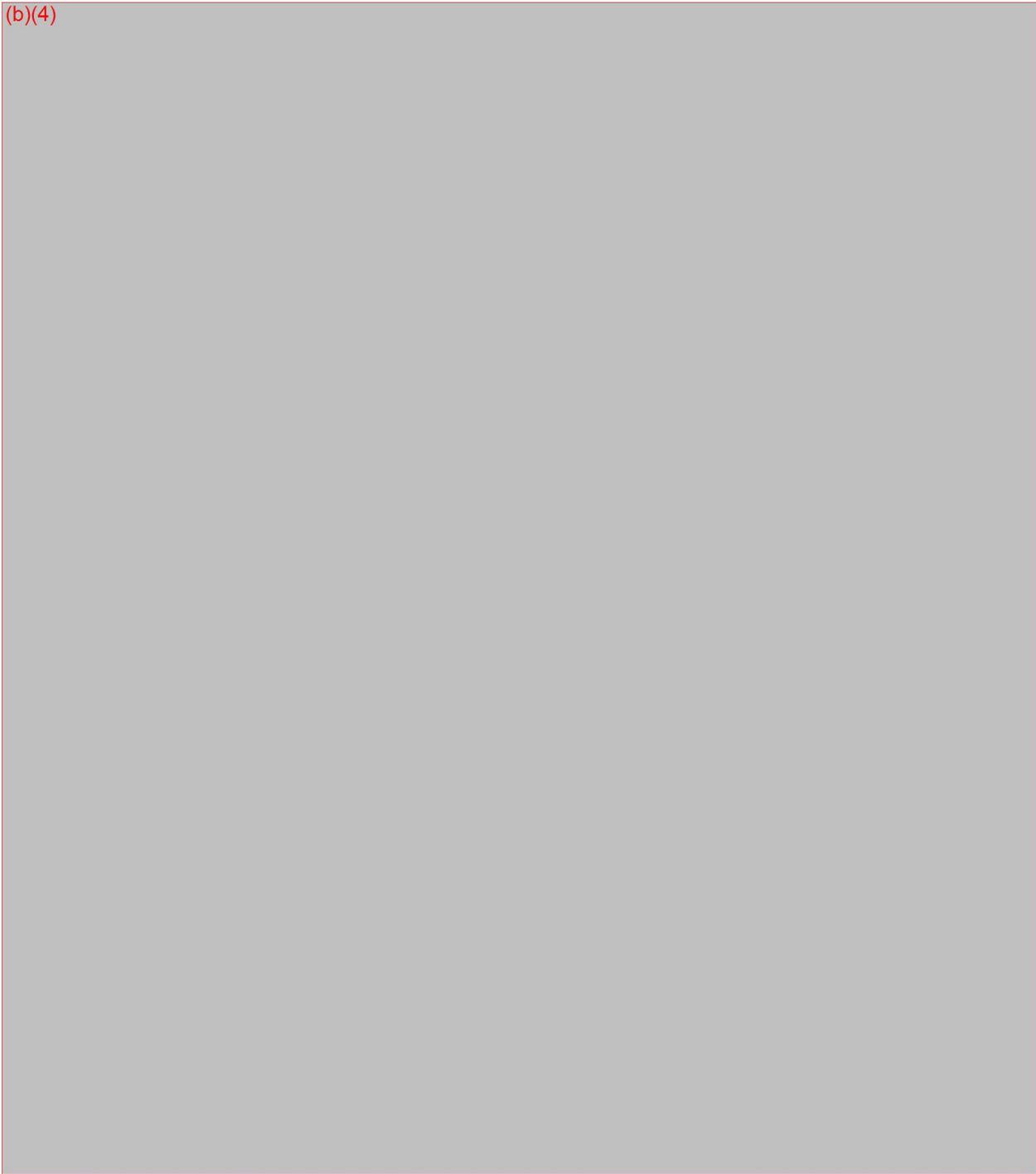
(b)(4)

Section of standard	Description	Acceptance criteria	Results	Pass Fail	Report #
(b)(4)					

(b)(4)

Performance Testing – Bench

(b)(4)



(b)(4)



Table 1: evGuide TLS Electrical Adaptor

Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
(b)(4)				

Table 2: evGuide TLS Electrical Adaptor and Arrow-Johans Adaptor (connected via alligator-snap connector)

Test and test methodology	Acceptance criteria	Sample size	Summary of performance data	Pass Fail
(b)(4)				

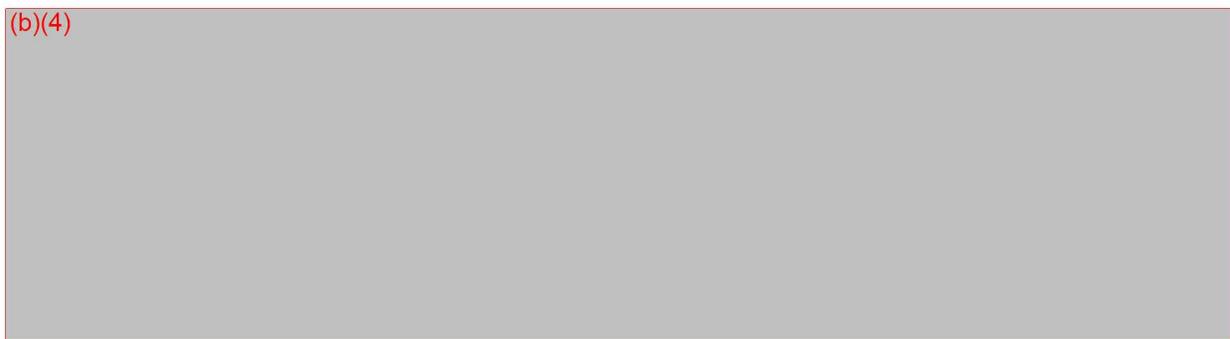
Performance Testing – Human Factors

(b)(4)



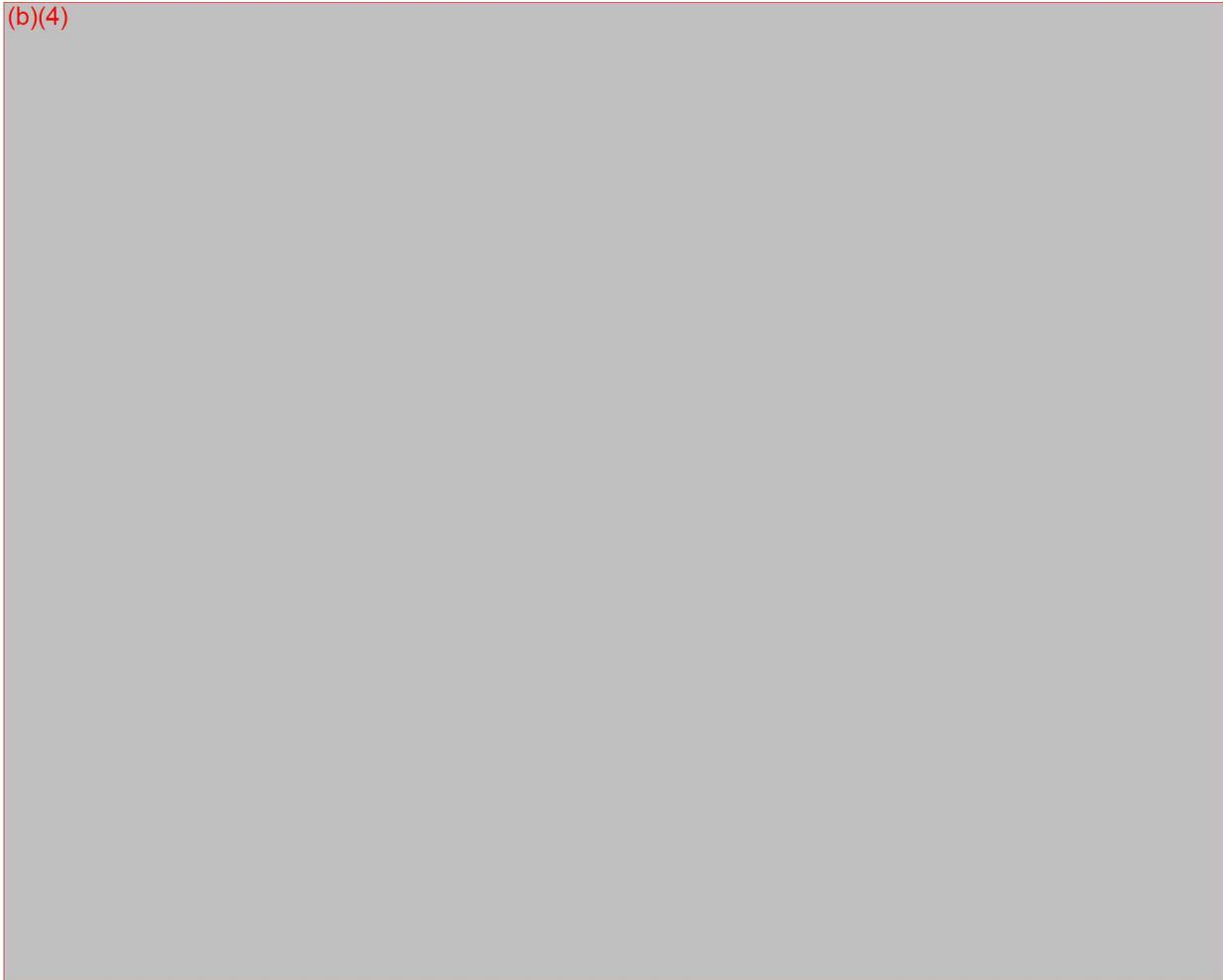
Background

(b)(4)

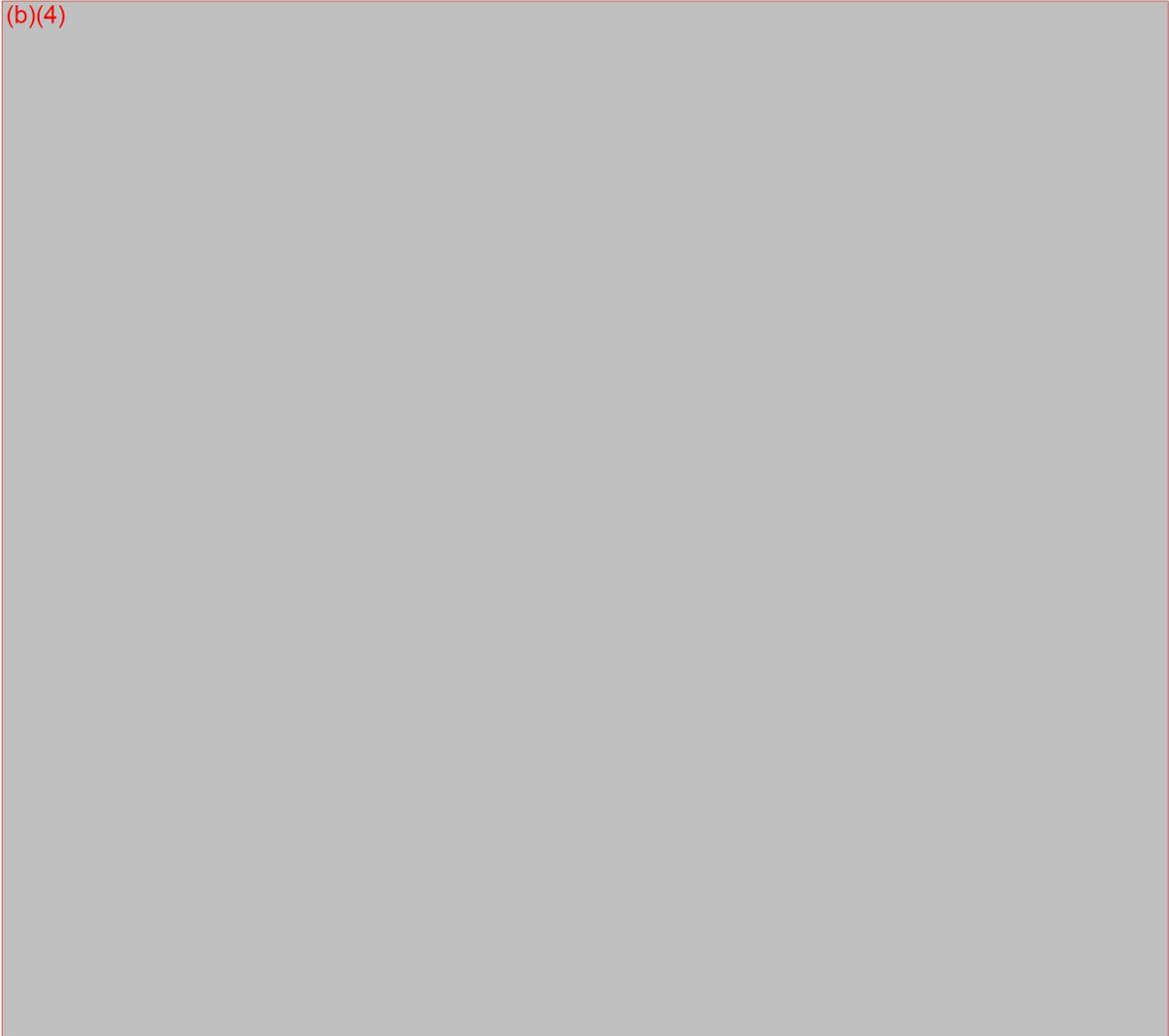


Results Summary / Conclusion

(b)(4)



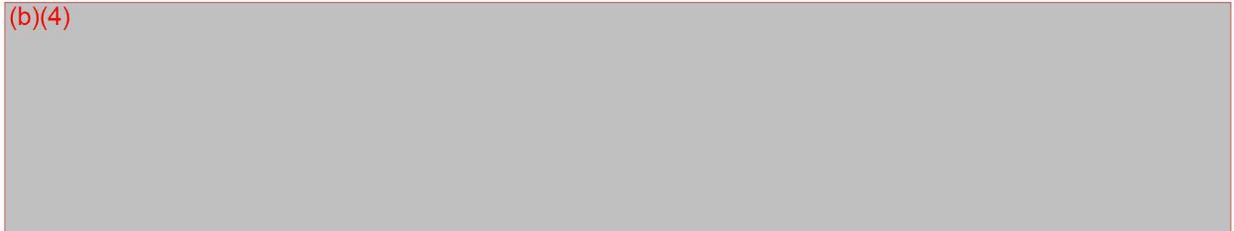
(b)(4)



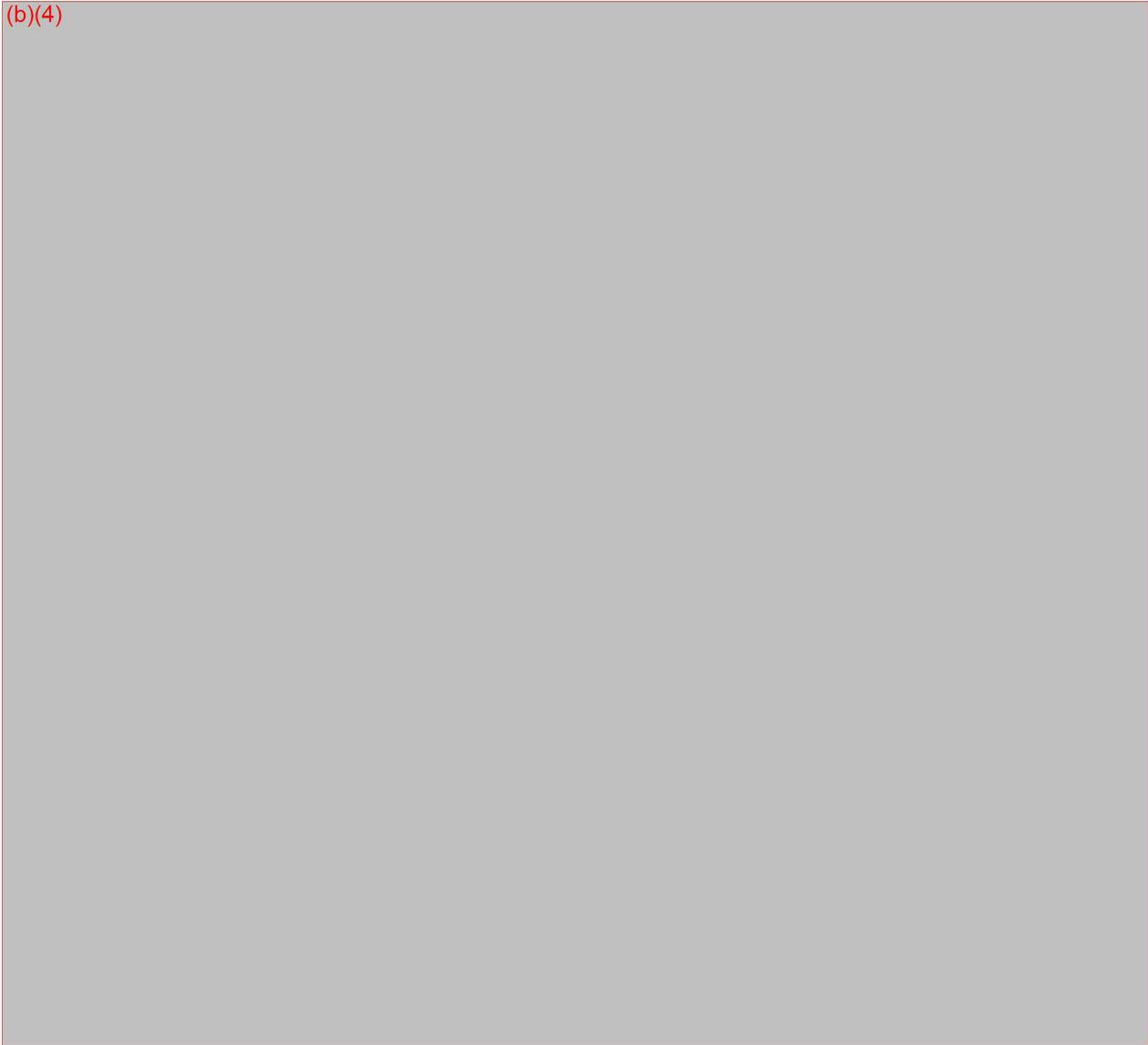
(b)(4)



(b)(4)



(b)(4)



Performance Testing – Animal & Clinical

(b)(4)

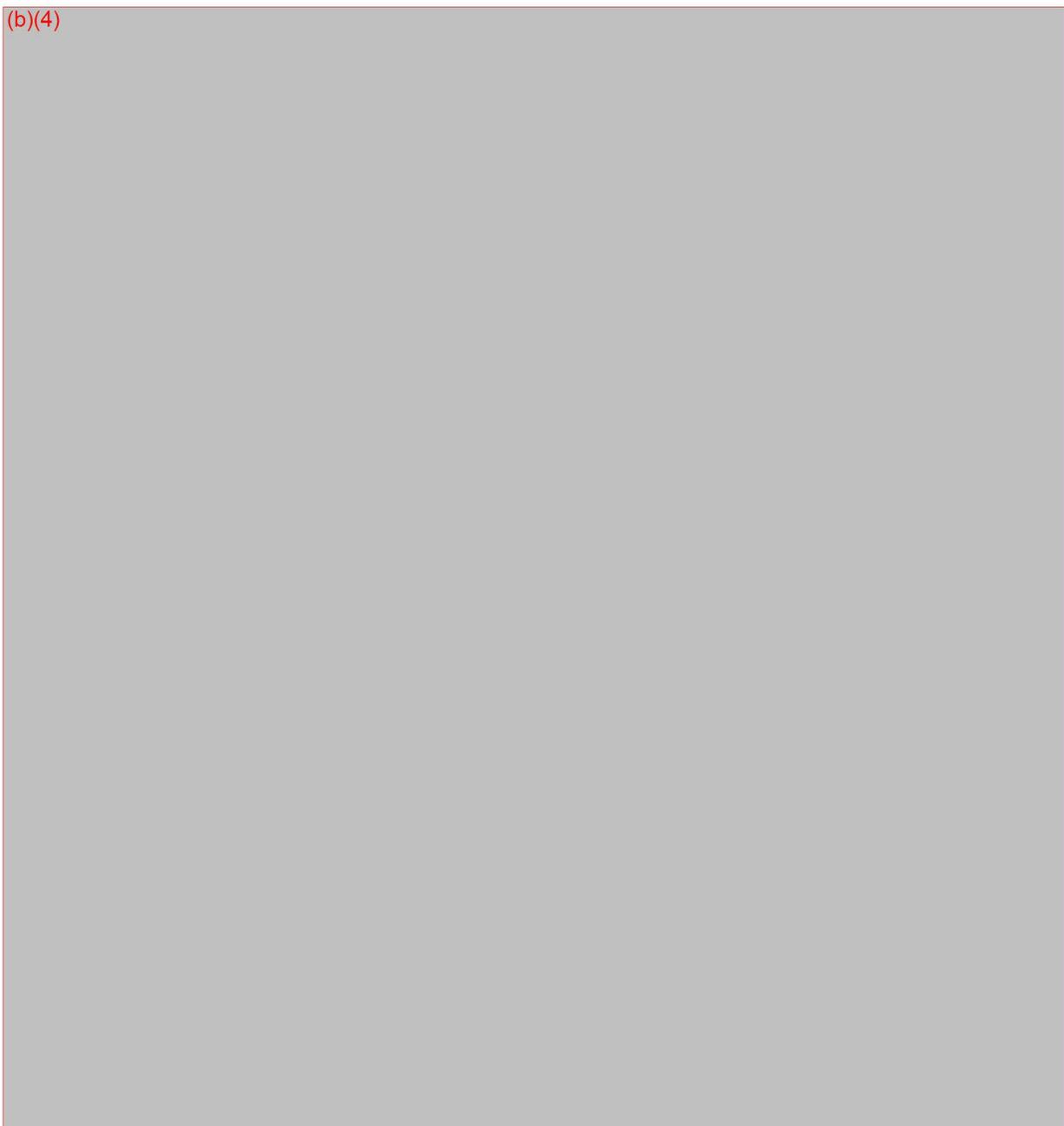


Table 16: Summary of evGuide/Sapiens TLS studies demographics

Patient demographics	Post Market (b)(4)	Human Factors/Usability (b)(4)	Total (b)(4)
(b)(4)			

The following wording has been added to the Indications for Use statement (Attachment 13) in order to identify the specific patients and clinical scenarios where this device should / should not be used:

Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Labeling was updated to identify the specific patients and clinical scenarios where this device should / should not be used. The following wording has been added to the User's Manual in Section 1.4 "Warnings and Precautions" (Attachment 1: evGuide-Sapiens TLS Users Manual).

Warning: *The Sapiens™ TLS User's Manual provides information about ECG waveforms and their correspondence with specific locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Warning: *In patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Warning: *In patients undergoing central venous catheterization using venous access through the saphaneous or the femoral veins, the catheter tip will typically not reach the right atrium and the caval atrial junction. In such a situation, the ECG waveforms described by this manual cannot be used for catheter guidance and placement and the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

Warning: *In certain patients, unstable ECG waveforms may be detected because of the manipulation of the Sapiens™ TLS Adaptor by the user. Verify that the connection between the Sapiens™ TLS Adaptor and the central venous catheter and the connection between the Sapiens™ TLS Adaptor and the ECG cable are free from contact with any other material and refrain from touching the Sapiens™ TLS Adaptor and any of its connections. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip*

location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: *In certain patients no ECG waveforms may be detected because of very specific impedance mismatch between the patient and the ECG electrodes. Be sure to use the Instructions for Use provided by the manufacturer of the skin electrodes. Verify the connection between the patient's skin and the electrodes, between the electrodes and Sapiens™ TLS ECG cable, and between the Sapiens™ TLS Adaptor and the Sapiens™ TLS ECG cable. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

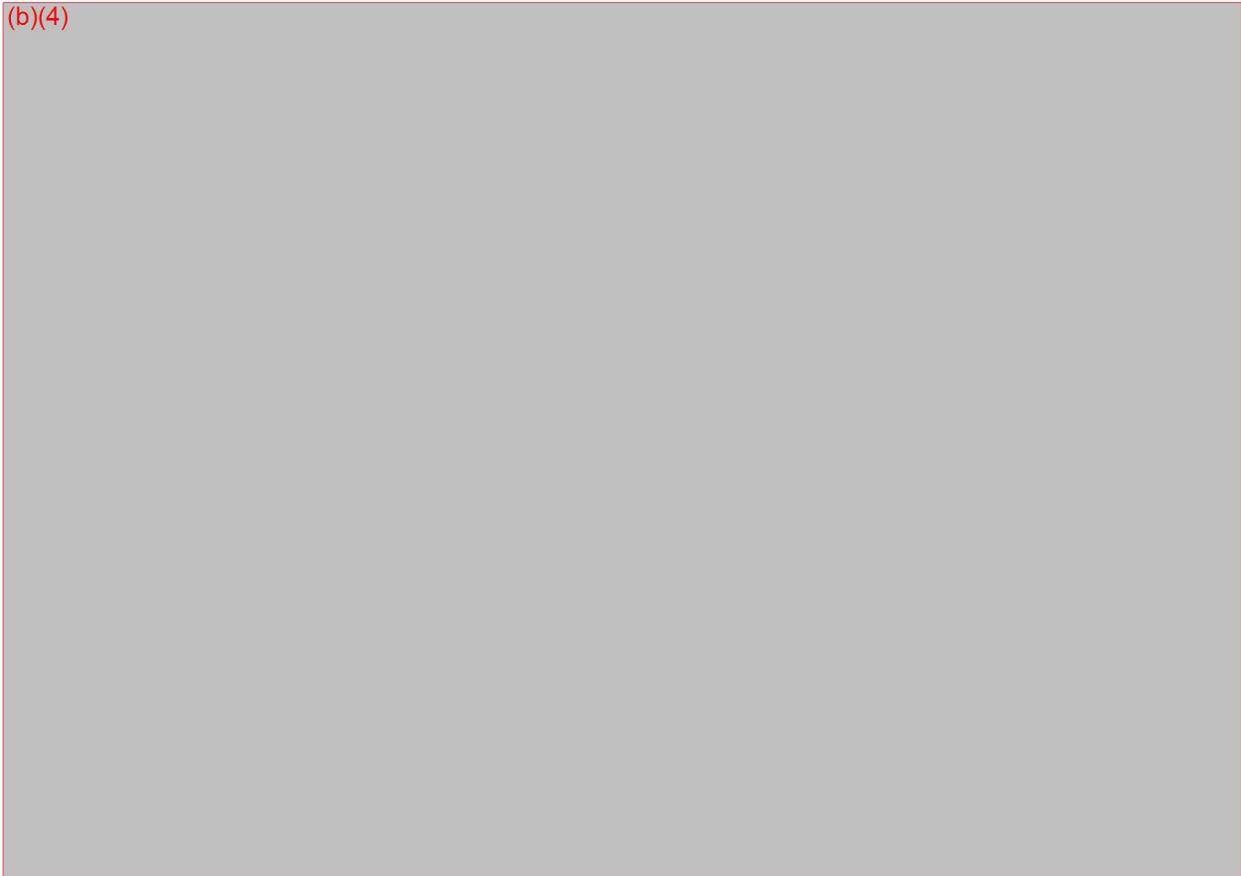
Warning: *In neonates unstable ECG waveforms may be detected because of patient's movements or manipulation by the user. In such a situation, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.*

(b)(4)



Device type	Number of devices	Device brands
(b)(4)	(b)(4)	

(b)(4)



Non-clinical Testing Summary:

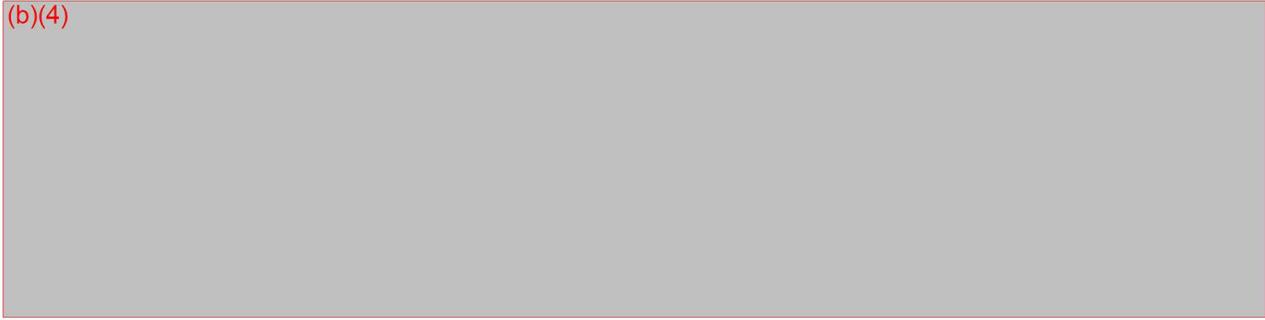
Electrical impedance measurement	Acceptance Criteria	Result
(b)(4)		

ECG waveform measurements	Acceptance Criteria	Result
(b)(4)		

(b)(4)

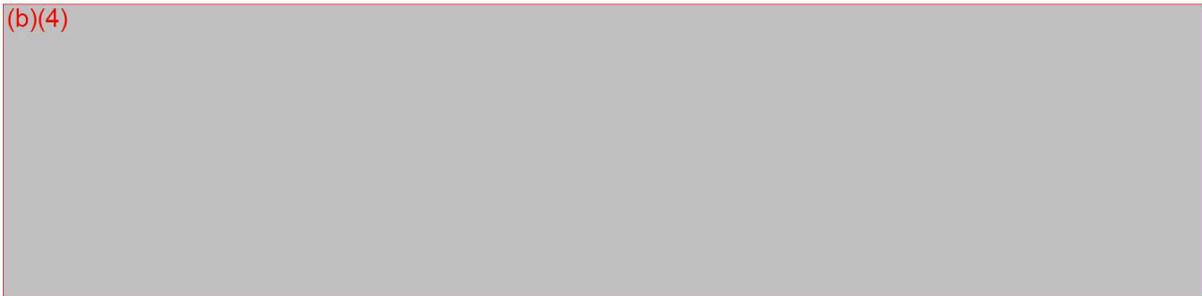
Clinical Evaluation Summary

(b)(4)



	Case	Physician assessment
1	(b)(4)	
2		
3		
4		
5		
6		
7		
8		
9		

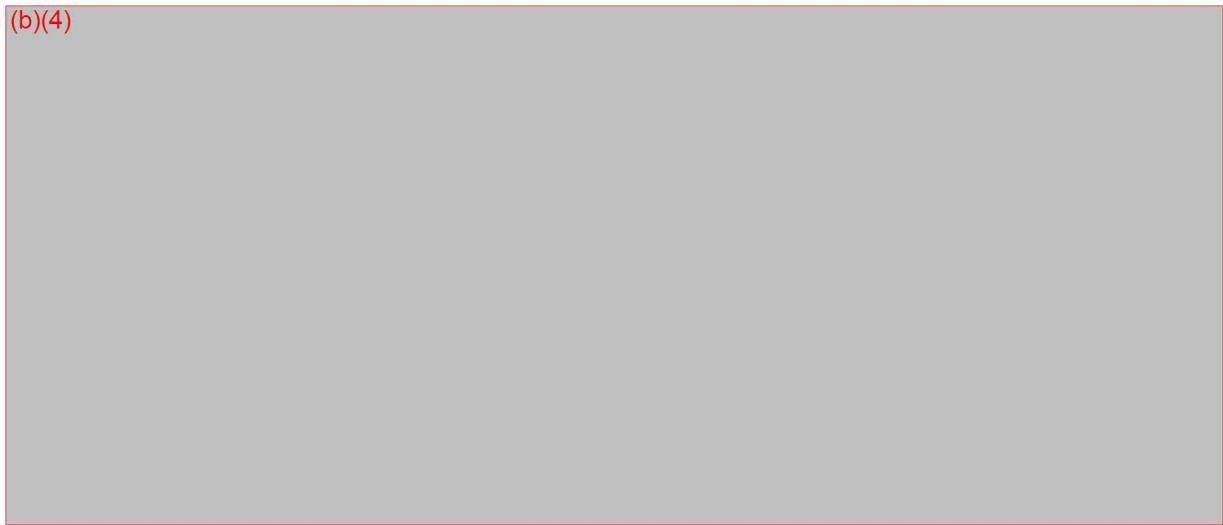
(b)(4)



(b)(4)



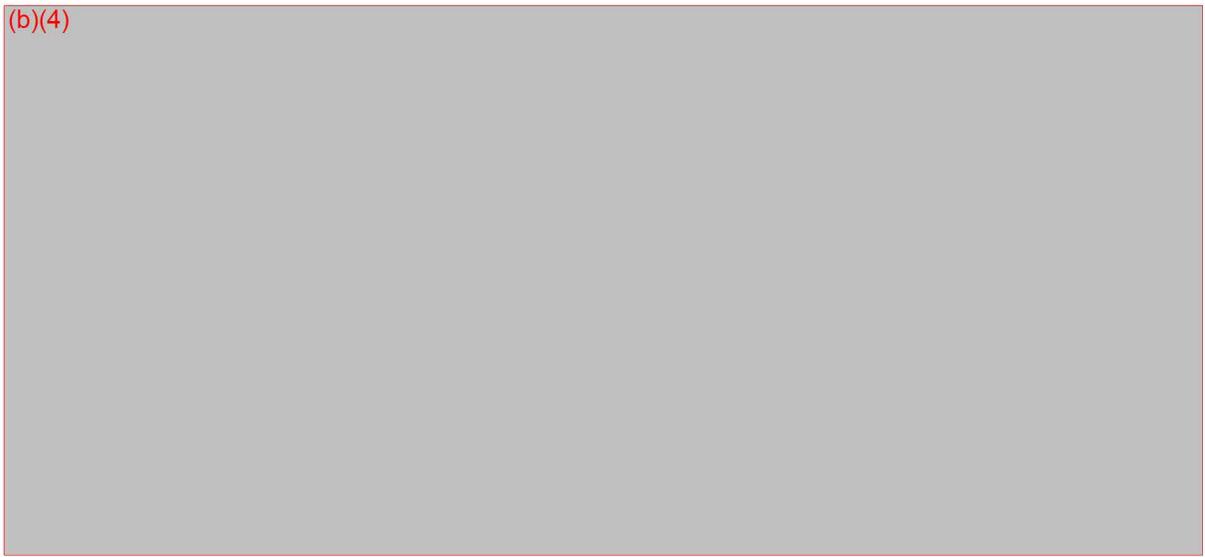
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A summary of the comparison results are provided below.

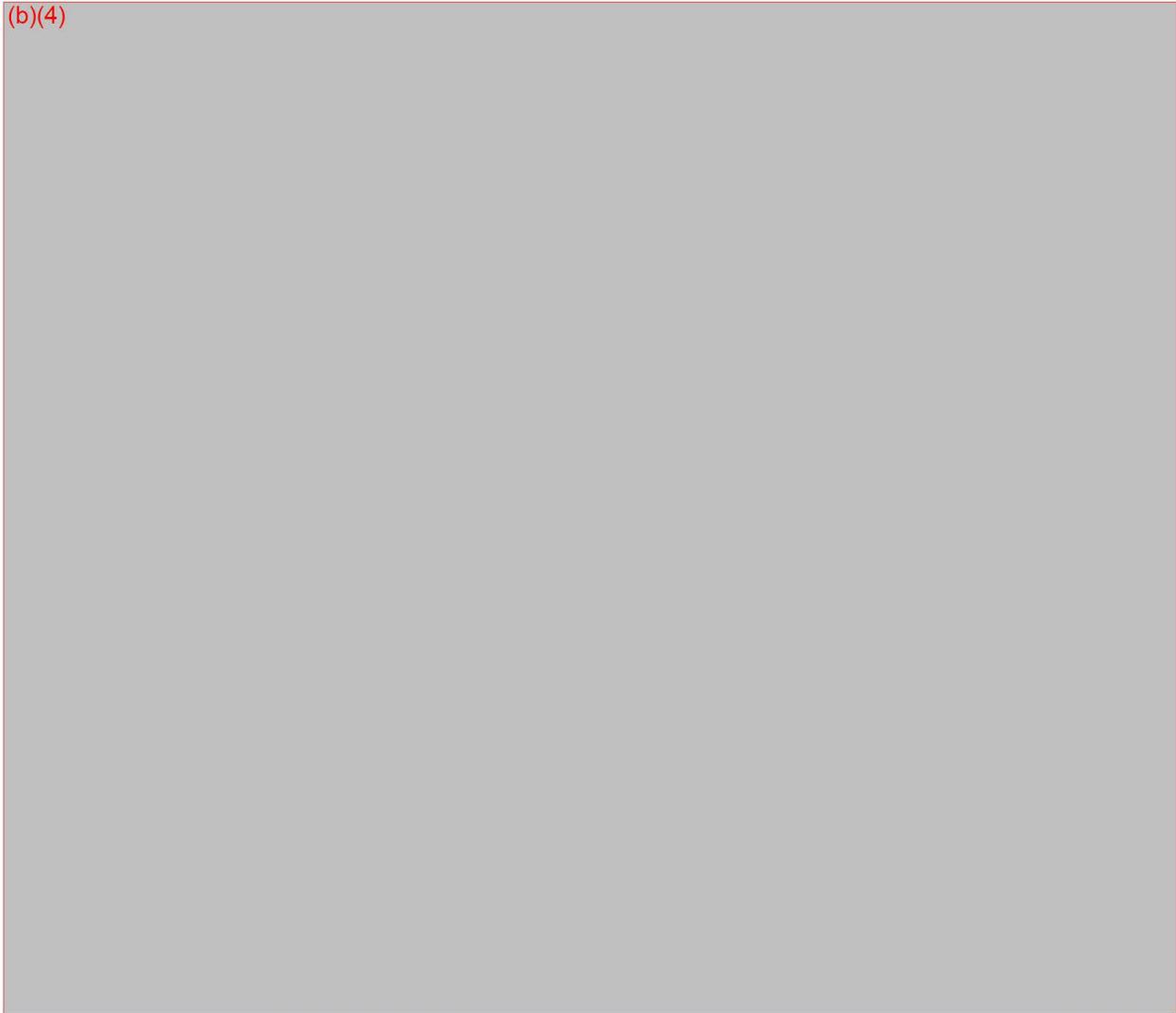
B1: BENCH TOP TEST – ELECTRICAL IMPEDANCE EQUIVALENCE

(b)(4)



B2: BENCH TOP TEST – WAVEFORM EQUIVALENCE

(b)(4)



	Test Case Waveform Measurement	Equivalent: Pass / Fail
1	(b)(4)	
2		
3		
4		
5		
6		
7		
8		
9		
10		

B3: NON-CLINICAL STUDY – WAVEFORM EQUIVALENCE

(b)(4)

ECG waveform measurements	Acceptance Criteria	Result
---------------------------	---------------------	--------

(b)(4)

B4: CLINICAL STUDY – WAVEFORM EQUIVALENCE

(b)(4)



	Guided device	Date	Physician ECG waveform accuracy assessment: Certodyn vs. evGuide	Pass Fail
1	(b)(4)			
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				

ATTACHMENT 1

EVGUIDE-SAPIENS TLS USERS MANUAL

evGuide-Sapiens™ TLS USER'S MANUAL

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evGuide-Sapiens™ TLS USER'S MANUAL

Note: The names evGuide™ TLS and Sapiens™ TLS will be used interchangeably in this document.

1. Overview

1.1 Indications for Use

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

1.2 The ECG Method for Catheter Guidance

Guiding the placement of central venous catheter using cardiac electric signals is an accepted clinical method as practiced in many health care institutions and as documented in many papers including:

- a. *Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation*, by Nancy Moureau et al. published in the Journal of the Association for Vascular Access in 2010, JAVA Vol. 15 No. 1 2010, pp. 9-15
- b. *The ECG method for positioning the tip of PICCs: results from two preliminary studies*, by Mauro Pittiruti et al. published in the Journal of the Association for Vascular Access in 2008, JAVA Vol. 13 No. 4 2008, pp. 112-119

Figure 1 illustrates the different ECG waveforms at different locations in the venous system as currently accepted and documented by the clinical community. The basic principle of the ECG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an endovascular electrode which replaces the "red" or "right shoulder" electrode of the standard surface ECG. When an ECG monitor is connected to the endovascular electrode,

the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the endovascular electrode (i.e. the tip) to the sino-atrial node. A "giant" P wave - as high as the QRS - indicates that the tip is inside the right atrium; when the P wave is as small as in the surface ECG, the tip of the electrode is in the superior cava vein or above; a P wave whose height is half of the QRS is considered indicative of the caval-atrial junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava).

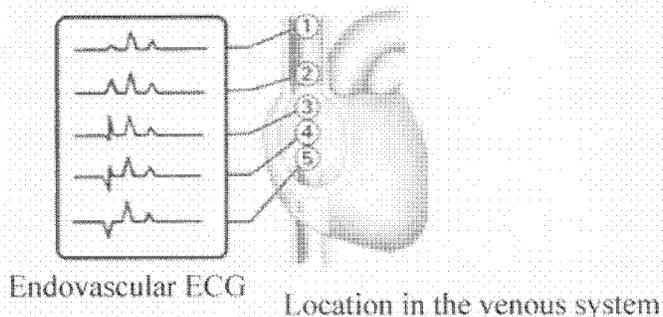


Figure 1: Changes in the ECG waveform as function of location in the vasculature

Thus, simply by monitoring the height and polarity of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium. Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy.

1.3 Sapiens™ TLS Description

The Sapiens™ TLS consists of the Sapiens™ TLS Electrical Adaptor, an ECG Module and an ECG cable, a laptop, and the Sapiens™ TLS application software. The Sapiens™ TLS components excluding the Sapiens™ TLS Adaptors are also referred to as the Sapiens™ TLS System. An optional printer can be connected to the laptop for documentation purposes. The Sapiens™ TLS Saline Adaptor can be connected to an Arrow-Johans Adaptor (Teleflex) to be used according to the saline column method as described herein. The Sapiens™ TLS Saline Adaptor with the Arrow-Johans Adaptor can be connected to any commercially available central venous catheters and the Sapiens™ TLS Electrical Adaptor to any commercially available stylets or guidewires used for the placement of central venous catheters. The Sapiens™ TLS system displays cardiac electrical signals (also known as endovascular ECG, RA-ECG, or intracavitary ECG) waveforms on the graphical user interface. These waveforms are generated at the distal tip of the central venous catheter and

acquired in real time through the Sapiens adaptors. Thus, the waveforms presented on the Sapiens™ TLS graphical user interface can aid the placement of central venous catheters.

The Sapiens™ TLS System is shipped in two subsystems: laptop running the Sapiens™ TLS software and the Sapiens™ TLS ECG module together with the corresponding cables.

Store the Sapiens™ TLS System indoors at room temperature and condition.

Figure 2 shows the system components:

1. PC/Laptop running Sapiens™ TLS software
2. ECG module
3. USB connection cable to the ECG module
4. ECG cable
5. Sterile Sapiens™ TLS Electrical Adaptor connected to an Arrow-Johans Adaptor placed between a syringe and a catheter
6. Skin ECG electrodes
7. Optional label printer
8. Optional remote control

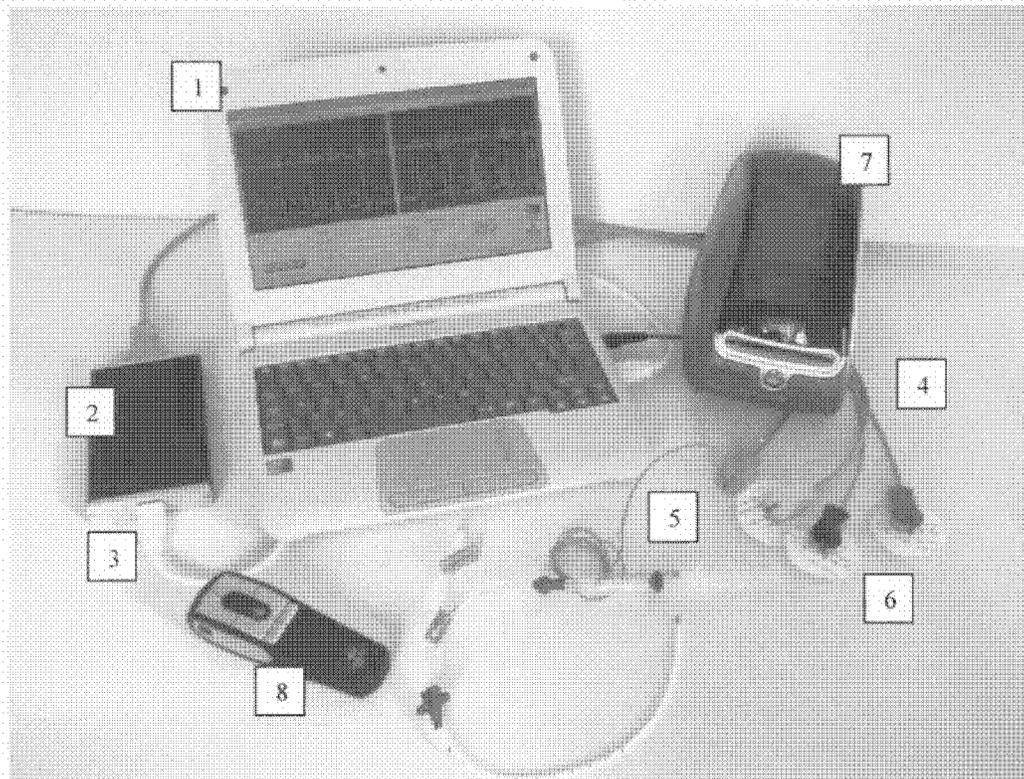


Figure 2: Sapiens TLS System Configuration

1.4 Warnings and Precautions

A Warning indicates that the personal safety of the patient or physician may be involved. Disregarding a Warning could result in injury to the patient or physician. A Caution indicates that particular service procedures or precautions must be followed to avoid possible damage to the product.

Warnings

- Warning:** Before using the Sapiens™ TLS System for the first time, be sure to read and understand all of the information in this User's Manual.
- Warning:** Failure to abide by the precautions detailed below causes the system and its use to be out of compliance with regulations and places the patient and the user at risk of injury or death.
- Warning:** When using the Sapiens™ TLS System with the Sapiens™ TLS Adaptors, always follow the Instructions for Use provided with the Sapiens™ TLS Adaptor. When using the Arrow-Johans Adaptor, always follow the Instructions for Use provided with the Arrow-Johans Adaptor.
- Warning:** The Sapiens™ TLS System should only be used by physicians and nurses trained in central lines placement procedures and in assessing the ECG information provided by the Sapiens™ TLS System.
- Warning:** The Sapiens™ TLS User's Manual provides information about ECG waveforms and their correspondence with specific locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** Place skin electrodes carefully at locations indicated by this User's Manual and ensure good skin-electrode contact. Failure to do so may cause unstable ECG waveforms and/or ECG waveforms which are not described in this Manual. In such a case, the use of an additional and/or different method may be required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** In patients where alterations of cardiac rhythm significantly change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Warning:** In patients undergoing central venous catheterization using venous access through the saphenous or the femoral veins, the catheter tip will typically not reach the right atrium and the caval atrial junction. In such a situation, the ECG waveforms described by this manual cannot be used for catheter

guidance and placement and the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In certain patients, unstable ECG waveforms may be detected because of the manipulation of the Sapiens™ TLS Adaptor by the user. Verify that the connection between the Sapiens™ TLS Adaptor and the central venous catheter and the connection between the Sapiens™ TLS Adaptor and the ECG cable are free from contact with any other material and refrain from touching the Sapiens™ TLS Adaptor and any of its connections. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In certain patients, no ECG waveforms may be detected because of very specific impedance mismatch between the patient and the ECG electrodes. Be sure to use the Instructions for Use provided by the manufacturer of the skin electrodes. Verify the connection between the patient's skin and the electrodes, between the electrodes and Sapiens™ TLS ECG cable, and between the Sapiens™ TLS Adaptor and the Sapiens™ TLS ECG cable. If the problem persists, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: In neonates, unstable ECG waveforms may be detected because of patient's movements or manipulation by the user. In such a situation, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Warning: The Sapiens™ TLS system is not intended to diagnose or treat disease.

Warning: Monitor catheter tip placement during insertion procedure and verify catheter tip location placement using your institution's guidelines.

Warning: Do not place and/or use the Sapiens™ TLS system in the presence of strong magnetic fields such as Magnetic Resonance Imaging (MRI) devices. The high magnetic fields created by an MRI device will attract the equipment with a force sufficient to cause death or serious personal injury to persons between the equipment and the MRI device. This magnetic attraction may also damage the equipment. The magnetic and the RF fields associated with the MRI environment may interfere with the display of ECG waveforms. Consult the MRI manufacturer for more information.

Warning: Do not use the Sapiens™ TLS system at the same time with a defibrillator. Disconnect any Sapiens™ TLS Adaptor from any catheter and any Sapiens™ TLS ECG cable connection from any ECG skin electrode before using a defibrillator.

- Warning:** Always use controls, make adjustments and perform procedures with Sapiens™ TLS as specified in this User's Manual.
- Warning:** The Sapiens™ TLS system is password protected to avoid accidental changes in the software and system configuration. Do not install any software on the Sapiens™ TLS System unless instructed to do so by qualified Romedex personnel and under the guidance of qualified Romedex personnel. Failure to do so may result in patient and user harm and system damage.
- Warning:** The Sapiens™ TLS system must be powered only by the batteries provided with the Sapiens™ TLS Laptop. Batteries may not be charged while using the Sapiens™ TLS system in a medical procedure.
- Warning:** Charge the Sapiens™ TLS system only when the system is Off using a medical grade power adaptor.
- Warning:** All optional system components including the optional printer must be powered by, and only by a medical grade power adaptor if they are connected to the Sapiens™ TLS system during the clinical procedure.
- Warning:** Do not use additional cables, extension cords or outlets with the Sapiens™ TLS System.
- Warning:** This device is not to be used in the presence of combustible or flammable gases, anesthetics, or cleaners/disinfectants.
- Warning:** Do not remove system covers. To avoid electrical shock, use only the power cord supplied with the system and connect only to properly grounded wall outlets. Only Romedex qualified personnel should service the system.
- Warning:** Maximum care should be taken in checking that all connecting cables and connections, such as alligator clips, are electrically insulated and do not come into contact with other electrical cables or metal surfaces
- Warning:** No part of the body of the patient must be in direct or indirect uninsulated contact with metal surfaces.

Cautions

- Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician
- Caution:** Active electric motor driven equipment, such as pumps, may interfere with the display of the ECG waveforms. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.
- Caution:** Equipment such as CT scanners, X-rays and fluoroscopy systems, cauterizers and diathermy equipment, operating in close proximity may emit strong electromagnetic or radio frequency interference (RFI) which

could interfere with the display of ECG waveforms by Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Caution: Electric equipment which requires direct contact with the patient may interfere with the display of ECG waveforms by Sapiens™ TLS. Do not use electric cauterization, electric scalpels, and ablation equipment while using Sapiens™ TLS. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

1.5 Sapiens TLS System Limitations

When using the Sapiens™ TLS Electrical Adaptor, a stylet or a guidewire typically provided with the kit of the vascular access device must be used in order to ensure an electrically conductive path between the proximal and the distal ends of the vascular access device.

When using the saline adaptor configuration of Sapiens™ TLS, the user needs to ensure that the catheter lumen is constantly filled with saline and in contact with the Arrow-Johans Adaptor, such that electrical conductivity through the catheter lumen is ensured from the proximal to the distal end of the vascular access device.

When using the saline adaptor configuration, instability of the endovascular electrical signal baseline may occur if the user makes hand contact with the proximal end connection of the Arrow-Johans Adaptor.

The Sapiens™ TLS system must be battery powered when used in a clinical case, i.e., as long as ECG electrodes are connected to the patient. The system battery lasts for approximately two hours. Recharging the battery must be done in between clinical cases.

The Sapiens™ TLS system uses data processing algorithms to enhance the quality of the endovascular ECG signal. In situations when electrodes have been disconnected and reconnected again, e.g., when the red clip electrode is connected to the sterile adaptor, it may take several seconds for the system to transition from a no-signal to a stable signal state. Please wait while the system makes this transition and do not touch the electrical connections of the adaptor during this time.

The Sapiens™ TLS system uses a serial communication protocol and a USB-Serial converter between the laptop and the ECG module. If the USB connector is not connected when the Sapiens software application starts up or if the USB connector is

disconnected before shutting down the Sapiens software application, under certain circumstances the Sapiens application must be restarted.

In order to prevent accidental installation of software on the Sapiens™ TLS laptop computer, the user does not have administrative rights to install software. Only Romedex personnel have the administrative rights to perform software installation on the Sapiens™ TLS laptop.

2. Sapiens™ TLS procedure workflow

2.1 System setup

Find an appropriate location for the system. Ensure the Sapiens™ TLS System is placed no more than 4 feet away from the patient outside the sterile field.

Ensure that all the individual power switches to the Laptop, optional printer, and medical grade power supply, where appropriate, are turned OFF. Connect the ECG module to the Laptop via the USB cable provided with the system. Connect the ECG cable to the ECG module via the ECG cable connector.

The laptop and the ECG module can run on the laptop battery. If the optional printer is not used, then there is no need to connect the medical grade power supply to the power outlet. Fully charging the laptop battery should be accomplished before any procedure if the system runs on battery. A full battery charge lasts for approximately two hours.

Turn the system on by turning on the power switches on of the individual systems in the following order:

- a. Optional printer
- b. Laptop

Once the Laptop power up sequence is finished, the Sapiens™ TLS software will be launched automatically. The startup screen is shown in Figure 3.



Figure 3: Sapiens™ TLS Screen Layout

1 - Toolbar containing controls for play / pause the data acquisition, load / save ECG files, printing to file / printer, settings and help. The following functions are available on the toolbar:

- a) Pause/Play the ECG waveform in acquisition and playback modes.
- b) Save the case to file. When clicking the “Save” icon, all ECG waveforms for the entire duration since the beginning of the case or since last save are saved in a file. The default name of the file is the name of the patient to which the date and time are appended. The default directory is C:/Data created when installing the Sapiens™ TLS application.
- c) Print to file. Click on the button to select (highlight) it, click again to unselect it. When this button is selected, the printer output will be redirected to a file using a default name and location.
- d) Print. By clicking the printer icon, the print preview will be displayed. The desired information needs to be first frozen on the right hand side screen before it can be printed. The printer output will be redirected to the default printer. A default label printer is preinstalled on the system.
- e) Clicking on the Help button brings up the User's manual and information about the Sapiens™ TLS software.
- g) By dragging the question mark to a screen location, certain hints will be provided depending on the location.
- h) Closes the Sapiens™ TLS application before turning off the computer. If the user accidentally closes it and needs to reopen it again, double click on the Sapiens TLS icon on the desktop.

- 2 - Main screen where the real-time ECG waveforms are displayed: the reference skin ECG waveform (lead III in Einthoven's reference system) and the guiding ECG waveform at the tip of the catheter (lead II in Einthoven's reference system).
- 3 - Available commands accepted by the device and respective parameters
- 4 - 'Patient name', 'institution', 'catheter type' and 'inserted length' information that will be shown on printed label.
- 5 - Status bar displaying information about the ECG module status
- 6 - Scroll bar used for changing the scroll speed of the ECG waveform display
- 7 - Color and visibility setting for channels.
- 8 - Frequency of R-Peaks measured in number of peaks / minute.
- 9 - Scale setting used to amplify the signals received from device.
- 10 - Pressing this button will save the current image shown in Main screen.
- 11 - Pressing this button will copy the current image shown in Main screen to Secondary screen.
- 12 - Secondary screen used for freezing ECG waveforms for comparison.
- 13 - Tab container displays the 'Reference' page.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

To power off the system:

- a. Close the Sapiens™ TLS application
- b. Power down the Windows operating system on the laptop
- c. Turn off the optional printer

2.2 Patient preparation and vein puncture

Connect the ECG cable to the patient:

1. Before preparing the sterile field, take the ECG cable supplied with the Sapiens™ TLS System and wipe the cable down according to hospital's guideline.
2. Locate three new off-the-shelf ECG snap electrode patches and place one on the patient's lower left abdomen, one on the patient's lower right abdomen, and one on the patient's left shoulder or arm per the ECG electrodes instructions for use.
3. Connect the green clip connector of the provided ECG cable to the electrode snap on the patient's left lower abdomen.
4. Connect the black clip connector of the provided ECG cable to the electrode snap on the patient's left lower abdomen.
5. Connect the yellow clip connector of the provided ECG cable to the electrode snap on the patient's left shoulder or arm.

6. Leave the red clip connector of the provided ECG cable in a reachable location for the connection with the sterile adaptor during the procedure.

With the Sapiens™ TLS system running, the reference skin ECG waveform should be at this time visible and stable. It should be possible to unambiguously identify the ECG waveform elements, e.g., the P-wave and the R-wave, as represented in this User's Manual. If this is not the case, do not attempt to use Sapiens™ TLS for catheter guidance and positioning and use another method for catheter tip location verification as indicated by the institutional guidelines, e.g., chest X-ray or fluoroscopy.

Prepare the patient for central venous catheterization per institution's guidelines.

Perform vein puncture and venous access per institution's guidelines, if applicable under ultrasound imaging guidance.

2.3 Connecting the Sapiens™ TLS Adaptor or the Arrow-Johans adaptor

In order to obtain ECG waveforms at the tip of the central venous catheter, the non-sterile red clip connector of the provided ECG cable must be connected to the sterile central venous catheter. This connection is achieved using the Sapiens™ TLS Electrical Adaptor and/or the Arrow-Johans Adaptor. Please refer to the Instructions for Use of these adaptors for details.

When using the Sapiens™ TLS Electrical Adaptor, connect the alligator clip end of the Sapiens™ TLS Adaptor to the proximal end of the stylet or guidewire which is packaged with your venous access device or pre-inserted in one of the lumens of your venous access device. Connect the red clip connector of the provided ECG cable to the plug end of the sterile Sapiens™ TLS Electrical Adaptor.

When using the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor, connect the Arrow-Johans Adaptor similarly to the Sapiens™ TLS Saline Adaptor. Then connect the alligator clip of the Sapiens™ TLS Electrical Adaptor to the snap nipple connector of the Arrow-Johans Adaptor and then connect the red clip connector of the provided ECG cable to the plug end of the sterile Sapiens™ TLS Electrical Adaptor.

2.4 Electrical vs. saline adaptors

The choice between using the Sapiens™ TLS Electrical Adaptor or the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor is a matter of user preference and workflow optimization and is potentially subject to institutional guidelines. Please refer also to the Instructions for Use of the respective adaptors.

Typical situations for using the Sapiens™ TLS Electrical Adaptor are:

1. Placement of open-ended PICCs with pre-inserted stylets and luer-locks which allow for stylet position control
2. Implantable ports using open vein access with over-the-guidewire catheter placement
3. Any central venous catheter inserted over a guidewire with centimeter markings

Typical situations for using the combination between the Arrow-Johans Adaptor and the Sapiens TLS Electrical Adaptor are:

1. Any post-procedural tip location verification of any central venous catheter type
2. Placement of closed-end PICCs
3. Placement of central venous catheters using the modified Seldinger technique (MST) which do not have pre-inserted stylets, e.g., tunneled catheters like Broviac catheters.
4. Any central venous catheter inserted over a guidewire without centimeter markings, e.g., CVCs.
5. Hemodialysis catheters which may require tip location verification for both ends: the long distal end in the right atrium and the short distal end at the caval-atrial junction.

2.5 Display ECG waveforms

As soon as the Sapiens™ TLS adaptors and/or the Arrow-Johans Adaptor are connected to the catheter and to the ECG cable, the guiding ECG waveform is displayed (Figure 3).

The waveforms on the top in Figure 3 on both left and right hand side display windows represent the skin ECG or reference ECG. The waveforms on the bottom in Figure 3 on both left and right hand side display windows represent the electrical signal detected at the tip of the central venous catheter.

The right hand side window in Figure 3 is labeled "Reference". The reference window allows for saving the ECG waveforms at a desired location for further comparison. Clicking on the "Freeze" button below the Reference window or using the left arrow key on the keyboard freezes the display, such that the frozen ECG waveform can be used as a reference.

The scroll speed of the ECG waveform can be selected by using the scroll bar "Display speed" (6 in Fig 3). The amplitude scale for the ECG waveform can be manually selected by using the Scale scrollbar (9 in Fig 3) or the up/down arrow keys on the keyboard.

2.6 Document the catheter tip location

The ECG waveforms can be recorded real-time during the procedure by clicking on the "Record" button. The ECG waveforms are recorded in a file. The file name is

automatically generated by the computer if a patient ID is not input. If a patient ID is input the file name is generated based on the patient ID. The file can be copied to a USB memory stick or memory card as a removable storage device.

Clicking the "Print/Save" button sends a screen shot to the printer if attached and save the screen shot in a file in JPG format. The file name is assigned automatically if no patient ID is input and a name is assigned based on the patient ID if a patient ID is input.

Using Sapiens™ TLS it is possible to print the ECG waveforms at the chosen tip location in order to attach the print to the patient chart and document the catheter tip location. The alphanumeric information input by the user and the ECG waveforms displayed in the Reference window are printed using the print layout illustrated in Figure 4. The print layout is displayed when clicking on the printer icon on the command toolbar at the top of the screen. The reference skin ECG and the guiding ECG waveforms are displayed on the right hand side and respectively on the left hand side of the print layout. Between the two waveforms a heart symbol is printed in order to allow the user to mark with a pen on printed paper the location of tip where the corresponding ECG waveforms have been obtained.

The patient name, institution name, catheter type and length, are displayed as well as they were input in the corresponding fields of the graphical user interface.

The following information can be input in the corresponding fields on the graphical user interface at any time:

1. Patient name
2. Institution name
3. Catheter type
4. Inserted length

This information is printed out in the corresponding fields of the print layout in Figure 4.

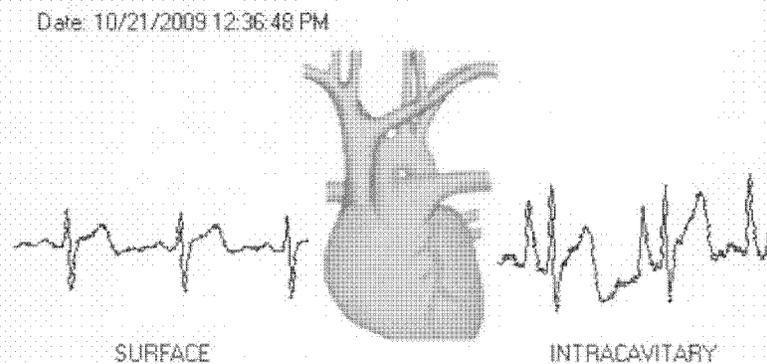


Figure 4: Print layout

To copy any file from the Sapiens™ TLS laptop to a removable storage medium, exit the Sapiens™ TLS application and use the Windows XP operating system to copy the desired file to the desired location.

3. Sapiens™ TLS Catheter Guidance

3.1 Outside the thoracic cavity

Outside the thoracic cavity the ECG signals are similar to the ones at the skin level. Figure 5 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located outside the thoracic cavity relative to the reference skin ECG.

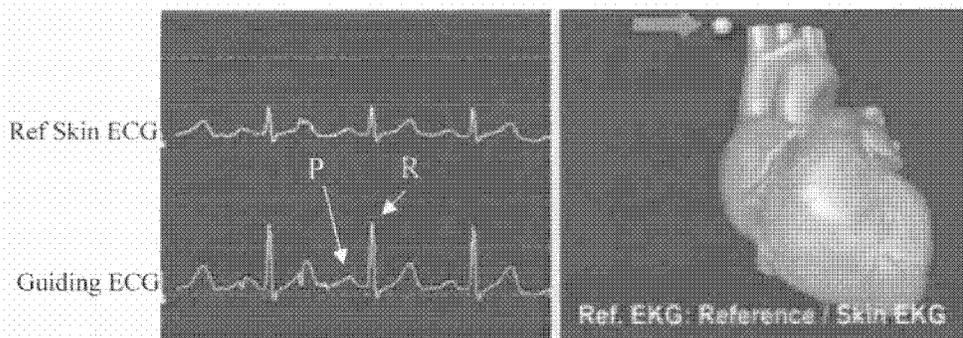


Figure 5: ECG waveform at the tip of the catheter outside the thoracic cavity.

3.2 Superior vena cava

Figure 6 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the upper superior vena cava (SVC). Compared to Figure 5 one can notice that the reference skin ECG waveform has not changed since this waveform does not depend on the location of the tip of the catheter. The amplitude and energy of the guiding ECG waveform have increase in Figure 6 when compared to Figure 5 indicating that the catheter tip is approaching the heart, i.e., a region of high electrical activity. Still, the shape of the ECG waveform has not changed significantly indicating that the catheter tip is not yet close to the sino-atrial node and the caval-atrial junction.

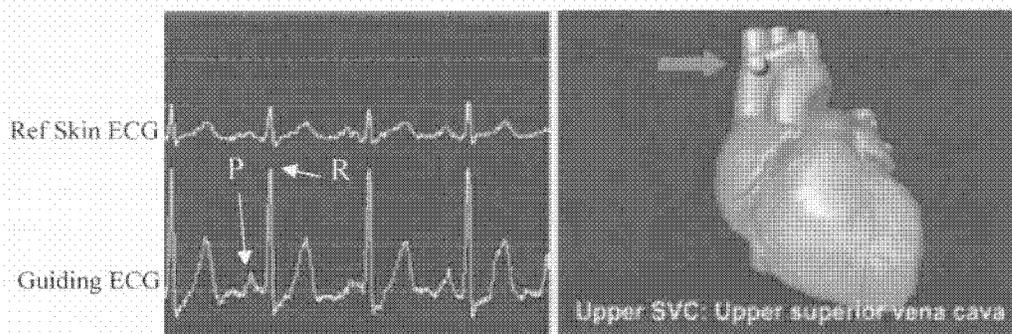


Figure 6: ECG waveform at the tip of the catheter in the upper SVC

3.3 Lower third of the superior vena cava

Figure 7 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in lower third of the upper superior vena cava. The P-wave has increased visibly when compared to Figure 6. The amplitude of the P-wave is about half size of the amplitude of the R-wave.

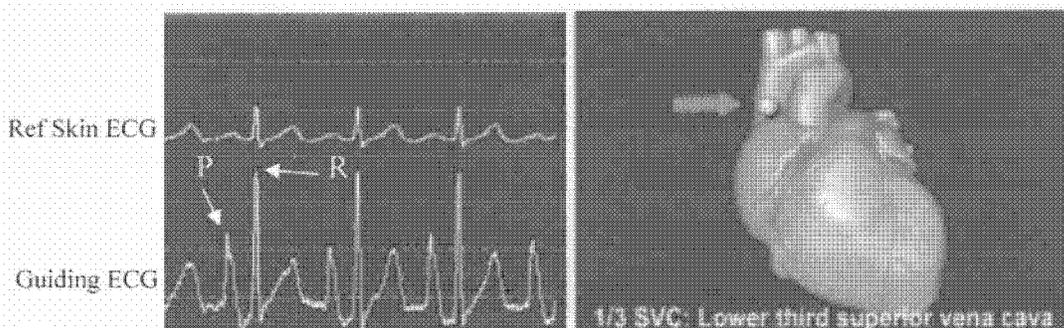


Figure 7: ECG waveform at the tip of the catheter in the lower third of the SVC

3.4 Caval-atrial junction

Figure 8 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located at the caval-atrial junction (CAJ) right below the sino-atrial node (SAN). The P-wave is bi-phasic, i.e., has a negative component. A negative component of the P-wave appears when the tip of the catheter is below the sino-atrial node (SAN). Since the P-wave has a negative component but the amplitude of the P-wave has not increased much compared to Figure 7, the ECG waveform in Figure 8 is typical of the caval-atrial junction with the tip of the catheter just below the SAN.

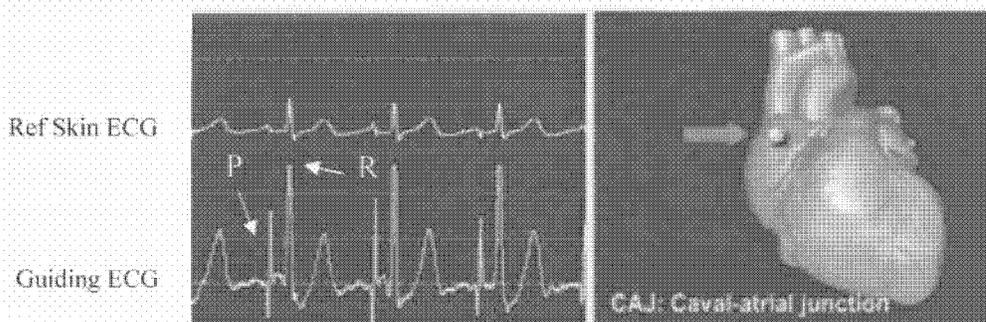


Figure 8: ECG waveform at the tip of the catheter at CAJ right below the SAN

3.5 Right atrium

Figure 9 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the right atrium (RA). The P-wave continues to have a negative component indicating that the catheter tip continues to be below the sino-atrial node. The P-wave amplitude has increased significantly when compared to Figures 7 and 8. This is an

indication that the tip of the catheter is in the middle of the right atrium where the P-wave intensity is maximal due to the right-atrial activity.

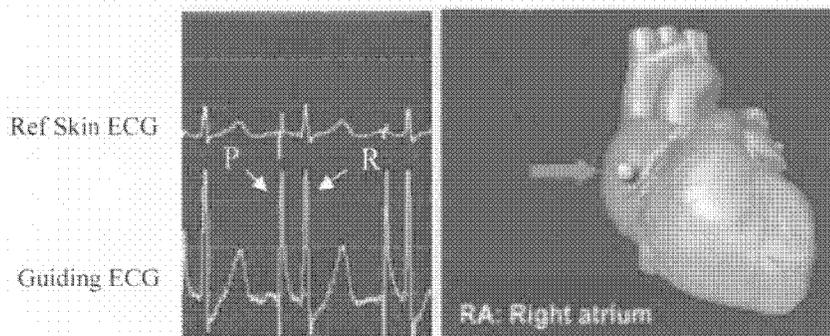


Figure 9: ECG waveform at the tip of the catheter in the RA.

3.6 Inferior Vena Cava

Figure 10 illustrates the guiding ECG waveform at the tip of the catheter when the tip is located in the inferior vena cava (IVC). The P-wave has changed polarity when compared to Figure 7. In Figure 7 the P-wave is positive whereby in Figure 10 the P-wave is negative. This is an indication that the catheter tip is approaching the inferior vena cava. The relatively high negative amplitude of the P-wave compared to the positive one in Figure 7 is an indication that the tip of the catheter is just entering the inferior vena cava coming from the right atrium.

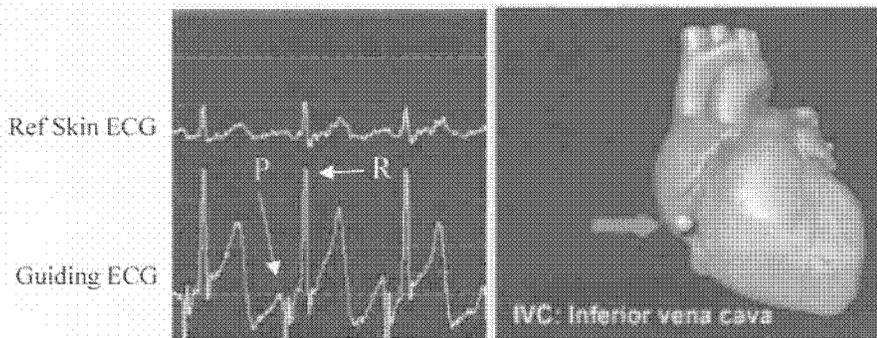


Figure 10: ECG waveform at the tip of the catheter in the IVC.

3.7 Catheter tip placement verification

As described in Section 3 of this Sapiens™ TLS User's Manual, using the Sapiens™ TLS the ECG waveforms can be unambiguously mapped to specific catheter tip locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described in Section 3.1.-3.6, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment.

Per institutional guidelines and in accordance with clinical judgment, in indicated patients, and under the conditions described by this User's Manual, Sapiens™ TLS may be used in conjunction with ultrasound-guided vein puncture or open vein access to replace chest X-ray and fluoroscopy for intra- and post-procedural central venous catheter tip location confirmation.

Using Sapiens™ TLS, central venous catheter tip location can be documented for the patient's chart either on paper or electronically.

Using Sapiens™ TLS, the location of the central venous catheter tip can be determined and documented as required by the different types of central venous catheters and by different institutional guidelines, for example:

1. When the tip of a PICC catheter must be placed in the lower third of the superior vena cava, the ECG waveforms illustrated in Figure 7 must be detected and documented at the tip of the PICC catheter.
2. When during intra-procedural catheter insertion or, at later times, during periodical post-procedural catheter tip verification, the long end of a hemodialysis catheter must be placed in the right atrium while its short end must be placed at the caval-atrial junction, then the ECG waveform in Figure 9 must be detected and documented at the long tip and, respectively, the ECG waveform in Figure 8 must be detected and documented at the short tip of the hemodialysis catheter.
3. When the tip of a central venous catheter (CVC) or of an implantable port must be placed at the caval-atrial junction, then an ECG waveform like the one in Figure 8 must be detected and documented at the tip of the catheter.

4. Error Messages and Troubleshooting

1. **Electrodes not connected**
If Sapiens™ TLS does not detect any connection of electrodes to the patient, a message is displayed on the status bar (5) in Figure 3. In such a case, verify that the skin electrodes are well attached to the patient's skin, that the ECG cable clips are well attached to the snap nipple on the electrodes and that the Sapiens™ TLS Adaptors are well connected to the red clip of the ECG cable. Verify that the ECG cable is well attached to the ECG module. If the error situation persists, you may replace the ECG skin electrodes with new ones. If the problem persists, contact your Romedex representative.
2. **ECG module not connected**
If Sapiens™ TLS does not detect the presence of an ECG module, a message is displayed on the status bar (5) in Figure 3. In such a case, verify that the USB cable between the ECG module and the laptop is well connected. Close and reopen the Sapiens™ TLS software. If the problem persists, contact your Romedex representative.
3. **Battery status**

The battery status is displayed on the task bar of the Windows operating system. To check battery status, close the Sapiens™ TLS software and point the mouse cursor to the battery icon on the Windows task bar. When finished, reopen the Sapiens™ TLS software.

4. Printer error

A printer error message is displayed when printing if the printer is not connected or if it is out of paper. Check the printer connection and paper status and try again. If the problem persists, contact your Romedex representative.

5. Cleaning and Disinfection

To clean the Sapiens™ TLS system:

1. Turn off the system
2. Dampen a nonabrasive cloth with either warm water or rubbing alcohol
3. Gently wipe the dampened cloth over the exterior surfaces of the ECG module and of the laptop.

For a list of disinfectants recommended for use please contact Romedex International.

Warning: Do not submerge the Sapiens™ TLS ECG module or the laptop or allow fluid to enter any of the connectors.

6. Warranty

The manufacturer, Romedex International Srl, warrants this product against defects in material and workmanship for a period of one year from the date of original purchase, and during such period agrees to repair, or at Romedex International's discretion, replace any defective unit free of charge. The warranty on the repaired or replaced unit continues from the purchase date of the original unit. This warranty does not cover damages resulting from misuse, abuse, modification, or alteration of the Sapiens™ TLS.

The following actions void the warranty of the Sapiens™ TLS:

1. Opening or servicing the ECG module or the laptop
2. Removal of system labels by anyone other than by Romedex authorized service personnel
3. Connecting the ECG module to any unauthorized laptop
4. Connecting any unauthorized peripheral to the laptop
5. Installing software on the laptop other than by authorized Romedex personnel or under authorized Romedex personnel guidance.

7. Service and Repair

For servicing information or to return your Sapiens™ TLS for repair, please contact Romedex International's technical support at service@romedex.com.

Warning: Only qualified personnel should attempt to service the Sapiens™ TLS system.

8. Technical Specifications

- | | |
|------------------------------|--|
| 1. Laptop: | ASUS Eee 900HA or better, 100-240V, 50/60 Hz |
| 2. Laptop power consumption: | Less than 40W |
| 3. Operating system: | Windows XP or later |
| 4. ECG module: | 4-lead, full patient isolation, defibrillation protected |
| 5. Dimensions ECG module: | 0.8" x 2.4" x 4" (2 cm x 6 cm x 10 cm) |
| 6. Connector type: | USB |
| 7. ECG cable: | 4-lead, 10 ft (3 m) |
| 8. IEC 60601-1: | Type CF Applied Part when used with the Sapiens TLS or Arrow-Johans Adaptors |

9. Disposal Information

To return the Sapiens™ TLS for end of life recycling please contact your nearest Romedex sales or distributor office in the country of purchase.

10. Contact Information

For additional information and training materials, please go to the Romedex International web site: www.romedex.com.

If you have any questions or comments regarding the use of this product please contact:

*Romedex International Srl
58 Aleea Arubium Str
Bucharest, 022944 Romania
Tel: +40.743.490.892
Fax: +40.317.107.048
Email: info@romedex.com*

11. References

- a. *Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation*, by Nancy Moureau et al. published in the Journal of the Association for Vascular Access in 2010, JAVA Vol. 15 No. 1 2010, pp. 9-15
- b. *The ECG method for positioning the tip of PICCs: results from two preliminary studies*, by Mauro Pittiruti et al. published in the Journal of the Association for Vascular Access in 2008, JAVA Vol. 13 No. 4 2008, pp. 112-119

ATTACHMENT 2

EVGUIDE-SAPIENS TLS ADAPTOR INSTRUCTIONS FOR USE

evGuide-Sapiens™ TLS ADAPTOR

Johans Adaptor.

INSTRUCTIONS FOR USE

DESCRIPTION:

- Sapiens™ TLS Adaptor is a family of sterile adaptors made of medical grade materials to facilitate placement of central venous access devices. Sapiens™ TLS adaptors are packaged in sterile individual pouches. Alternatively, the Sapiens™ TLS adaptors can be included in venous access device kits by the corresponding manufacturer of market available devices, e.g., PICC, CVC, hemodialysis catheters, implantable ports, and other central lines.
- The Sapiens™ TLS Adaptor must be used with the Sapiens™ Tip Location System. The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients. Limiting but not contraindicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous veins which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location. Please refer to the Sapiens™ TLS system User's Manual.
- The Sapiens™ TLS Electrical Adaptor, the adaptor is a sterile 39" long isolated stainless steel wire with a plug connector at one end and an alligator clip at the other end. The alligator clip is used to attach the Sapiens™ TLS adaptor to any commercially available stylet or guidewire used for central venous catheter placement. The plug connector is used to connect the adaptor to the ECG cable provided with the Sapiens™ TLS system.
- The Sapiens™ TLS Electrical Adaptor can also be used in combination with the Arrow-Johans Adaptor (Teleflex). In such a situation, the alligator clip of the Electrical Adaptor must be connected to the snap connector of the Arrow-

CONTRAINDICATIONS:

- All contraindications of central venous catheters apply as specified by the central venous catheter manufacturer.
- There are no contraindications specific to the Sapiens™ TLS Adaptor

POSSIBLE COMPLICATIONS:

- All complications indicated by the manufacturer of the central venous catheter should be considered when using the Sapiens™ TLS adaptor.
- There are no complications specific to the Sapiens™ TLS Adaptor.

WARNINGS:

- Refer to the Sapiens™ TLS User's Manual, its warnings and precautions when considering using Sapiens™ TLS for catheter tip placement confirmation.
- Monitor catheter tip placement per institutional policy.
- Release the central venous catheter after insertion according to your institution's guidelines.
- Do not release the central venous catheter based on Sapiens™ TLS information if the signal on the screen is unstable or does not show the ECG waveforms as illustrated in Figures 4 through 9 and according to the Sapiens™ TLS User's Manual. In such a case, use a different method for guiding the placement of your central line as indicated by the institutional guidelines and clinical judgement, e.g., chest X-ray or fluoroscopy.
- If the Sapiens™ TLS Adaptor becomes damaged, remove the adaptor with caution as to not change the position of the catheter.
- The Sapiens™ TLS Adaptor is for Single Use Only.
- Sapiens™ TLS Adaptor is sterilized by ethylene oxide (ETO).
- Do not re-sterilize the adaptor or accessories by any method.
- The manufacturer shall not be liable for any damages caused by reuse or re-sterilization of this adaptor or accessories.
- Contents are sterile in an unopened, undamaged package.
- Do not use adaptor or accessories if package is opened or damaged.

- The Sapiens™ TLS Adaptor is not intended to diagnose or treat disease.

PRECAUTIONS:

- Do not use sharp instruments near the adaptor.
- Adaptor may be damaged if clamps other than what is provided are used.
- Examine adaptor before each insertion for damage.
- Read instructions carefully before using this device. The adaptor should be manipulated by a qualified, licensed physician or other qualified health care professional.
- The medical techniques and procedures described in these instructions for use do not represent all medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgment in treating any specific patient.
- Use standard hospital protocols when applicable.
- Discard gloves and change to a new pair of sterile gloves after connecting the Adaptor to the Sapiens™ TLS System and completing the setup of the Sapiens™ TLS System per User's Manual.
- Beware of the adaptor wire. Tripping over the adaptor might cause malfunction of the adaptor, detachment of the adaptor connectors from the system or injuries for the user.

Note: After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations

Note: For detailed central venous catheter preparation and insertion information, follow the instructions stated in the catheter's Instruction for Use provided by the catheter manufacturer.

ELECTRICAL VS. SALINE ADAPTORS

The choice between using the Sapiens™ TLS Electrical Adaptor or the combination of the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor is a matter of user preference and workflow optimization and is potentially subject to institutional guidelines. Please refer also to the Instructions for Use of the respective adaptors.

Typical situations for using the Sapiens™ TLS Electrical Adaptor are:

1. Placement of open-ended PICCs with pre-inserted stylets and luer-locks which allow for stylet position control
2. Implantable ports using open vein access with over-the-guidewire catheter placement
3. Any central venous catheter inserted over a guidewire with centimeter markings

Typical situations for using the combination between the Arrow-Johans Adaptor and the Sapiens™ TLS Electrical Adaptor are:

1. Any post-procedural tip location verification of any central venous catheter type
2. Placement of closed-end PICCs
3. Placement of central venous catheters using the modified Seldinger technique (MST) which do not have pre-inserted stylets, e.g., tunneled catheters like Broviac catheters.
4. Any central venous catheter inserted over a guidewire without centimeter markings, e.g., CVCs.
5. Hemodialysis catheters which may require tip location verification for both ends: the long distal end in the right atrium and the short distal end at the caval-atrial junction.

WORKFLOW

1. Attach ECG skin electrodes as indicated by the Sapiens™ TLS User's Manual.
2. Prepare patient and insert the central venous access device according to institutional protocols and the device instructions for use.
3. When using the Sapiens™ TLS Electrical Adaptor, Figure 1, expose the stylet pre-inserted in the catheter at the distal end close to the touyh borst. Open the Adaptor package and take out the Sapiens™ TLS Adaptor wire. Attach the mini-grabber connector to the exposed stylet close to the touyh borst. Follow the catheter manufacturer's instructions regarding the use of the stylet during procedure. Place the catheter onto the patient where sterile field is established. Clip the Sapiens™ TLS Adaptor wire to the sterile drape to ensure the catheter stays in the sterile field.
4. When using the Sapiens™ TLS Electrical Adaptor in combination with the Arrow-Johans Adaptor, Figure 3, attach the alligator clip of the Electrical Adaptor to the snap clip of the Arrow-Johans Adaptor.
5. In either configuration, attach the plug connector of the Sapiens™ TLS Adaptor wire to the red lead of the ECG cable provided with the Sapiens™ TLS System according to

User's Manual.

- 6. The ECG patterns provided by the Sapiens™ TLS Adaptor and System, Figures 4 through 9, may be considered in assessing catheter tip location. Please refer to the Sapiens™ TLS User's Manual for detail information, warnings and precautions regarding tip location confirmation.

WARNING: Failure to verify catheter placement may result in serious trauma or fatal complications.

- 7. When using the Electrical Adaptor, disconnect the alligator clip from the stylet or guidewire. Remove stylet according to the manufacturer's instructions.
- 8. Record catheter length, catheter lot number, adaptor's lot number and tip position on patient's chart.
- 9. Record patient name, catheter length on the Sapiens™ TLS graphical user interface
- 10. Document tip location by printing using Sapiens™ TLS.

CATHETER TIP PLACEMENT VERIFICATION

As described herein and in the Sapiens™ TLS User's Manual, using the Sapiens™ TLS the ECG waveforms can be unambiguously mapped to specific catheter tip locations in the vasculature. In any situation in which the user cannot unambiguously identify ECG waveforms as described herein, the use of an additional and/or different method is required to confirm catheter tip location, e.g., chest X-ray or fluoroscopy as indicated by the institutional guidelines and clinical judgment. Per institutional guidelines and in accordance with clinical judgment, in indicated patients, and under the conditions described by this User's Manual, Sapiens™ TLS may be used in conjunction with ultrasound-guided vein puncture or open vein access to replace chest X-ray and fluoroscopy for intra- and post-procedural central venous catheter tip location confirmation.

Using Sapiens™ TLS, central venous catheter tip location can be documented for the patient's chart either on paper or electronically.

Using Sapiens™ TLS, the location of the central venous catheter tip can be determined and documented as required by the different types of central venous catheters and by different institutional guidelines, for example:

- 1. When the tip of a PICC catheter must be placed in the lower third of the superior vena cava, the ECG waveforms illustrated in Figure 7 must be

detected and documented at the tip of the PICC catheter.

- 2. When during intra-procedural catheter insertion or, at later times, during periodical post-procedural catheter tip verification, the long end of a hemodialysis catheter must be placed in the right atrium while its short end must be placed at the caval-atrial junction, then the ECG waveform in Figure 9 must be detected and documented at the long tip and, respectively, the ECG waveform in Figure 8 must be detected and documented at the short tip of the hemodialysis catheter.
- 3. When the tip of a central venous catheter (CVC) or of an implantable port must be placed at the caval-atrial junction, then an ECG waveform like the one in Figure 8 must be detected and documented at the tip of the catheter.

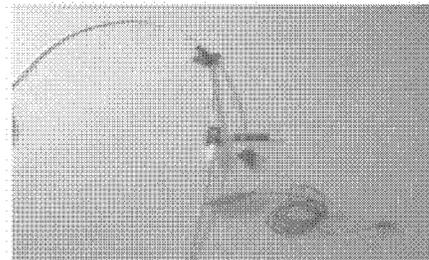


Figure 1: SAPIENS™ TLS Electrical Adaptor

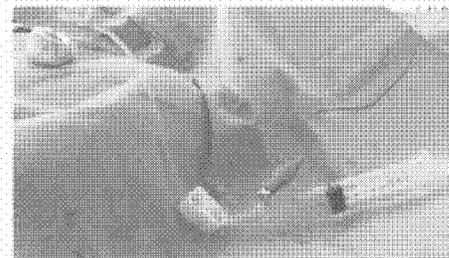


Figure 3: Sapiens™ TLS Electrical Adaptor in combination with Arrow-Johans Adaptor

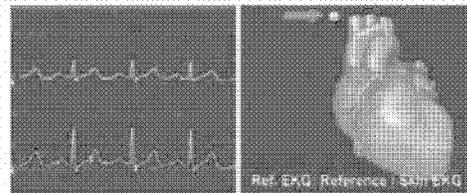


Figure 4: Tip outside thoracic cavity

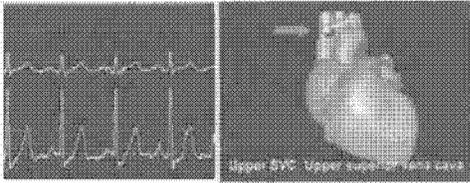


Figure 5: Tip in upper SVC

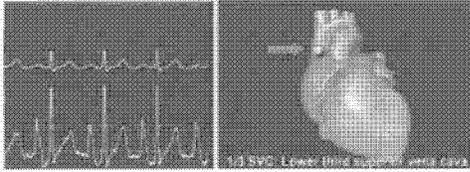


Figure 6: Tip in lower third of SVC

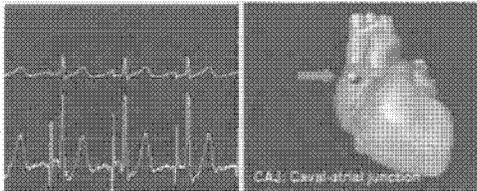


Figure 7: Tip at caval-atrial junction

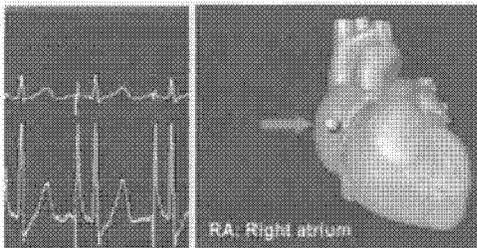


Figure 8: Tip in the right atrium

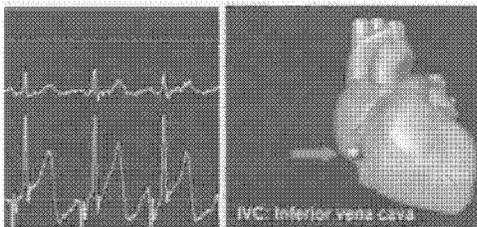


Figure 9: Tip in the inferior vena cava

If you have any questions or comments regarding this product, contact

Romedex International Srl
58 Aleea Arubium Str
Bucharest, 022944 Romania
Tel: +40.743.490.892
Fax: +40.317.107.048
Email: info@romedex.com

CONTACT INFORMATION

For additional information, please go to the Romedex International web site:
www.romedex.com.

ATTACHMENT 3

ROMEDEX (b)(4) STERILIZATION VALIDATION PROTOCOL

ATTACHMENT 5

EVGUIDE-SAPIENS STERILIZATION TEST RESULTS

ATTACHMENT 6

BIOBURDEN VALIDATION FOR ROMEDEX – PROTOCOL

ATTACHMENT 7

BIOBURDEN VALIDATION FOR ROMEDEX – REPORT

ATTACHMENT 8

EVGUIDE-SAPIENS SHELF-LIFE TEST PROTOCOL

evGuide Shelf Life Test Protocol

Originator: Sorin Grunwald

Date: 3/25/10

Protocol Approval:

Name	Title	Signature	Date
Sorin Grunwald			

1.0 PURPOSE

- 1.1. The purpose of this document is to provide an overall protocol for evaluating the packaging and shelf life of the Romedex International evGuide™ / Sapiens™ TLS Electrical Adaptor. The integrity of packaging of the evGuide™ / Sapiens™ TLS Electrical Adaptor will be challenged. The evGuide™ / Sapiens™ TLS Electrical Adaptor will seek for 1-year shelf life after sterilization and accelerated ageing by completing testing as described in this document.

2.0 SCOPE

- 2.1. This protocol applies to the evGuide™ / Sapiens™ TLS Electrical Adaptor and is a required test in the verification process.

3.0 REFERENCES

(b)(4)



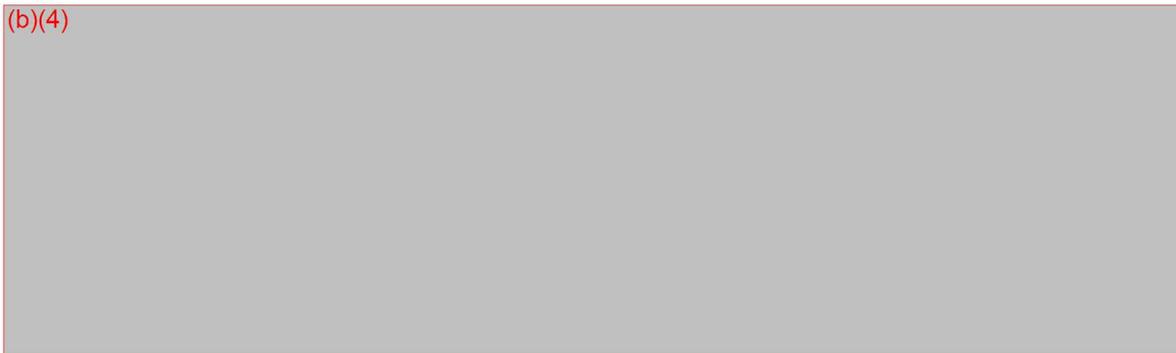
4.0 EQUIPMENT

(b)(4)



Table 1. Description of test articles

(b)(4)

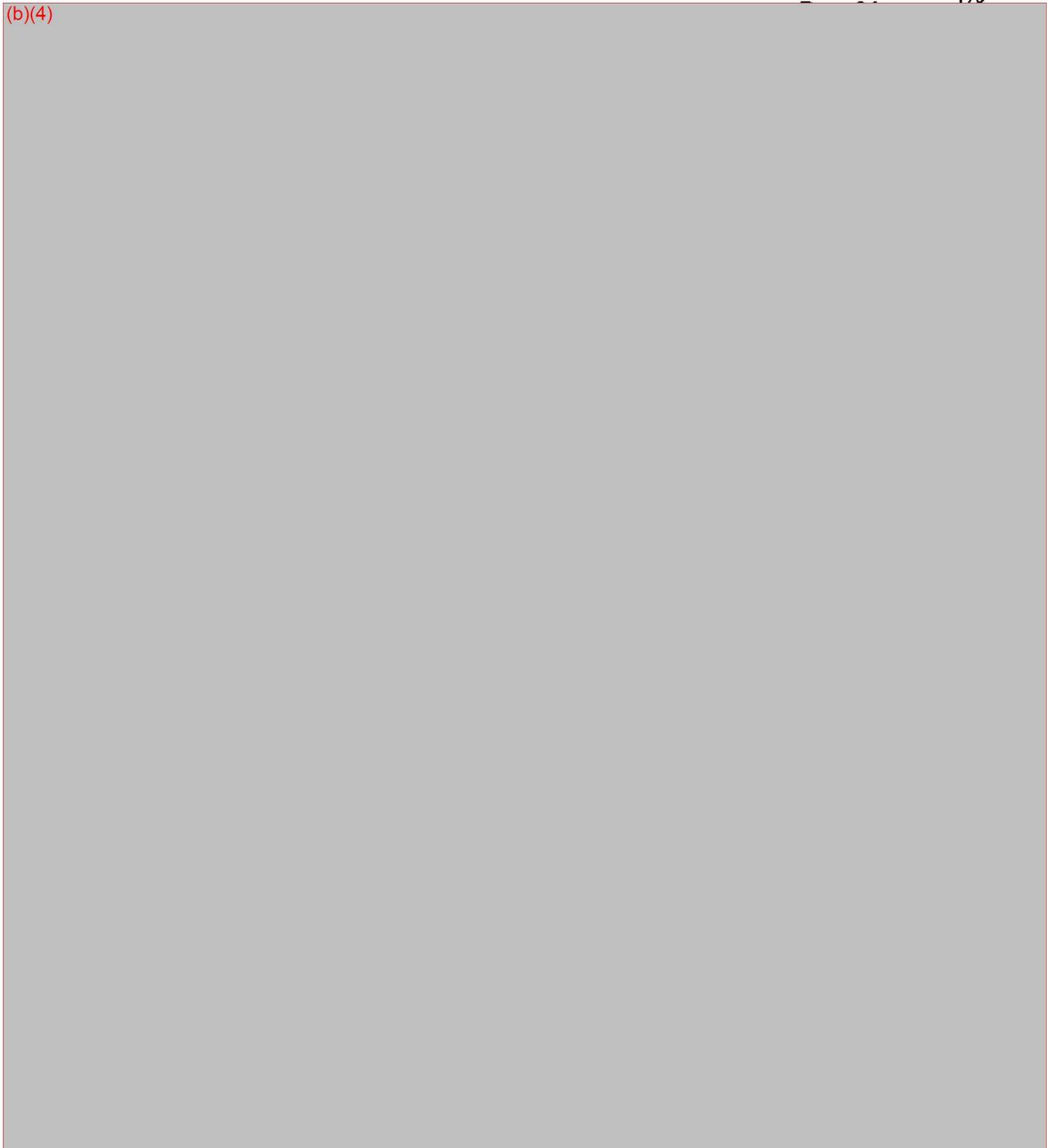
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5.0 METHODS AND STRATEGY



Figure 1. Study flow chart.

(b)(4)

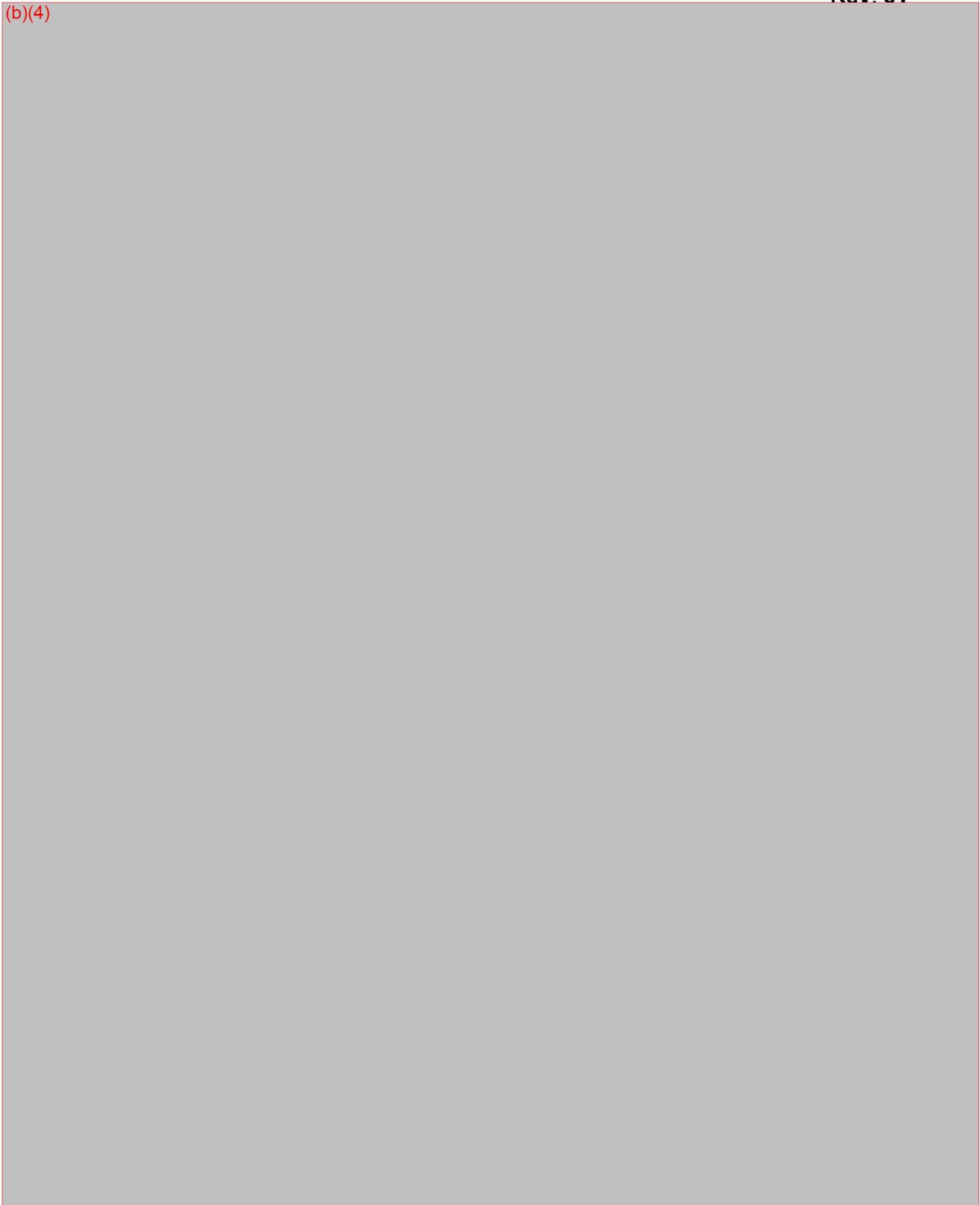


6.0 SUMMARY OF TESTING AND SAMPLING PLANS

(b)(4)



(b)(4)



(b)(4)

7.0 ACCEPTANCE CRITERIA

(b)(4)

8.0 EXISTING PROTOCOLS and DEVIATIONS

(b)(4)

9.0 RESULTS

(b)(4)

10.0 REVISION HISTORY

Section	Description	Author/Date

APPENDIX A
Deviation Records Log Sheet

Name / Date	Section	Deviated Action

**APPENDIX B
Data Sheets**

Date:	Location:	Tester (s):	Report:
-------	-----------	-------------	---------

T=0 group visual inspection

Sample	Label is Legible P/F	Label is affixed P/F	Seal is not peeling P/F	Comments
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				

Test Operator: _____

Reviewed: _____

Date: _____

Date: _____

APPENDIX B: Data Summaries

Date:	Location:	Tester (s):	Report:
-------	-----------	-------------	---------

Sample	Pouch Dye Penetration	Pouch Seal Peel
	Pass/Fail	Pass/Fail
1		
2		
3		
4		
5		
6	(b)(4)	
7		
8		

Reviewed: _____ Date: _____

Technician: see specific test data

APPENDIX B: Data Summaries

Date:	Location:	Tester (s):	Report:
-------	-----------	-------------	---------

Sample #	Pouch Dye Penetration	Pouch Seal Peel
	Pass/Fail	Pass/Fail
9	(b)(4)	
10		
11		
12		
13		
14		
15		
16		

Reviewed: _____ Date: _____

Technician: see specific test data

ATTACHMENT 9

BIOCOMPATIBILITY SUMMARY FOR THE ARROW-JOHANS ADAPTOR

ATTACHMENT 14

EVGUIDE-SAPIENS ECG WAVEFORM ACCURACY TEST REPORT

ATTACHMENT 10

EVGUIDE-SAPIENS SYSTEM HUMAN FACTORS
AND USABILITY VALIDATION REPORT

Romedex International Srl	Title: evGuide / Sapiens System Human Factors / Usability Validation Report	Part# DCO #: Rev: Release Date: xx/xx/xxxx
---------------------------	---	--

evGuideTM / SapiensTM System
Human Factors / Usability Validation Report

REVISION HISTORY

Section	Description	Author	Date
ALL	Initial Release	Sorin Grunwald	3/10/10

Romedex International Srl	Title: evGuide / Sapiens System Human Factors / Usability Validation Report	Part# DCO #: Rev: Release Date: xx/xx/xxxx
----------------------------------	--	---

1 Introduction

As emphasized in the FDA guidance document “Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management”, issued July 18th, 2000, hazards associated with medical device use are a common and serious problem. According to this guidance document, use-related hazards occur for one or more of the following reasons:

- Devices are used in ways that were not anticipated
- Devices are used in ways that were anticipated, but inadequately controlled for
- Device use requires physical, perceptual, or cognitive abilities that exceed those of the user
- Device use inconsistent with the user’s expectations or intuition about device operation
- The use environment effects device operation and this effect is not understood by the user
- The user’s physical, perceptual, or cognitive capacities are exceeded when using the device in a particular environment.

This evGuide™ / Sapiens™ TLS human factors and usability retrospective validation study is integrated into the overall risk management of the evGuide™ / Sapiens™ TLS. It is meant to help identify, understand, control, and prevent failures that can result in hazards when people use the evGuide™ / Sapiens™ TLS system.

In this document, the names evGuide™ TLS and Sapiens™ TLS will be used interchangeably.

2 Goal and Objectives

The goal of this human factors / usability retrospective validation study is to demonstrate that the intended user (nurses and physicians) can use the evGuide™ / Sapiens™ TLS system and adaptors safely and effectively.

The study focuses on usability testing. According to the FDA guidance, usability testing (also called user testing) is a powerful technique used to assess user’s interaction with the product. The central advantage of usability testing is that device use is realistic. For the purpose of the study at hand, the testing involved systematic collection of data from users (participants) using the evGuide™ TLS in real clinical situations.

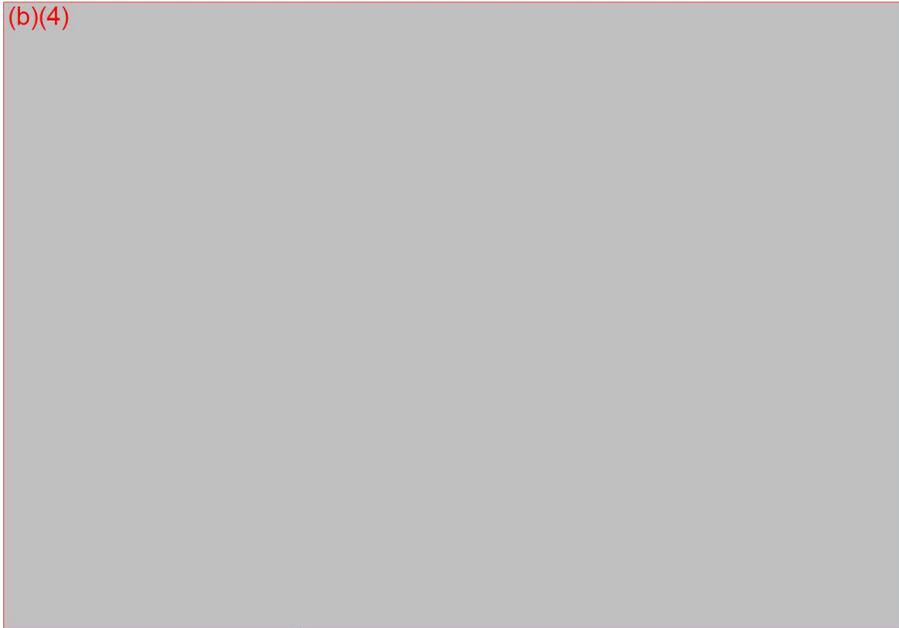
The study and the task selection focus on the high risk use scenarios as identified in the evGuide™ risk analysis and the FMEA for the evGuide™ TLS system, adaptors, and software. From a perspective of human factors engineering in medical device use, the risk

ATTACHMENT 11

EVGUIDE-SAPIENS POST-MARKET CLINICAL STUDY REPORT

evGuide-Sapiens™ TLS Post-Market Clinical Study Report

(b)(4)



REVISION HISTORY

ORIGINATOR	ECO#	REVISION	EFFECTIVE DATE	CHANGE
S. Grunwald		A	5/28/2010	Initial version
(b)(6)			6/3/2010	Reviewed version

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2. Study Summary 3

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 2.2. Objective..... 3

3. Methodology..... 4

4. Patient Selection Criteria 4

 4.1. Inclusion Criteria 4

 4.2. Exclusion Criteria 4

 4.3. Determination of Study Eligibility..... 4

5. Study Results 5

6. Conclusion 5

1. Overview and purpose

(b)(4)



2. Study Summary

2.1. Indications for Use

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphenous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location

2.2. Objective

(b)(4)



3. Methodology

(b)(4)



4. Patient Selection Criteria

(b)(4)



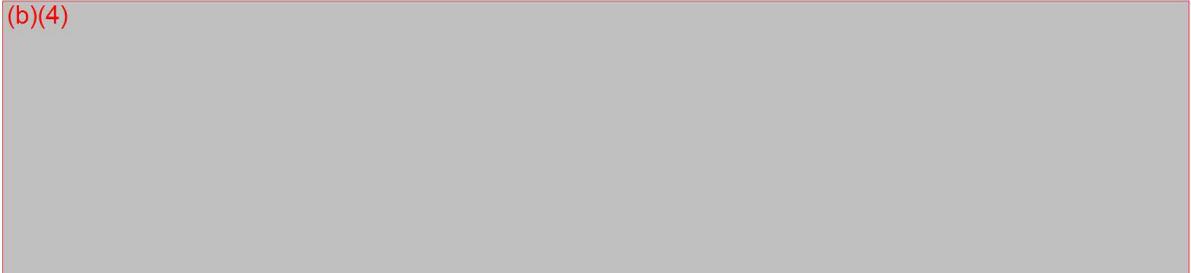
5. Study Results

(b)(4)



6. Conclusion

(b)(4)



ATTACHMENT 12

K093775 – UPDATED SUBMISSION COVER SHEET

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Date of Submission 12/8/2009	User Fee Payment ID Number MD6046572-956733	FDA Submission Document Number (if known) K093775
---------------------------------	--	--

SECTION A TYPE OF SUBMISSION				
PMA <input type="checkbox"/> Original Submission <input type="checkbox"/> Premarket Report <input type="checkbox"/> Modular Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment <input type="checkbox"/> Licensing Agreement	PMA & HDE Supplement <input type="checkbox"/> Regular (180 day) <input type="checkbox"/> Special <input type="checkbox"/> Panel Track (PMA Only) <input type="checkbox"/> 30-day Supplement <input type="checkbox"/> 30-day Notice <input type="checkbox"/> 135-day Supplement <input type="checkbox"/> Real-time Review <input type="checkbox"/> Amendment to PMA & HDE Supplement <input type="checkbox"/> Other	PDP <input type="checkbox"/> Original PDP <input type="checkbox"/> Notice of Completion <input type="checkbox"/> Amendment to PDP	510(k) <input checked="" type="checkbox"/> Original Submission: <input checked="" type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated (Complete section I, Page 5) <input type="checkbox"/> Additional Information <input type="checkbox"/> Third Party	Meeting <input type="checkbox"/> Pre-510(K) Meeting <input type="checkbox"/> Pre-IDE Meeting <input type="checkbox"/> Pre-PMA Meeting <input type="checkbox"/> Pre-PDP Meeting <input type="checkbox"/> Day 100 Meeting <input type="checkbox"/> Agreement Meeting <input type="checkbox"/> Determination Meeting <input type="checkbox"/> Other (specify):
IDE <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	Humanitarian Device Exemption (HDE) <input type="checkbox"/> Original Submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment	Class II Exemption Petition <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Evaluation of Automatic Class III Designation (De Novo) <input type="checkbox"/> Original Submission <input type="checkbox"/> Additional Information	Other Submission <input type="checkbox"/> 513(g) <input type="checkbox"/> Other (describe submission):

Have you used or cited Standards in your submission? Yes No (If Yes, please complete Section I, Page 5)

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name Romedex International Srl		Establishment Registration Number (if known) 3007923075	
Division Name (if applicable)		Phone Number (including area code) 650.209.4838	
Street Address 58 Aleca Arubium		FAX Number (including area code) 650.887.0348	
City Bucharest	State / Province	ZIP/Postal Code 022944	Country ROMANIA
Contact Name Sorin GRUNWALD PhD			
Contact Title Managing Director		Contact E-mail Address sorin@romedex.com	

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Division Name (if applicable)		Phone Number (including area code) 650.209.4838	
Street Address 175 Colorado Av.		FAX Number (including area code) 650.887.0348	
City Palo Alto	State / Province CA	ZIP Code 94303	Country USA
Contact Name Sorin GRUNWALD PhD			
Contact Title US FDA Agent for Romedex International Srl		Contact E-mail Address sorin@romedex.com	

SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE		
<input type="checkbox"/> New Device <input type="checkbox"/> Withdrawal <input type="checkbox"/> Additional or Expanded Indications <input type="checkbox"/> Request for Extension <input type="checkbox"/> Post-approval Study Protocol <input type="checkbox"/> Request for Applicant Hold <input type="checkbox"/> Request for Removal of Applicant Hold <input type="checkbox"/> Request to Remove or Add Manufacturing Site	<input type="checkbox"/> Change in design, component, or specification: <input type="checkbox"/> Software / Hardware <input type="checkbox"/> Color Additive <input type="checkbox"/> Material <input type="checkbox"/> Specifications <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Location change: <input type="checkbox"/> Manufacturer <input type="checkbox"/> Sterilizer <input type="checkbox"/> Packager
<input type="checkbox"/> Process change: <input type="checkbox"/> Manufacturing <input type="checkbox"/> Packaging <input type="checkbox"/> Sterilization <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Labeling change: <input type="checkbox"/> Indications <input type="checkbox"/> Instructions <input type="checkbox"/> Performance Characteristics <input type="checkbox"/> Shelf Life <input type="checkbox"/> Trade Name <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Report Submission: <input type="checkbox"/> Annual or Periodic <input type="checkbox"/> Post-approval Study <input type="checkbox"/> Adverse Reaction <input type="checkbox"/> Device Defect <input type="checkbox"/> Amendment
<input type="checkbox"/> Response to FDA correspondence:		<input type="checkbox"/> Change in Ownership <input type="checkbox"/> Change in Correspondent <input type="checkbox"/> Change of Applicant Address
<input type="checkbox"/> Other Reason (specify):		

SECTION D2 REASON FOR APPLICATION - IDE		
<input type="checkbox"/> New Device <input type="checkbox"/> New Indication <input type="checkbox"/> Addition of Institution <input type="checkbox"/> Expansion / Extension of Study <input type="checkbox"/> IRB Certification <input type="checkbox"/> Termination of Study <input type="checkbox"/> Withdrawal of Application <input type="checkbox"/> Unanticipated Adverse Effect <input type="checkbox"/> Notification of Emergency Use <input type="checkbox"/> Compassionate Use Request <input type="checkbox"/> Treatment IDE <input type="checkbox"/> Continued Access	<input type="checkbox"/> Change in: <input type="checkbox"/> Correspondent / Applicant <input type="checkbox"/> Design / Device <input type="checkbox"/> Informed Consent <input type="checkbox"/> Manufacturer <input type="checkbox"/> Manufacturing Process <input type="checkbox"/> Protocol - Feasibility <input type="checkbox"/> Protocol - Other <input type="checkbox"/> Sponsor	<input type="checkbox"/> Response to FDA Letter Concerning: <input type="checkbox"/> Conditional Approval <input type="checkbox"/> Deemed Approved <input type="checkbox"/> Deficient Final Report <input type="checkbox"/> Deficient Progress Report <input type="checkbox"/> Deficient Investigator Report <input type="checkbox"/> Disapproval <input type="checkbox"/> Request Extension of Time to Respond to FDA <input type="checkbox"/> Request Meeting <input type="checkbox"/> Request Hearing
<input type="checkbox"/> Report submission: <input type="checkbox"/> Current Investigator <input type="checkbox"/> Annual Progress Report <input type="checkbox"/> Site Waiver Report <input type="checkbox"/> Final		
<input type="checkbox"/> Other Reason (specify):		

SECTION D3 REASON FOR SUBMISSION - 510(k)		
<input checked="" type="checkbox"/> New Device	<input type="checkbox"/> Additional or Expanded Indications	<input type="checkbox"/> Change in Technology
<input type="checkbox"/> Other Reason (specify):		

SECTION E

ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	LJS	2	LDF	3	DQY	4	DQY
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

- 510 (k) summary attached
 510 (k) statement

Information on devices to which substantial equivalence is claimed (if known)

	510(k) Number		Trade or Proprietary or Model Name		Manufacturer
1	K091324	1	Sherlock 3CG TPS	1	Bard Access Systems
2	K032613	2	Transvenous Pacemaker Placement Assist Device	2	Peter Rothenberg
3	K973371	3	Conduction Anesthesia Kit - Certodyn	3	B. Braun Medical
4	K843263	4	Arrow-Johans ECG Adaptor	4	Teleflex/Arrow International
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Vascular Access Catheter Accessories

	Trade or Proprietary or Model Name for This Device		Model Number
1	Sapiens Tip Location System (TLS)	1	
2		2	
3		3	
4		4	
5		5	

FDA document numbers of all prior related submissions (regardless of outcome)

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

 Laboratory Testing Animal Trials Human Trials

SECTION G

PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code LJS	C.F.R. Section (if applicable) 880.5970	Device Class <input type="checkbox"/> Class I <input checked="" type="checkbox"/> Class II <input type="checkbox"/> Class III <input type="checkbox"/> Unclassified
Classification Panel General Hospital		

Indications (from labeling)

The Sapiens Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients. Limiting but not contra-indicated situations are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm and in central venous catheterization procedures performed through femoral or saphenous veins which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.

FDA Document Number (if known)

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

(b)(4)		Facility Establishment Identifier (FEI) Number		(b)(4)	
Company / Institution Name			Establishment Registration Number		
(b)(4)			(b)(4)		
Division Name (if applicable)			Phone Number (including area code)		
			(b)(4)		
Street Address			FAX Number (including area code)		
(b)(4)			(b)(4)		
City		State / Province		ZIP Code	Country
(b)(4)					(b)(4)
Contact Name		Contact Title		Contact E-mail Address	
(b)(4)		(b)(4)		(b)(4)	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		Facility Establishment Identifier (FEI) Number		(b)(4)	
Company / Institution Name			Establishment Registration Number		
(b)(4)					
Division Name (if applicable)			Phone Number (including area code)		
(b)(4)			(b)(4)		
Street Address			FAX Number (including area code)		
(b)(4)			(b)(4)		
City		State / Province		ZIP Code	Country
(b)(4)					(b)(4)
Contact Name		Contact Title		Contact E-mail Address	
(b)(4)		(b)(4)		(b)(4)	

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		Facility Establishment Identifier (FEI) Number		<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer <input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler	
Company / Institution Name			Establishment Registration Number		
Division Name (if applicable)			Phone Number (including area code)		
Street Address			FAX Number (including area code)		
City		State / Province		ZIP Code	Country
Contact Name		Contact Title		Contact E-mail Address	

Note: Complete this section if your application or submission cites standards or includes a "Declaration of Conformity to a Recognized Standard" statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
1	13485	ANSI/AAMI/ISO	Medical devices - quality management systems - requirements for regulatory devices	2003	
2	14971	ANSI/AAMI/ISO	Medical devices - application of risk management to medical devices	2007	
3	11135-1	ISO	Sterilization of health care products - ethylene oxide - part 1: Requirements for development, validation, and routing control of a sterilization process for medical devices	2007	
4	10993 -4, -5, -6, -7, -10	ISO	Biological evaluation of medical devices - Part 1: Evaluation and testing	2002, 1999, 1994, 2008, 2002	
5	60601-1-1 60601-1-2	IEC/EN	Safety standards for electrical medical equipment	2000/2001 2003/2006	
6	594-2	ISO	Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment - Part 2: Lock fittings	1998	
7	1041	BS EN	Information supplied by the manufacturer of medical devices	2008	

Please include any additional standards to be cited on a separate page.

Public reporting burden for this collection of information is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of the Chief Information Officer (HFA-710)
5600 Fishers Lane
Rockville, Maryland 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

CDHR PREMARKET REVIEW SUBMISSION COVER SHEET
Romedex International Srl
EvGuide Tip Location System
SECTION I - ADDITIONAL STANDARDS CITED IN THE SUBMISSION

FDA forms 3654 are attached in Appendix L

8	Standards No.	Standards Organization	Standards Title	Version	Date
	980	EN	Graphical symbols for use in labeling of medical devices	2008	June 2008
9	Standards No.	Standards Organization	Standards Title	Version	Date
	55011	EN	Industrial, scientific and medical RF equipment – radio disturbances characteristics – limits and methods	2007	May 2007
10	Standards No.	Standards Organization	Standards Title	Version	Date
	730	IEEE	Software Quality Assurance	1998	June 1998
11	Standards No.	Standards Organization	Standards Title	Version	Date
	829	IEEE	Software test documentation	1998	1998
12	Standards No.	Standards Organization	Standards Title	Version	Date
	830	IEEE	Recommended practices for software requirements specification	1998	1998
13	Standards No.	Standards Organization	Standards Title	Version	Date
	1058	IEEE	Software Project management	1998	1998
14	Standards No.	Standards Organization	Standards Title	Version	Date
	1074	IEEE	Developing software life cycle	1997	1997
15	Standards No.	Standards Organization	Standards Title	Version	Date
	J-STD-06	IEEE	Software development plan	1995	1995

ATTACHMENT 13

K093775 – UPDATED SECTION 4 – INDICATIONS FOR USE STATEMENT

SECTION 4: INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K093775

Not known at this time _____

Device Name: Sapiens™ TLS

Indications for Use:

The Sapiens™ Tip Location System (TLS) is indicated for guidance and positioning of central venous catheters such as PICCs, CVCs, implantable ports, and hemodialysis catheters. The Sapiens™ TLS provides real-time catheter tip location information by using the patient's cardiac electrical activity. Sapiens™ TLS is indicated for use as an alternative method to chest X-ray and fluoroscopy for central venous catheter tip placement confirmation in adult patients.

Limiting but not contraindicated situations for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm, and in central venous catheterization procedures performed through femoral or saphaneous vein access which change the presentation of the P wave. In such patients, who are easily identifiable prior to central venous catheter insertion, the use of an additional method is required to confirm catheter tip location.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE
OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)
Page of
(Posted November 13, 2003)

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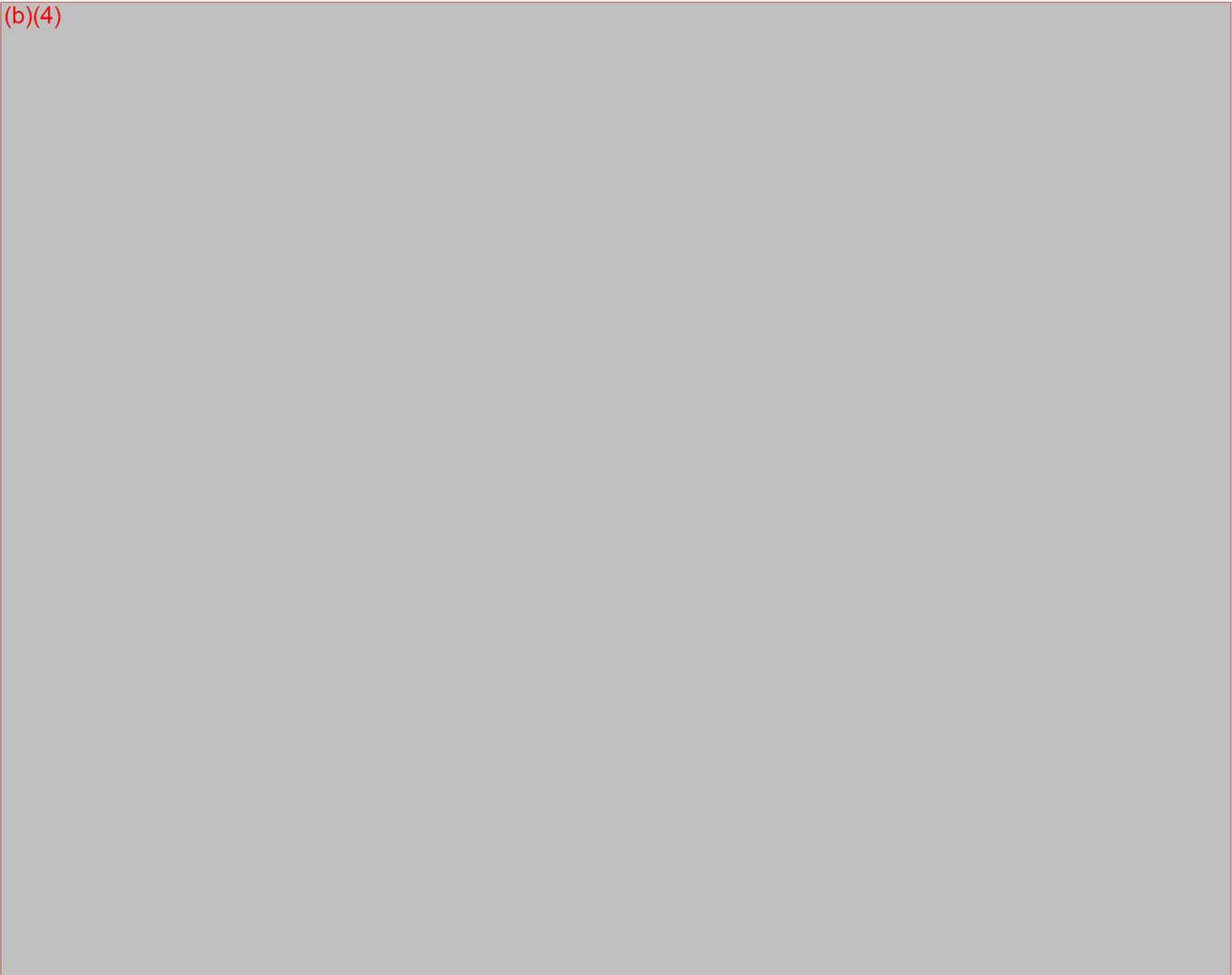
1. Purpose & Scope

The purpose of the ECG accuracy comparison described by this protocol is to demonstrate that:

- a) the evGuide™ TLS system can detect ECG waveforms with the same level of accuracy as the predicate devices B.Braun Certodyn (K973371), Arrow-Johans (K843263) and Pacer Assist (K032613)
- b) the evGuide™ TLS system can detect ECG waveforms with the same level of accuracy using the Electrical Adaptor and a combination of the Electrical Adaptor and the predicate device Arrow-Johans Adaptor (K843263)

2. Overview of the Test Methods

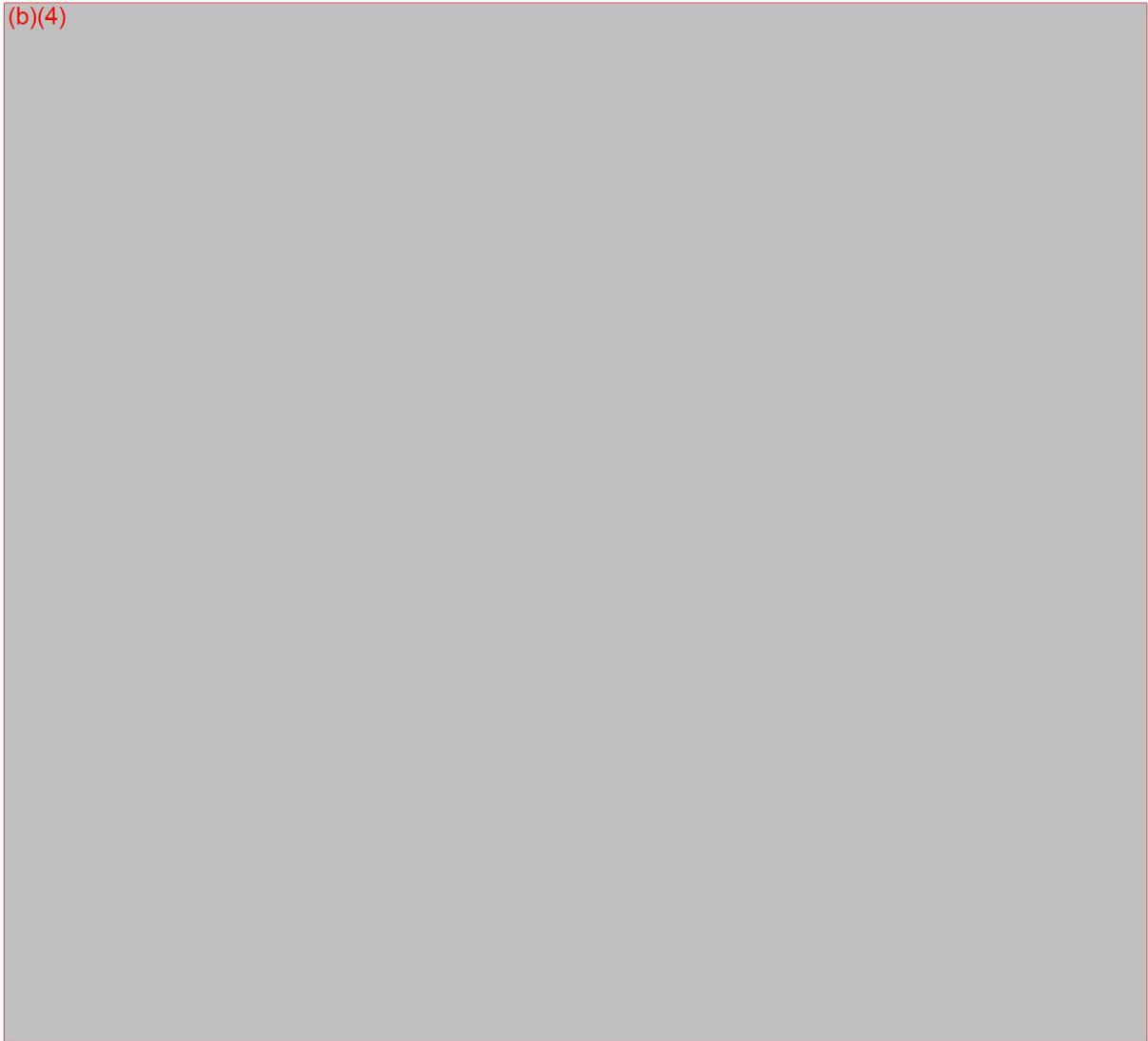
(b)(4)



3. Acceptance Criteria

3.1. Bench top testing

(b)(4)



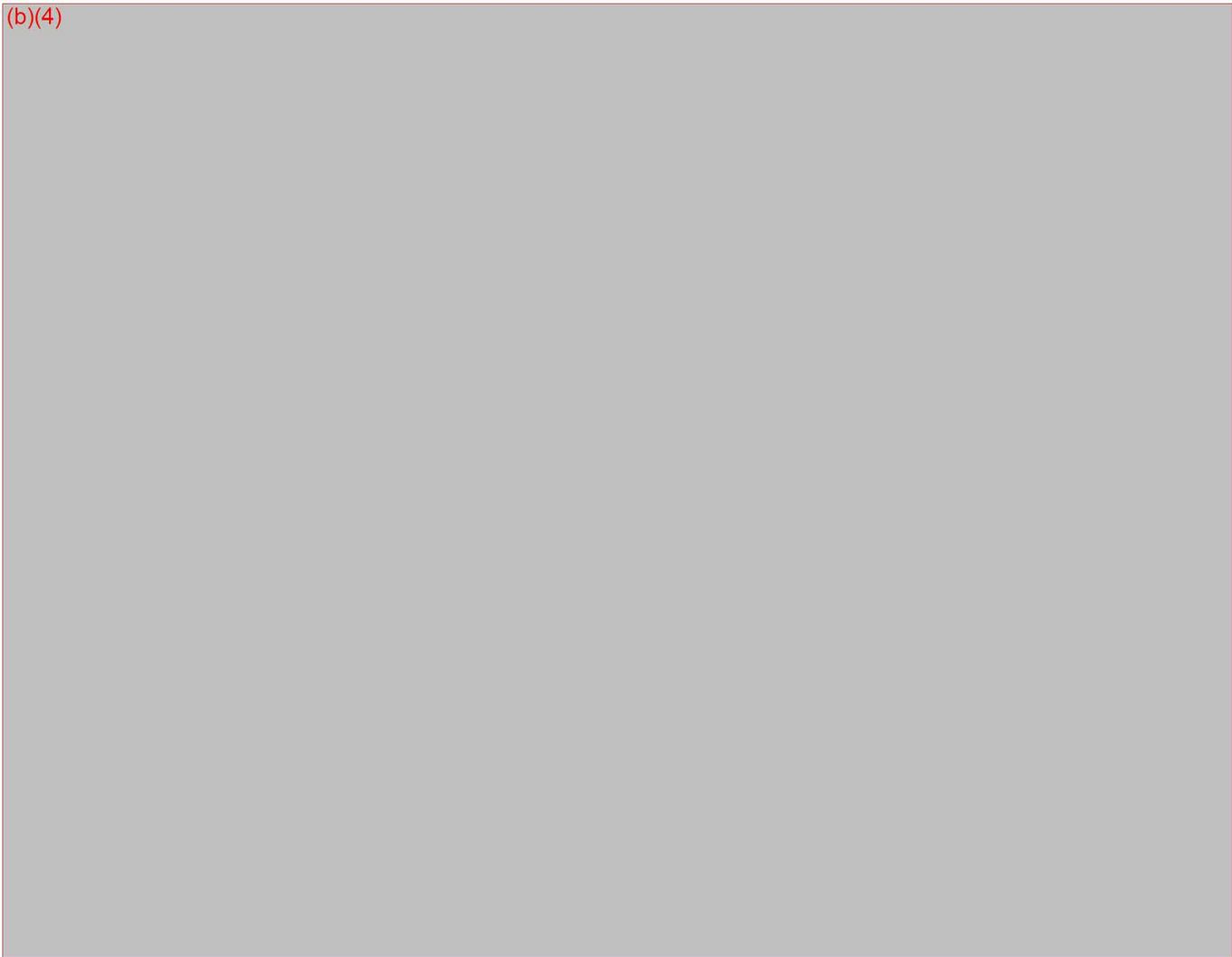
3.2. Animal Study

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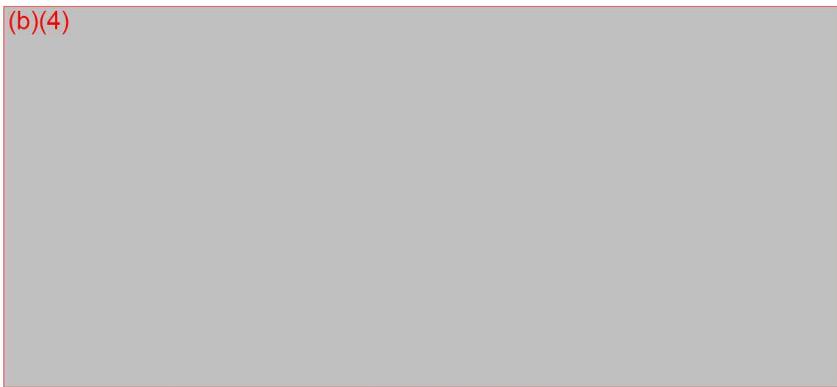
3.3. Clinical Settings

(b)(4)



4. Equipment, Material & Setup

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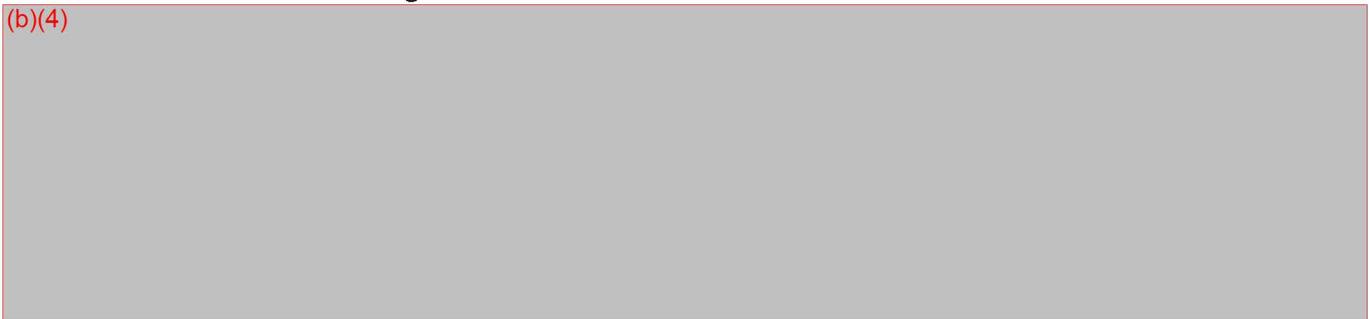
5. References

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6. Test Protocol and Results - Bench Top

6.1. Electrical Testing

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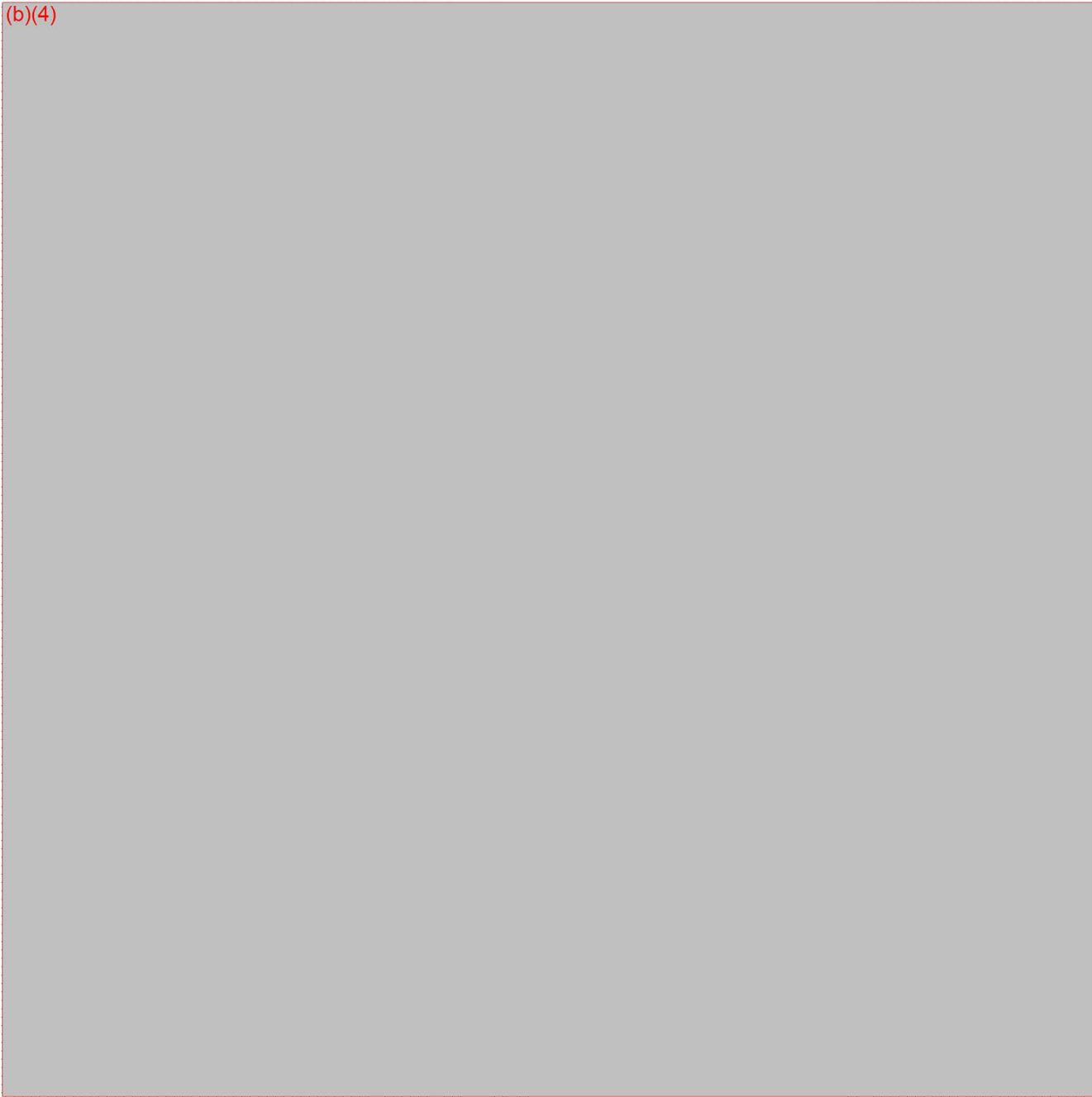


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6.2. Waveform Measurement

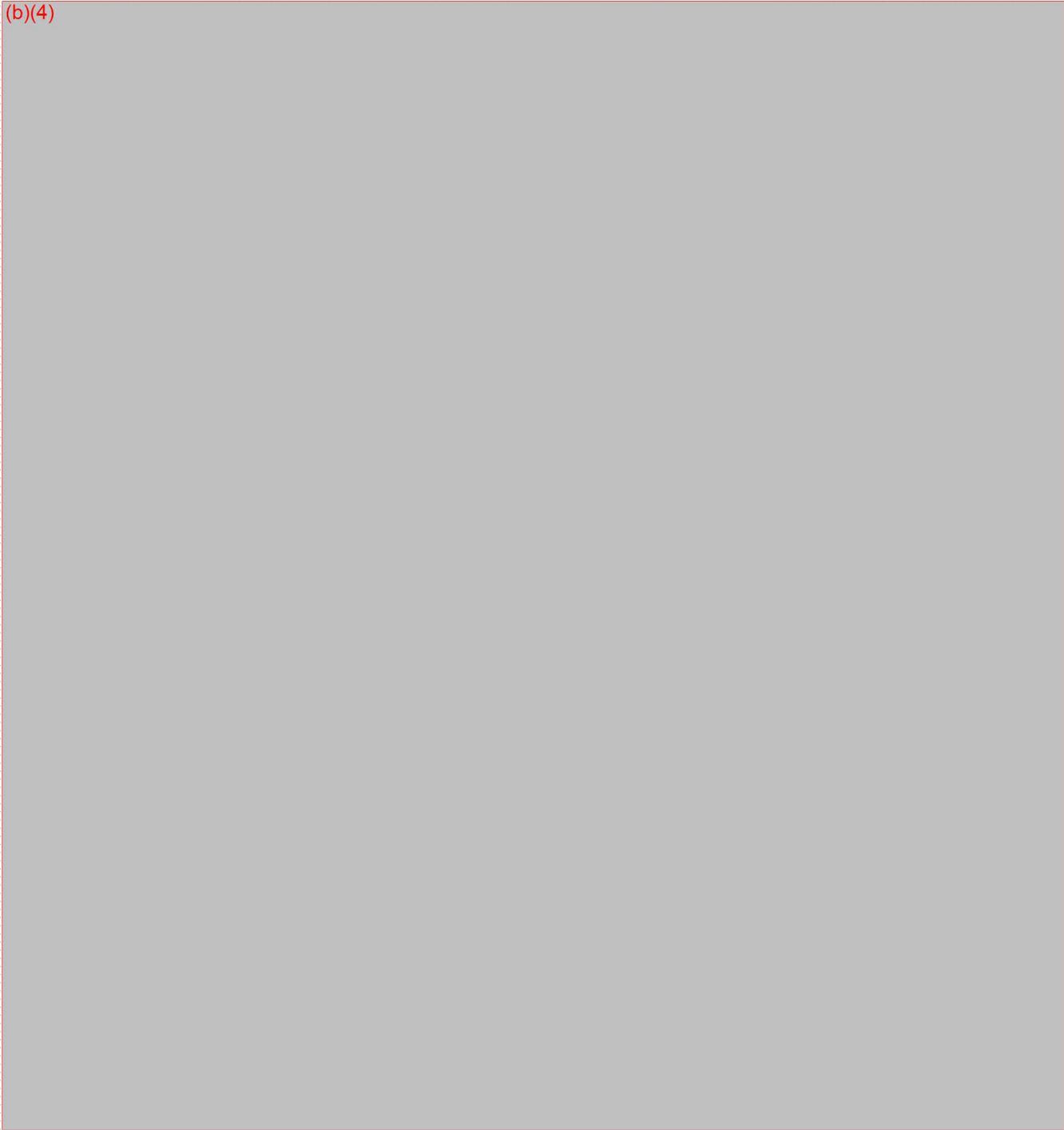
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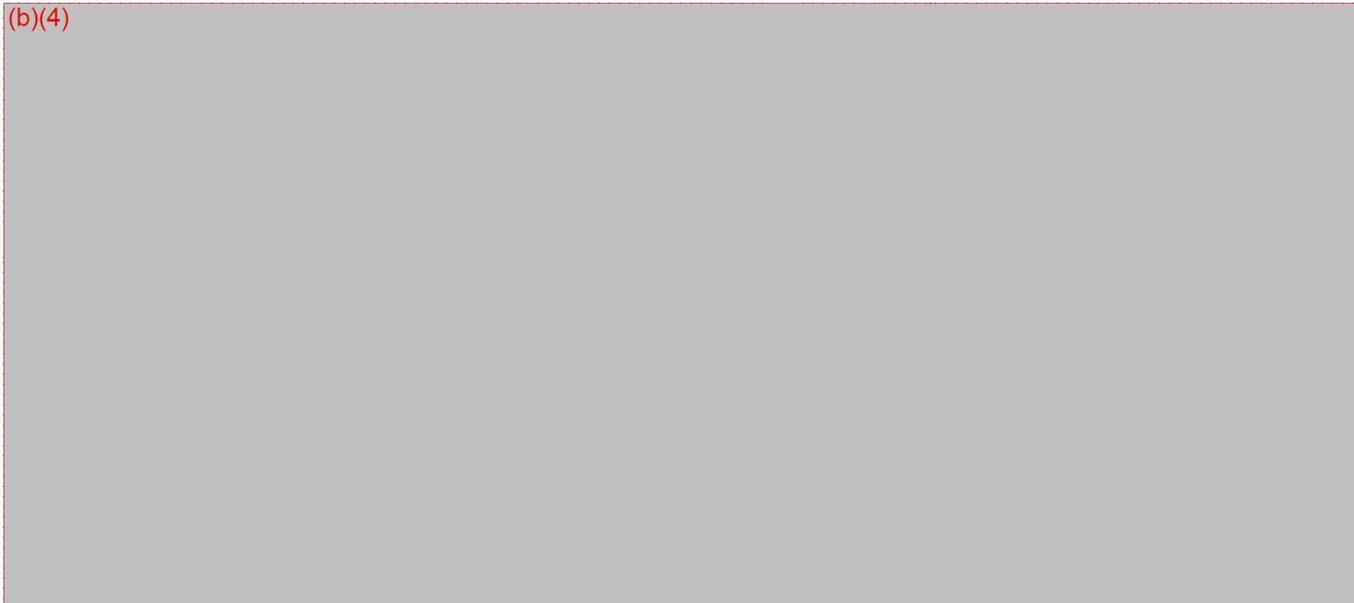


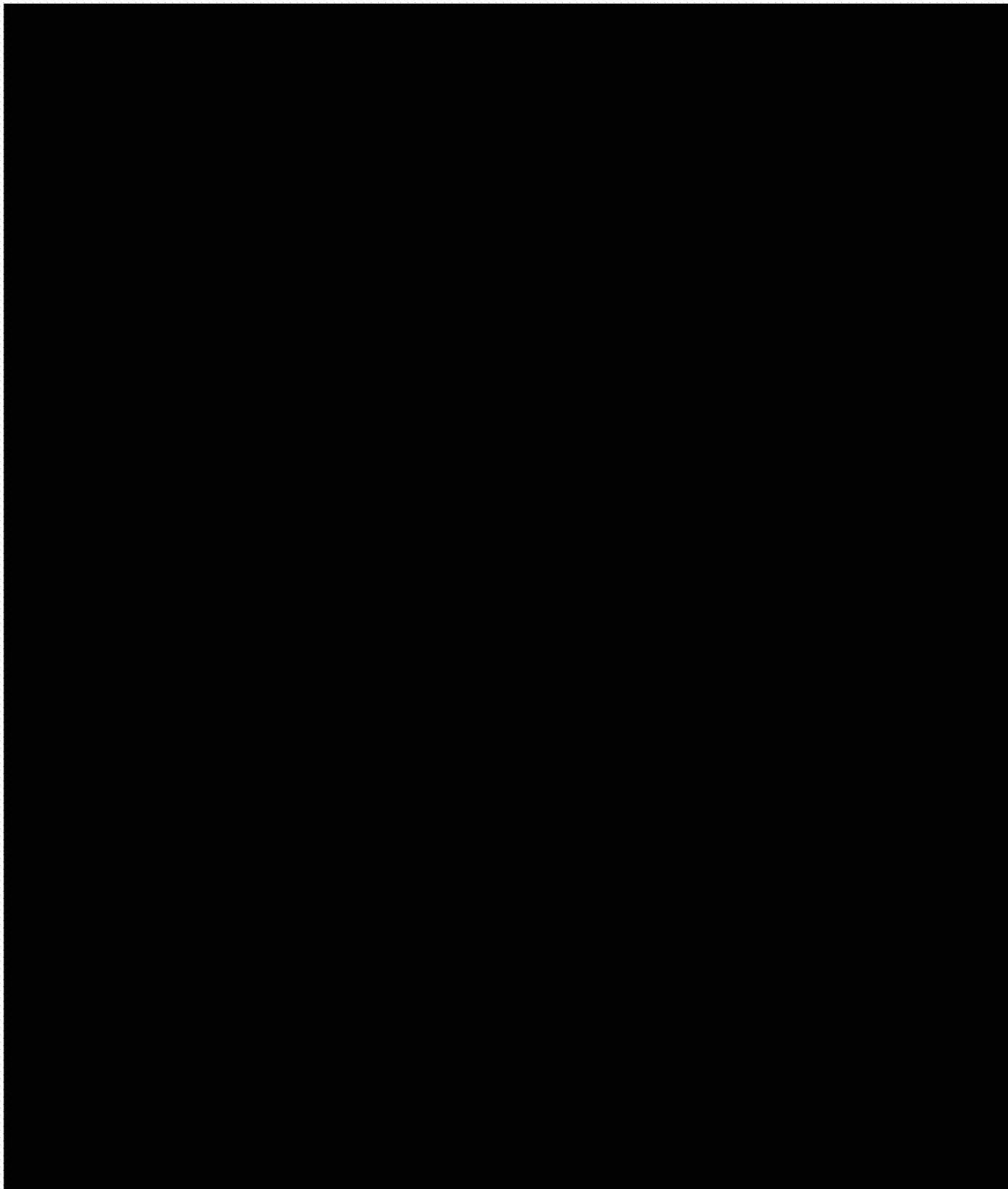
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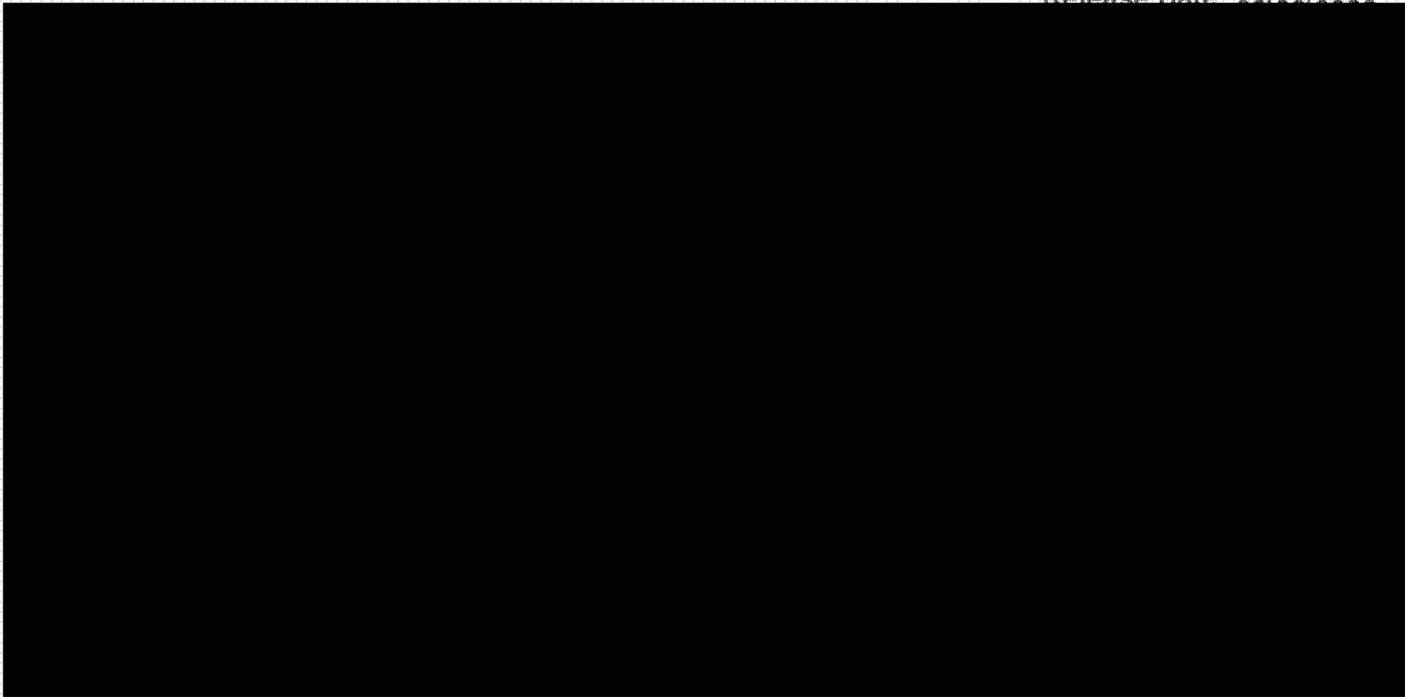


7. Test Protocol and Results – Animal Study

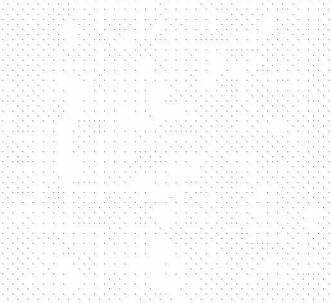
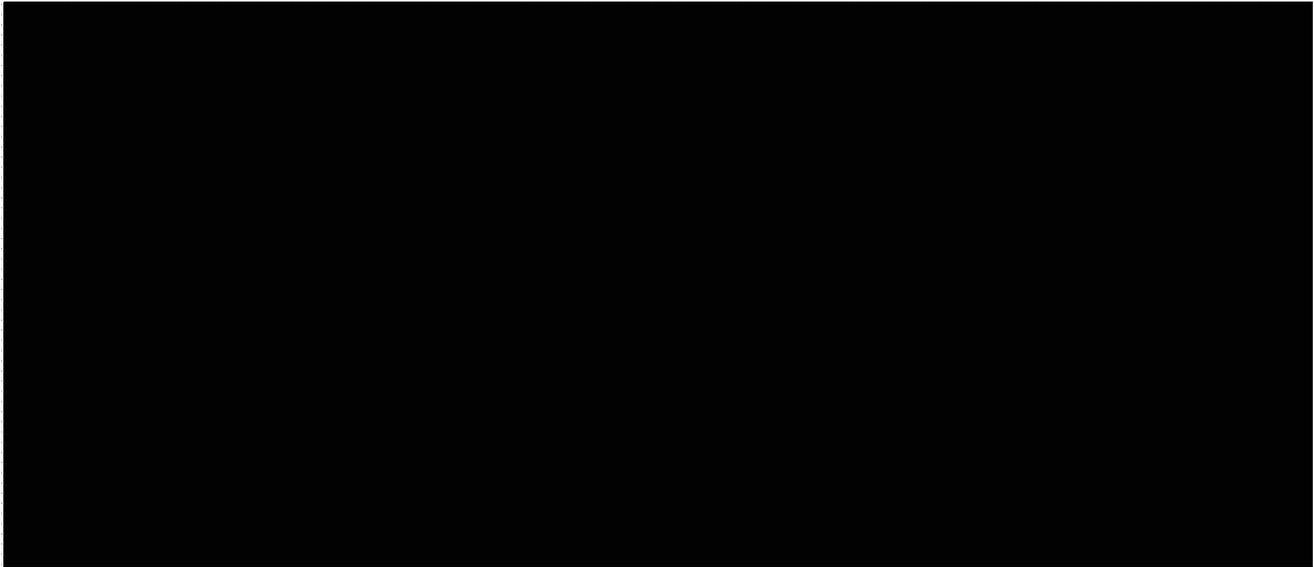
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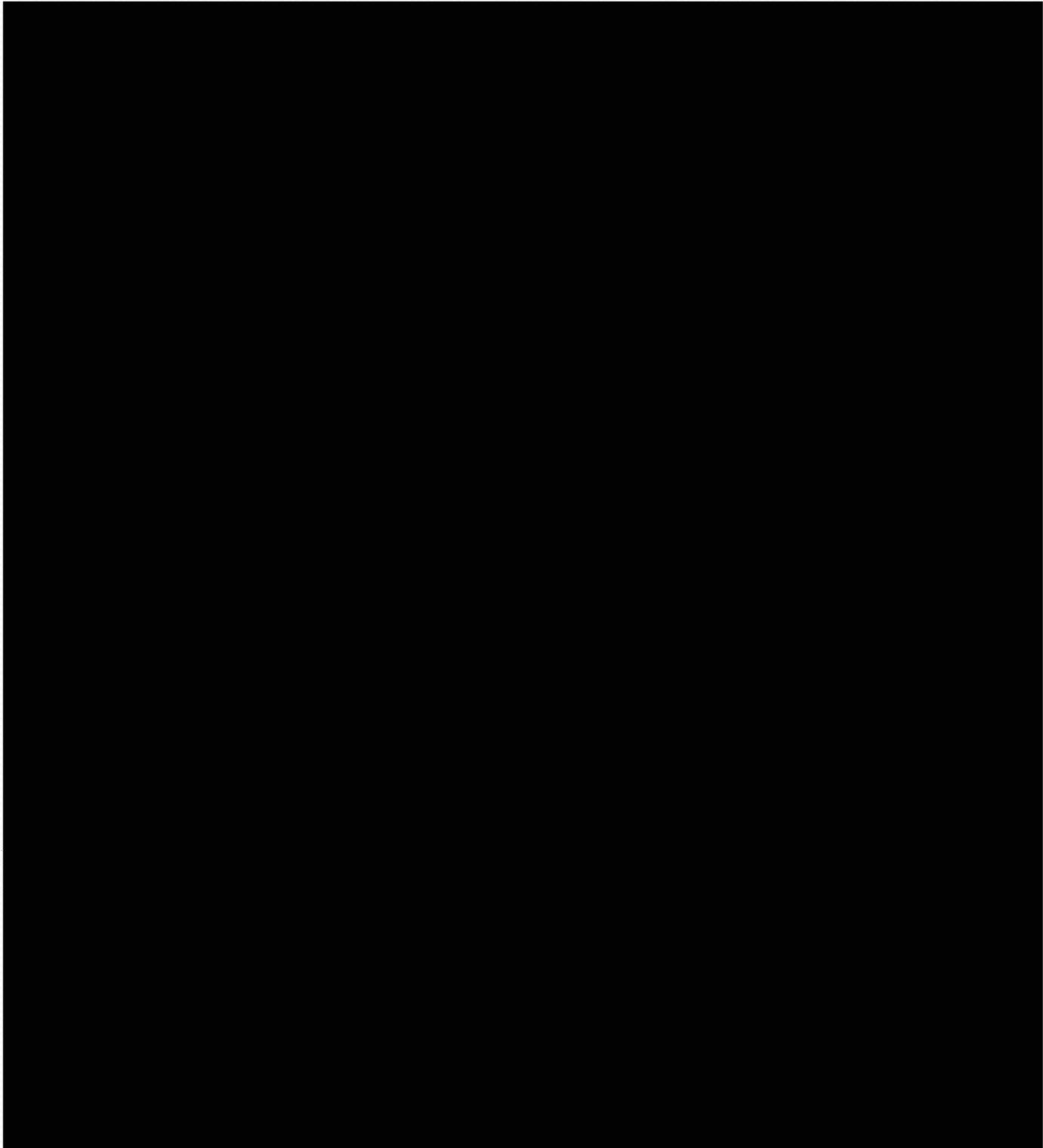


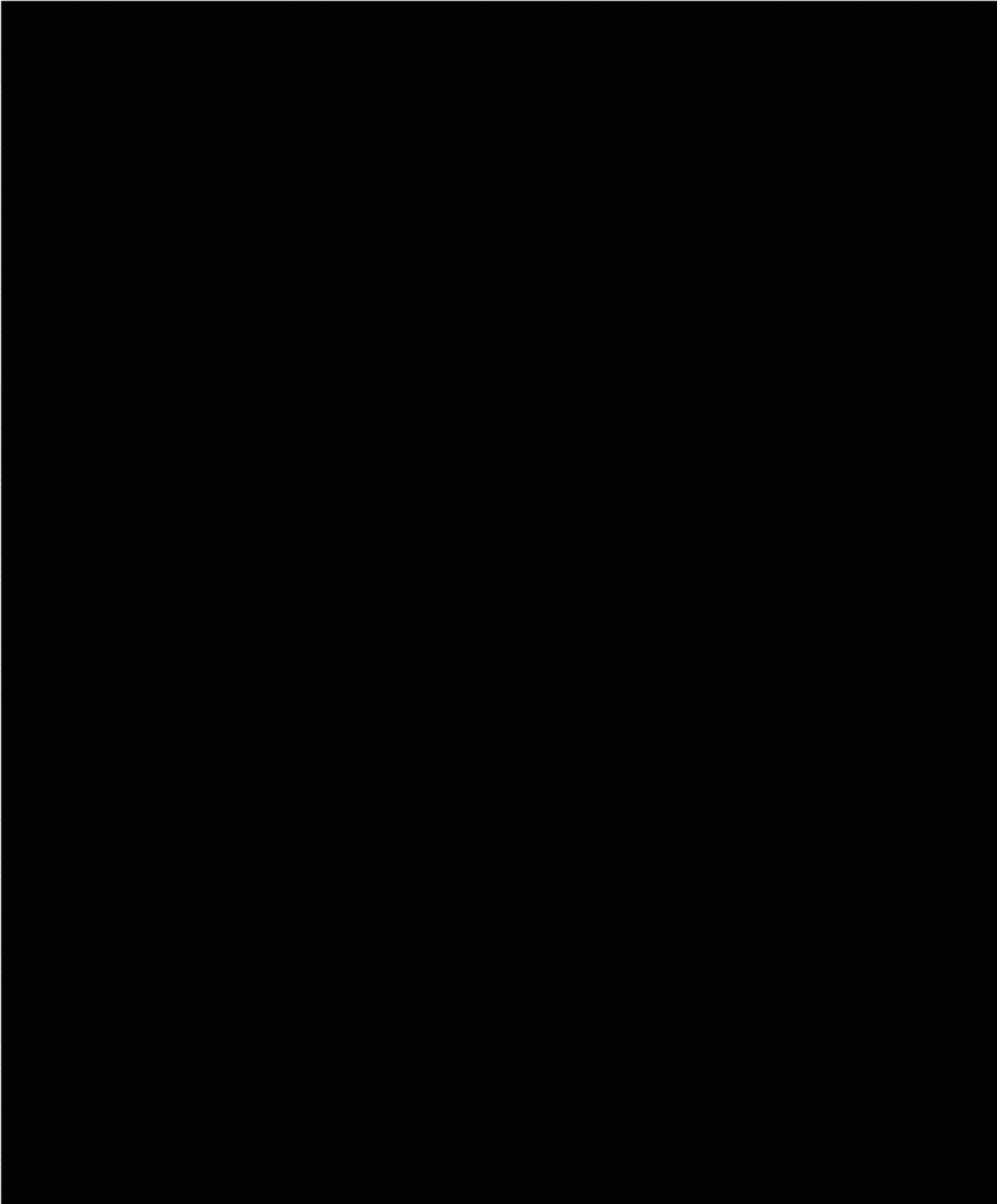




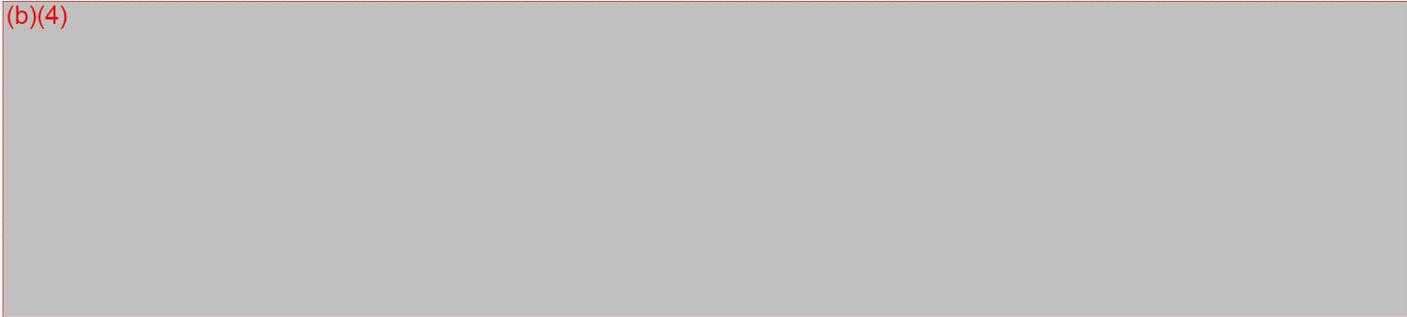
8. Test Protocol and Results – Clinical Setting







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8.2. evGuide Saline Adaptor

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9. Conclusion

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ATTACHMENT 15**ELECTROCARDIOGRAM (EKG) GUIDED PERIPHERALLY INSERTED
CENTRAL CATHETER PLACEMENT AND TIP POSITION: RESULTS OF A
TRIAL TO REPLACE RADIOLOGICAL CONFIRMATION**

**BY NANCY MOUREAU ET AL. PUBLISHED IN THE JOURNAL OF THE
ASSOCIATION FOR VASCULAR ACCESS IN 2010, JAVA VOL. 15 No. 1
2010, PP. 9-15**



Electrocardiogram (EKG) Guided Peripherally Inserted Central Catheter Placement and Tip Position: Results of a Trial to Replace Radiological Confirmation

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Abstract

Background: The current standard of care for Peripherally Inserted Central Catheters (PICCs) is radiological confirmation of terminal tip location. Tip location practices in Europe have used electrocardiographic (EKG) guided positioning for central venous catheters for more than twenty years with tip positioning safely confirmed over thousands of insertions (Madias, 2003). The goal of this group was to confirm the findings of a study performed by Pittiruti and his team; and to establish safe function in the use of EKG guidance for verification of terminal tip position with PICCs placed at McKenzie Willamette Medical Center.

Methods: In 2008/2009 McKenzie Willamette Medical Center conducted a study to determine whether or not EKG guidance can be used as a reliable means to accurately place and confirm terminal tip location of PICCs. A group of trained nurses performed PICC placement using EKG guidance followed by radiological confirmation of SVC position. All PICCs placed from October 2008 to December 2009 were included in the study. Tip location was confirmed using either radiological confirmation alone, EKG plus radiological confirmation, or EKG alone.

Results: A total of 417 PICCs were placed during the study period. EKG guidance alone was used in the placement and confirmation of 168 PICCs. Both EKG and chest x-ray confirmation were used in the placement of 82 of the PICCs; 240 of the PICCs were placed with the use of EKG and then position correlated using the traditional chest x-ray procedure.

Discussion: EKG guided PICC placement proved accurate in consistently guiding the terminal tip to the superior vena cava (SVC). The procedure was easily taught and duplicated by members of the PICC team. The study demonstrated a definite correlation between the height (size) of the P-wave and the location of the terminal tip within the SVC. With knowledge of this correlation, transition from placing PICCs using EKG guidance with chest x-ray confirmation to confirmation of tip placement using just EKG guidance without chest x-ray confirmation was attained. Application of EKG placement/confirmation performed during insertion saves time previously spent waiting for x-ray confirmation readings, saves cost of chest x-ray, prevents patient exposure to radiation and saves time required for tip repositioning of malpositioned tips found after the end of the procedure.

Background

While radiographic imaging is the current standard of care for Peripherally Inserted Central Catheter (PICC) tip confirmation (Scott, 1995), electrocardiographic (EKG) guided positioning, which has been widely used throughout the world in conjunction with central venous catheters (CVCs), is applicable for position confirmation of

PICCs (Chu, et al., 2004; Jalaiean, Mottahedi, Ghanad, & Peyvandi, 2005; Pittiruti, et al., 2008). With the number of PICC placements increasing, a more accurate and efficient means of tip confirmation is needed. PICCs are placed primarily through the veins of the arm. One of the primary reasons for chest x-ray (CXR) is to rule out the presence of insertional complications such as malposition (Jalaiean, et al., 2005). Use of EKG guidance for placement of PICCs can speed time to first usage by reducing time required for x-ray interpretation and by reducing repositioning delays (Francis, Picard, Fajardo, & Pizzi, 1992; Tiernay, Katke, & Langer, 2000).

Chest x-rays are used to verify the terminal tip after CVC

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placement as well as to rule out the presence of pneumothorax, a complication occurring with subclavian or internal jugular catheters. While EKG tip location does not address the presence of a pneumothorax, PICCs consistently demonstrate reduced insertional risk without pneumothorax. When patient symptoms demonstrate respiratory complications following CVC placement, a CXR is easily performed to identify the origin of the problem.

The challenge with small diameter PICCs is to locate the terminal tip and have consistent interpretation of where the distal superior vena cava is positioned. Radiographic films taken with portable equipment use the anterior/posterior (A/P) view to verify position of the terminal CVC tip. Radiographic interpretation variations occur with positioning, anatomic aberrations, arterial placement and obesity providing a false sense of security with the A/P view. A corresponding lateral view has been noted by several authors as necessary in determining accurate placement of CVCs and PICCs but is rarely employed in daily practice (Lum, 2004; Madias, 2003; Royer, 2001). Variation is also present in landmarks used to interpret radiographic results and distal SVC position on 2-D radiographic films (Vesely, 2003). A more accurate means of tip position confirmation has been extensively studied throughout the world, primarily with CVCs, but more recently with PICCs (Chu, et al., 2004; Jalaiean, et al., 2005; Pittiruti, et al., 2008). Pittiruti and his team of physicians and nurses performed multiple EKG confirmation studies on open and closed ended PICCs validating accurate distal SVC position. The methods used included guidewire and saline infusion for electrical conductivity represented in the p-wave of an electrocardiogram (EKG) rhythm. When a normal sinus rhythm is visible on an EKG monitor, the p-wave is seen just prior to the QRS complex (QRS). With intracavitary monitoring of electrical activity the p-wave changes and becomes amplified or taller as a catheter is advanced into the SVC. When the p-wave peaks, the tip is at the SVC/right atrial junction (SVC/RA). This study is thought to be the first published nursing- based PICC EKG tip location study performed in the United States (US), confirming the findings of Pittiruti and his team while demonstrating application with US based equipment.

Methods

In 2008/2009 McKenzie Willamette Medical Center conducted a study of EKG guided placement of PICCs followed by radiological confirmation of SVC position to determine if the procedure could be duplicated with accuracy and dependability. Peripherally inserted central catheters used in the study included both closed-ended (Groshong™ Bard Access, SLC Utah) and open-ended (Power PICC™ Bard Access, SLC Utah) catheters. A review of EKG literature available at the time of the study revealed 95-100% accuracy with EKG guided CVC or PICC placement into the superior vena cava (SVC) (Francis, et al., 1992; Hoffman, et al., 1988; Karaaslan, Altinisik, Peker, Nayir, & Ozmen, 2009; W. T. McGee, et al., 1993; Pittiruti, et al., 2008; Schummer, et al., 2004). The desire to recreate this study was based on the level of success reported in the literature.

Following a Critical Care Committee review and approval, patients undergoing PICC placement from October 2008 through December 2009 received verification of tip placement with either radiological confirmation alone, EKG and radiological

confirmation, or EKG alone. The first ten patients involved in the study used the EKG tip location method and a secondary confirmation with chest x-ray method. After the initial ten patients, PICCs were placed using the EKG method only, with verification based on the judgment of the clinician reading the EKG during placement. When chest x-ray was necessary for other reasons, catheter tip location was also reviewed and findings were correlated with results of EKG tip location method.

Criteria for patients' inclusion with EKG tip location study included all of the following: a) any adult 18 years or older; b) with a normal sinus rhythm; c) a clearly visible p-wave; d) who were scheduled to receive a PICC for prescribed treatment. Criteria which excluded patients from the EKG placement study included: a) the presence of an arrhythmia resulting in lack of p-wave or indistinguishable QRS complex, or b) the dependency on a pacemaker for heart function. Initially a conservative approach was applied at this institution for selection of PICC candidates for use of EKG tip location. Placement of catheters was performed by PICC trained experienced radiological nurses using the guidewire and saline EKG location techniques. Radiographic confirmation was verified by interventional cardiologists for consistency with this study. EKG equipment included an EKG adapter (Pacerview, San Clemente, CA) and a cable with alligator clamp (Pacerview, Grabber, San Clemente, CA)

When placing a PICC using the EKG tip location method, a conductor is required within the tip of the catheter. Two methods of creating conductivity within the catheter include: use of a guidewire within the catheter or filling the catheter with a saline solution. Both of these methods are described below and were used as steps in the study.

Steps for placing EKG guided PICC with guidewire technique:

1. Attach 3 or 5 lead monitor to patient (always apply all new leads); determine if the patient is in Normal Sinus Rhythm (NSR), atrial fibrillation or is dependently paced. If the patient is in NSR, proceed with EKG guided PICC insertion.
2. Detach the left leg lead from the patient and attach it (red lead) to the EKG adapter lead button.
3. Select the vein for PICC insertion using ultrasound scanning.
4. Measure selected vein to estimated location of Superior Vena Cava (SVC).
5. Set up sterile field; prep and drape patient.
6. Don personal protective equipment (PPE).
7. Trim the PICC to the desired length making sure guidewire is at the very distal end of the PICC but not extended outside the catheter. Flush PICC with normal saline.
8. Place the EKG cable into sterile cover/sleeve. Remember the cable is unsterile and must be covered.
9. Insert the PICC using ultrasound guided modified Seldinger technique (MST).
10. When the PICC is approximately 50% to its intended goal of the distal SVC/caval atrial junction, attach the EKG Alligator cable to the guide wire in the PICC, carefully punching the tip of the grabber through the sterile sleeve and covering the connection with a sterile 4x4.
11. Flush the PICC again with normal saline.

12. An inverted QRS complex should appear on the monitor. The p-wave is normal size initially, increasing in amplitude as the PICC is advanced. Compare p-wave size from initial normal complex to peak level. (Note: Size may vary with QRS complex comparison with p-wave and be larger than QRS. The determinant is p-wave change measured to peak with biphasic notch.)
13. When the p-wave is about $\frac{1}{4}$ of the full peaked level, approx $\frac{3}{4}$ the size of the QRS, the PICC tip is in the lower or distal SVC (also known as proximal SVC in relation to the heart).
14. When the p-wave is fully peaked or at the highest amplitude, it is at the caval atrial junction (SVC/RA).
15. When a small positive wave spike is seen in the p-wave, the tip is in the right atrium.
16. When the p-wave becomes biphasic (expands beyond the baseline up and down), the PICC tip is in the low right atrium/high right ventricle. This is known as an atrial spike.
17. If no QRS pattern is seen during advancement of the catheter, the PICC has malpositioned in the internal jugular or contra-lateral in the opposite subclavian vein. Attempts to reposition can be made until the inverted QRS is seen on the monitor.
18. Print final strip with P-wave at the same amplitude as QRS to confirm location of the tip. Include this EKG strip as part of the patient's record.

(Note: You may see some respiratory variation in the wave form.)

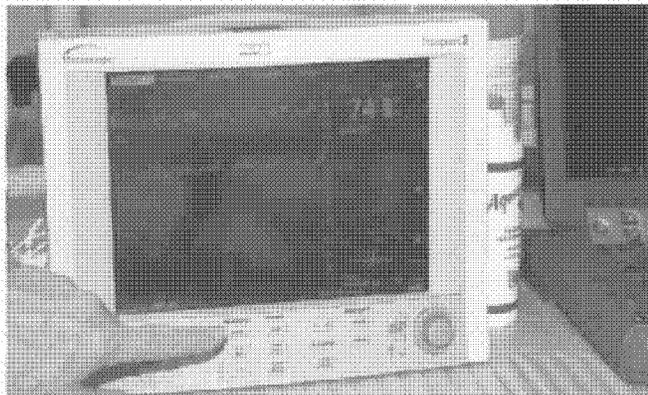


Photo 1 EKG Interpretation of PICC tip location. Note p-wave amplitude near amplitude of inverted QRS. This demonstrates PICC tip location near the Caval Atrial Junction. G Dennis

Steps for placing EKG guided PICC with saline filled lumen:

1. Attach 3 or 5 lead monitor to patient (always apply all new leads; do not use any currently in use with other monitors); determine if the patient is in Normal Sinus Rhythm (NSR), atrial fibrillation, or is dependently paced. If the patient is in NSR, proceed with EKG guided PICC insertion.
2. Detach the left leg lead from the patient and attach it (red lead) to the EKG adapter lead button.
3. Select the vein for PICC insertion using ultrasound scanning.

4. Measure selected vein to estimated location of Superior Vena Cava (SVC).
5. Set up sterile field; prep, and drape patient. Drop a sterile injection cap with needle penetration septum onto the sterile field.
6. Don personal protective equipment (PPE).
7. Prefill a 20cc syringe with saline and attach a steel needle.
8. Trim the PICC to the desired length; remove the guidewire and apply the injection cap with needle septum. Flush the PICC with normal saline.
9. Place the EKG cable in sterile cover/sleeve.
10. Insert the PICC using ultrasound guided modified Seldinger technique (MST).



Photo 2 Sterile sleeve covering the EKG alligator cable. G Dennis

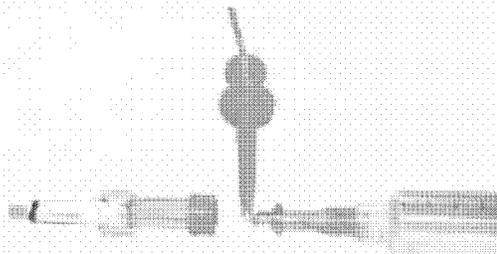
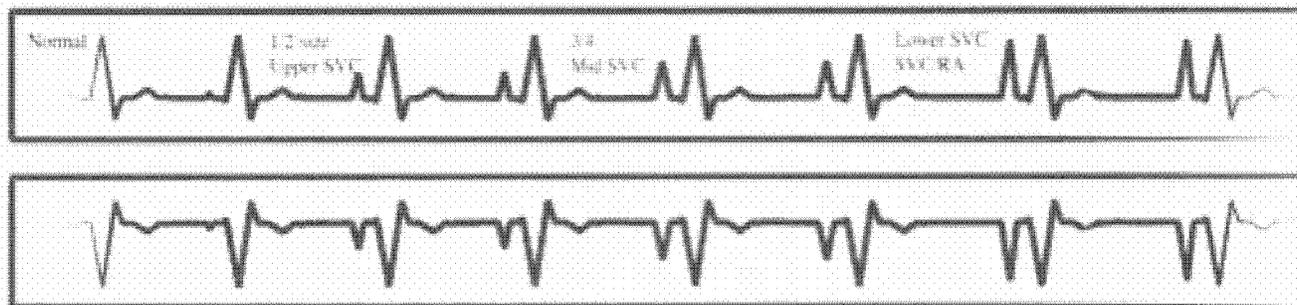


Photo 3 Close up of EKG alligator cable clipped to steel needle shaft for saline-only method of EKG tip placement. G Dennis

11. When the PICC is approximately 50% to its intended goal of the distal SVC/caval atrial junction, attach the alligator cable to the needle shaft (the needle is inserted through the injection cap) carefully punching the tip of the grabber through the sterile sleeve, and covering the connection with a sterile 4x4.
12. Flush the PICC again with normal saline 5-10ml.
13. An inverted QRS complex appears on the monitor. The p-wave is normal size initially, increasing in amplitude as the PICC is advanced. Compare p-wave size from initial normal complex to peak level. (Note: Size may vary with QRS complex comparison with p-wave and be larger than QRS. The determinant is p-wave change measured to peak with biphasic notch.)
14. When the p-wave is about $\frac{1}{4}$ the size of the QRS, the PICC tip is in the lower SVC.
15. When the p-wave is the same amplitude as the QRS, it is at the caval atrial junction.
16. When a small positive wave spike is seen in the p-wave,

Figure 1: P-Wave Simulated Interpretation (used with permission PICC Excellence, Inc.)



the tip is in the right atrium.

17. When the p-wave becomes biphasic (expands beyond the baseline), the PICC tip is in the low right atrium/high right ventricle. This is known as an atrial spike.
18. If no QRS pattern is seen during insertion procedure, the PICC has malpositioned in the internal jugular or is contralateral in the opposite subclavian vein. Attempts to reposition can be made until the QRS is seen on the monitor.
19. Print final strip with P-wave at peak amplitude as QRS to confirm location of the tip. Include this EKG strip as part of the patient's record.

(Note: You may see some respiratory variation in the wave form)

Results

A total of 417 PICCs were placed from October 2008 through December 2009 in this 100 bed facility. EKG tip location was used in 250 (60%) of PICC placements. Of those correlated with CXR results by the interventional cardiologist, 240 agreed and 8 disagreed (3%) with optimal position in the SVC. Valved catheters composed the largest PICC group with 399 (96%).

Left-sided placements were in only 76 of the 417 placements (18%) and basilic vein was used in 346 (83%) placements. Position verified as distal/lower SVC or caval/atrial junction with 367 placements (88%). Other placement locations in 50 (12%) placements included SVC 2 (.4%), mid-SVC 18 (4%), axial 4 (.9%) and other 26 (6%).

The most common reasons for the inability to use EKG were:

- a) The presence of atrial fibrillation
- b) Rhythm that prevented or impaired p-wave interpretation
- c) Patient dependence on a pacemaker.

The study confirmed when using the EKG method to place PICCs the terminal tip location could be predicted based on the size of the p-wave, relative to the peak level and QRS complex. These findings were confirmed through correlation with chest x-rays after placement with EKG.

A learning curve was present in gaining proficiency in interpretation and with application of all advantages of EKG PICC tip guidance. Specific details for the learning period in this study were the following:

- Four catheters required repositioning in December 2008. Three PICCs were located in the right atrium, and one looped in the innominate vein extending contralateral. All four locations required retraction or repositioning of the catheter.

- Two catheter placements failed to visualize QRS complex or p-wave changes with one curled in the basilic vein and the other repositioned from azygos vein twice prior to correct positioning with EKG. Both placements were then confirmed using chest x-ray.
- One of the eight PICCs listed as uncorrelated from EKG to CXR had a position in the distal SVC; retraction of 5cm was originally advised by radiologist.

Discussion

Throughout the 15 month period of this study, EKG guidance was used in positioning and confirming placement for PICCs. In the most difficult placements, EKG reduced the number of chest x-rays needed and provided immediate feedback to the clinician to speed placement. Analysis of p-wave amplitude to note peak configuration and biphasic activity during advancement through the SVC and RA junction requires training and experience to reach 100% accuracy in interpretation.

Respiratory variations, ventilator vibration and action, muscle twitching or excessive patient movement caused signal interruptions or inability to interpret tracing of EKG and p-wave. Closed ended catheters require a continuous infusion of saline or flushing of saline to keep the valve open and the signal somewhat consistent. Even with a steady infusion, breaks may occur with valved catheters where signal is lost but should return with continued flow of saline to reopen valve. Application of new leads to each patient resulted in improved signal.

Variables to this study included:

1. Poor initial understanding of biphasic spike and presentation of p-wave in right atrium at the beginning of the study period.
2. Adding 4 new clinicians during the course of the 2008/2009 study may have caused variation and reduction of accuracy in data interpretations.
3. Multiple physicians interpreting PICC tip chest x-rays in different acceptable locations.
4. Use of the data category "other" with failure to specify in 4% of final tip location results. Data collection categories overlapped. (distal SVC, Caval atrial junction, mid SVC, lower SVC, SVC, axial, other) and greater clarity was needed in the study for correct final placement.

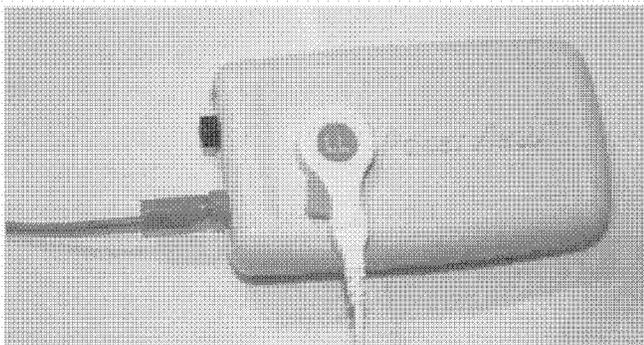


Photo 4. Pacerview device. Note EKG lead LL attached to Pacerview unit. G Dennis

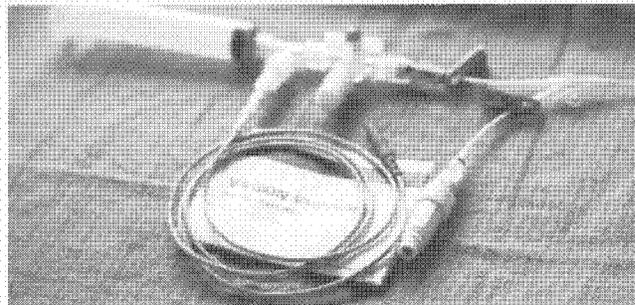


Photo 5. Vygon/Advanced Medical Vyocard and cable connection for catheter and EKG monitor. PICC Excellence, Inc

Table 1

EKG Device Company	Name of Device	FDA Indication/European CE
Arrow International www.arrowintl-europe.com	Adapter: Arrow-Johans™ JAdapter for Right Atrial Electrocardiography	FDA Clearance: pending CE Mark: Yes
B. Braun www.cvc-partner.com	Certodyn, Alphacard	FDA Clearance: unknown CE Mark: Yes
Pacerview www.pacerview.com	Pacerview device and Grabber	FDA Clearance: Yes No longer available for purchase
Romedex International SRL www.romedex.com	Sapien Tip Location System TLS	FDA Clearance: pending CE Mark: Yes
Vasonova www.vasonova.com also has doppler	Vasonova Visual Positioning System (VPS)	FDA Clearance: Yes CE Mark: unknown
Vygon/Advanced Medical www.vygonusa.com	Vyocard and cable	FDA Clearance: pending CE Mark: Yes



Photo 6. B Braun Alphacard. PICC Excellence, Inc.

The current standard of radiographic interpretation of CVC/PICC tip location by chest x-ray is often imprecise and subject

to observer variability. In this study, variation was noted in the tip determinations by different radiologists and in their definition of optimal placement location. Differing anatomic landmarks (carina, right superior heart border) are used to identify optimal location in the SVC with interpretation changing from person to person, some desiring SVC/RA junction and others opting for mid-SVC rather than deeper placement (Vesely, 2003). When viewing a chest x-ray flat film or even a digital film, the exact desired location is difficult to pin-point; typically there is a range of acceptable options and even those can be debated. Manufacturer recommendations for central line placement specify placement in the SVC and not the right atrium. FDA central venous catheter working group identified distal SVC as optimal location for non-dialysis catheters (Scott, 1995). EKG guidance provides a precise SVC position in more than 95% of placements (Francis, et al., 1992; D. McGee & Gould, 2003; W. T. McGee, et al., 1993; Schummer, et al., 2004) also reducing the need to reposition catheters (Gebhard, et al., 2007). In this study accuracy of correlated EKG/CXR position reached 97%. Validation of EKG positioning correlates with the gold standard for positioning when using the transesophageal imaging (Chu, et al, 2004). While it is

prudent to recheck tip position with a chest x-ray when abnormal symptoms arise following CVC or PICC placement, consensus is that EKG virtually eliminates the need to confirm tip position by chest x-ray (Madias, 2003). CXR may be necessary for CVCs other than PICCs and certainly for those patients in which the p-wave is not discernable. EKG guidance has demonstrated superior performance in guiding a catheter to the right location and confirming safe position.

Recommendations

During the process of this study, certain pinpointed actions saved time and improved accuracy of the process. Key points included:

1. Always use new leads that you apply to the patient even if this means you add a second set. It is better not to use leads of a monitored patient since connection to your monitor may cause the telemetry staff to lose their signal.
2. Connect to the same monitor for all patients. Use of a single monitor reduces variation and inaccuracies in interpretation.
3. Do not hold cables or EKG connectors; attach them and move on to other things. If the signal continues to be noisy and difficult to interpret, move the contact point of the alligator connector by sliding it down on the wire or needle confirming firm connection.
4. Understand that the presence of biphasic activity of the p-wave at the opposite side under baseline denotes entry into the right atrium. A negative or biphasic spike with elongation indicates advancement through the right atrium into the ventricular region. Identification and evaluation of biphasic activity is crucial to accurate position of the catheter tip.
5. If no Normal Sinus Rhythm is present, the catheter is not in the area of the SVC or if no p-wave variation occurs, the patient is on a dependent pacer.

EKG guidance provided other time saving benefits. On the average, time to release of the PICC resulted in time reduction of 30 minutes when EKG confirmation was used rather than waiting for chest x-ray confirmation. With an average of 10% repositioned for PICCs in prior months, use of EKG reduced repositioning after placement for time savings of 21 hours (417 x 10% reposition rate x 30 minutes/reposition). Time savings would likely be more significant for larger non-radiology PICC based facilities.

EKG adapter unit and cable used for positioning are available through multiple companies (see Table 1). The device used for this study (Pacerview) is no longer commercially available. Other companies carry CE mark for European usage (similar to FDA clearance) and are pending with the United States with Food and Drug Administration (FDA) submission.

Conclusion

EKG guided PICC placement proved accurate in consistently guiding the terminal tip to the superior vena cava (SVC). The procedure was easily taught and duplicated by members of the PICC team. The study demonstrated a definite correlation between the peak height (size) of the p-wave and the location of the terminal tip within the distal SVC. With knowledge of this correlation, transition from placing PICCs using EKG guidance

with chest x-ray confirmation to confirmation of tip placement using just EKG guidance without chest x-ray confirmation was easily attained. The incorporation of EKG guidance to current PICC and CVC insertions provides improvements in flow process by reducing delays. Application of EKG placement/confirmation performed during insertion saves time previously spent waiting for x-ray confirmation readings and saves time required for tip repositioning of malpositioned tips found after the end of the procedure by allowing the inserter to guide the terminal tip to the desired location by watching the p-wave activity. Additionally, EKG placement saves the cost of a chest x-ray and saves the patient exposure to radiation by eliminating the need for x-ray confirmation of tip position. The EKG guided PICC placement confirmation used in this study provided precise positioning demonstrating that previous studies are clearly reproducible.

Acknowledgement: The authors would like to acknowledge Dr. Peter Rothenberg, President of Pacerview Inc. for his assistance and encouragement in developing skills and perfecting technique for using EKG guided PICC placement, and to Dr. Mauro Pittiruti and the team of GAVeCeLT for their contributions to advancing EKG guidance with PICCs.

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ATTACHMENT 16

THE ECG METHOD FOR POSITIONING THE TIP OF PICCs: RESULTS FROM
TWO PRELIMINARY STUDIES

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The EKG method for positioning the tip of PICCs: results from two preliminary studies

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Abstract

Two preliminary studies were conducted to determine feasibility of using the electrocardiography (EKG) method to determine terminal tip location when inserting a peripherally inserted central catheter (PICC). This method uses the guide-wire inside the catheter (or a column of saline contained in the catheter) as an intracavitary electrode. The EKG monitor is then connected to the intracavitary electrode. The reading on the EKG monitor reflects the closeness of the intracavitary electrode (the catheter tip) to the superior vena cava (SVC). The studies revealed that the EKG method was extremely precise; all tips placed using the EKG method and confirmed using x-ray were located in the superior vena cava. In conclusion, the EKG method has clear advantages in terms of accuracy, cost-effectiveness, and feasibility in conditions where x-ray control may be difficult or expensive to obtain. The method is quite simple, easy to learn and to teach, non-invasive, easy to reproduce, safe, and apt to minimize malpositions due to failure of entering the SVC.

Background

The importance of the position of the tip of any central venous access device (VAD) was stressed in 1998 by the Position Statement of the National Association of Vascular Access Network (NAVAN, now AVA). This position states the optimal position of the tip of a central VAD (excluding the VADs designed for hemodialysis) is the lower third of the superior vena cava (NAVAN, 1998; Scott, 1988; Scott, 1995). Though guidelines from other USA and European associations (Royal College of Nurses, Infusion Nursing Society, Society of Interventional Radiology, American Society of Parenteral and Enteral Nutrition, European Society of Parenteral and Enteral Nutrition, etc.) have offered different definitions of the optimal tip position, there is wide agreement that no central VAD should have its tip above the middle third of the superior vena cava or below the mid-portion of the right atrium (McGee and Gould, 2003; Taylor and Palagiri, 2007). In fact, positioning of the tip of a central line in an inappropriate site of the venous system is associated with a significant increase in the risk of malfunction, fibrin sleeve formation and venous thrombosis.

A 'short' catheter - i.e. a catheter whose tip is located in the upper or middle third of the superior vena cava (SVC) or in the innominate veins - has a 10 to 50 percent increased risk of central venous thrombosis (Caers et al., 2005) (Table I). Also, a high position of the tip of the VAD is associated with intimal damage due to mechanic irritation of the endothelium, with erosion and even perforation to the walls of the vein. Formation of a fibrin sleeve around the catheter occurs more frequently with a short catheter; this is typically associated with VAD malfunction (persistent withdrawal occlusion, or ball valve obstruction). In addition to these complications, the presence of a sudden or sustained increase of central venous pressure such as coughing, vomiting, etc, has been known to cause the 'short' catheter to dislocate, also known as 'tip migration' (Puel et al., 1993).

Conversely, a 'long' catheter, a catheter whose tip is in the lower portion of the right atrium or in the right ventricle or beyond, may carry the risk of arrhythmias, tricuspid valve dysfunction, erosion, or atrial thrombosis (Korones et al., 1996).

Finally, the tip of the catheter may be inadvertently positioned in the subclavian vein, in the internal jugular vein, or in other thoracic veins (internal mammary vein, azygos, etc.). This type of malposition is almost constantly associated with pain on infusion, early VAD malfunction and subsequent venous thrombosis.

While correct positioning of the tip of the catheter is of great importance during any central venous cannulation, it plays a crucial role in mid-term and long term VADs such as peripher-

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ally inserted central catheters (PICC), tunneled catheters and ports, which are frequently inserted in patients requiring chemotherapy with vesicant drugs or hyper-osmolar nutritional solutions. Standard of Care for central venous catheters (CVC) dictates in the United States that the position of the tip must be confirmed by x-ray prior to use (INS 2006; NAVAN 1998). When the tip location cannot be confirmed in the superior vena cava, the catheter must be repositioned. Tip verification techniques have focused primarily on the x-ray. Other forms of tip verification have been used throughout Europe, with or without x-ray, incorporating electrocardiogram interpretation.

Methods for Preventing Malpositions

At present, the 'gold standard' for preventing malpositions and verifying the tip of the catheter is through radiology, either as intra-procedural fluoroscopy or as a post-procedural chest x-ray. On the fluoroscopic monitor or on the radiological film, the tip must be seen in the area correspondent to the lower third of the superior vena cava, i.e. no more than 2 cm below the image of the main right bronchus.

While confirmation of tip placement in the superior vena cava is mandatory, the radiological assessment of the tip position does have a few limitations and disadvantages:

- any type of radiological assessment is associated with x-ray exposure for the patient and/or for the health operator; such exposure can be relevant for intra-operative fluoroscopy or with repeated chest x-rays;
- the radiological landmarks used to determine catheter tip location may be unclear or significantly affected by physiological or pathological anatomic variations, false perspectives, or errors of interpretation (this is particularly true for intra-procedural fluoroscopy). In the case of post-procedural control, greater accuracy can be achieved by studying the chest in both the anterior-posterior view and in the lateral view. The use of dual views, while it increases accuracy, requires longer x-ray exposure and higher costs.
- In most cases, the radiological assessment requires the availability of an expensive and logistically cumbersome machine plus a radiology technician and/or a radiologist all adding to the procedural cost. This gives us an inappropriate cost-effectiveness ratio. Radiological assessment a problem with a PICC insertion which, in the United States, is most frequently performed by nurses at bedside. In this situation, the intra-procedural fluoroscopy may be difficult or impossible to adopt while the post-procedural chest x-ray carries a significant burden in terms of costs, organization and time delay. Also, in most cases the nurse who has inserted the PICC must rely on the intervention of the radiologist to interpret tip location.*

**This aspect might be overcome in some countries such as UK or USA, where there is a growing tendency to authorize nurses, if specifically trained, to interpret the x-ray. In April 2008, the Association for Vascular Access (AVA) published a Position statement on this subject. (AVA, 2008).*

Tip confirmation by chest x-ray is less expensive, safer and more commonly used than fluoroscopy, though, in some cases the catheter has to be repositioned. Catheter tip repositioning

Table 1: Incidence of catheter-related thrombosis and catheter dysfunction, depending on tip position (modified from Caers et al., 2005)

Tip position	# cases	Thrombosis	Dysfunction
Brachiocephalic vein	31	45.2%	6.5%
Cranial 1/3 SVC	42	19%	16.7%
Middle 1/3 SVC	142	4.2%	1.4%
Caudal 1/3 SVC	66	1.5%	0%
RA or IVC	18	5.6%	5.6%

requires a new procedure, a second radiological assessment, major discomfort for the patient and for the nurse or physician who has implanted the device, a significant time delay, repeated x-ray exposure, and increased costs.

Some non-radiological methods which can be useful in reducing the risk of malposition of the tip of the catheter include establishing the proper choice for venous access, using ultrasound for guidance, establishing baseline anthropometric estimates from landmarks, and using electromagnetic tools to detect direction of insertion.

1) Proper choice of the venous approach

In centrally inserted VADs, the supraclavicular approach to the right internal jugular vein, to the right subclavian vein or to the right innominate vein (by ultrasound guidance) is characterized by a lower incidence of malposition since the catheter almost invariably enters the superior vena cava vein. Nonetheless, the risk of malpositioning with a 'short' or 'long' catheter still persists.

2) Ultrasound Guidance

The use of ultrasound for needle guidance with CVC placement is known to increase success and reduce complications. Soon after PICC insertion, while the stylet is still inside the PICC, ultrasound examination of the internal jugular veins is a simple and reliable method to rule out a gross malposition, though it cannot give information about the correct length of the catheter. Post-procedural ultrasound control of tip position can be done by surface or trans-esophageal echocardiography, but the cost is high and requires specially trained operators.

3) Anthropometric estimates and surface landmarks.

There are several landmark methods for estimating the desired length of a central venous catheter or a PICC; usually, they are based on the assumption that the atrio-caval junction is located at the level of the third intercostal space, on the right parasternal border. The anthropometric methods utilized for central venous catheters apply formulas which are derived from large population studies. These measurements estimate the desired length of the catheter knowing the site of venipuncture and the height of the patient (Peres, 1990). Both anthropometry and surface landmark methods are quite precise in estimat-

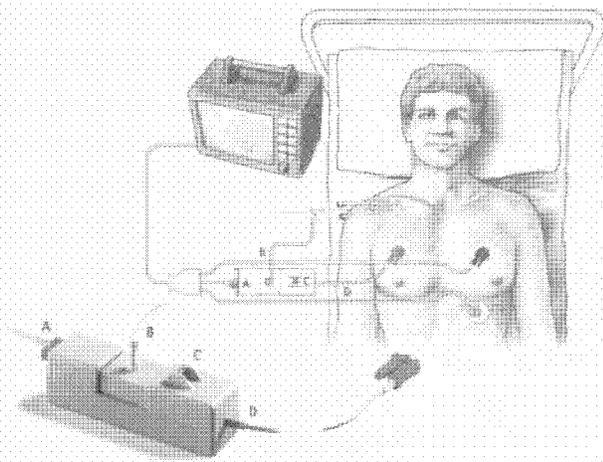


Fig. 1 – Diagram showing how the intracavitary electrode replaces the 'red' or 'right shoulder' electrode of the standard surface EKG (Figure reproduced by courtesy of BBraun. A = electrode connected with EKG monitor; B = cable connecting to intracavitary electrode; C = switch to shift from surface electrode to intracavitary electrode; D = surface electrode to the right shoulder of the patient)

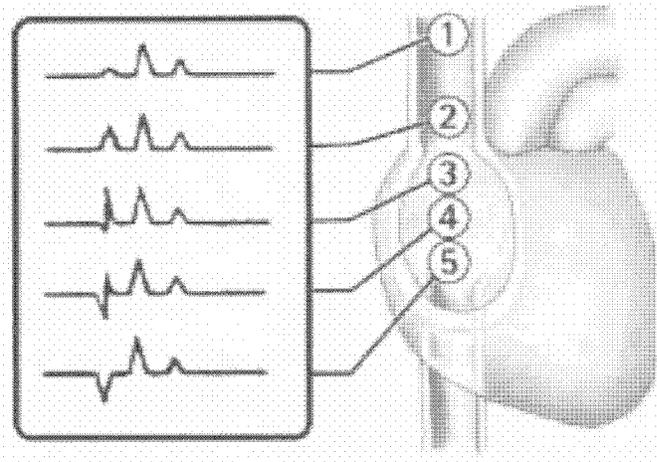


Fig. 2 – Changes of the P wave as a function of the tip of the intracavitary electrode (Figure reproduced by courtesy of BBraun)

ing the length of the catheter in the adult patients, but not in children. Measurements provide a possible length for catheter placement in the SVC without adjustment for anatomical variations, directional or functional malpositioning.

4) Electromagnetic tracking methods.

These usually consist of an electromagnetic signal from a wire installed in the catheter by means of a surface apparatus connected to a monitor (Navigator, manufactured by Viasys; Sherlock, manufactured by Bard; Cath-Finder, manufactured by Pharmacia Deltec). They are primarily used with PICCs and need a specific technological design of the catheter and/or of its stylet. Some authors have demonstrated a significant reduction in the incidence of malposition, from 13.4% down to 2.5%, using such devices (Naylor, 2007). Their main limitation is that, while they do ascertain that the PICC is in the right direction, they do not give information about the correct location of the catheter (Royer and Earhart, 2007).

The Electro-cardiographic Method for Positioning the tip of Central Lines

The "ideal" method for checking the position of the tip should have the following features:

1. It should provide a way to check the position of the tip both during the procedure (to avoid repositioning manoeuvres) as well as after the procedure (to confirm tip position of the VAD);
2. The method should be easily and autonomously performed by the inserter of the VAD, either a nurse or a physician;
3. The method should be accurate enough to ascertain that the catheter has gone in the *right direction* (straight along the axis internal jugular vein – innominate vein – SVC) and to

the *right depth* (not too long, not too short, but exactly at the atrio-caval junction);

4. It should be inexpensive, non-invasive, and easy to repeat with reproducible results;
5. It should be easy to learn and easy to teach;
6. It should provide a way to print and record the results to allow for documentation in the patient's records.

Correct determination of catheter terminal location, in addition to identification and correction of malpositioning are all necessary components of PICC or CVC placement. Finding a method to perform these processes with ease during the insertion procedure will reduce time, speed usage, and save the patient from additional exposure and cost. We suggest the method that most closely meets all of these requirements is the location of terminal tip by use of the electrocardiographic (EKG) method. This method interprets the location of the catheter tip by using EKG with an intracavitary electrode (Corsten et al., 1994; Francis et al., 1992; Cavatorta et al., 1999; Gebhard et al., 2007; Antonaglia et al., 2008; David et al., 2005; Schummer et al. 2005; Cavatorta et al., 2001; Dionisio et al., 2001).

The basic principle of the EKG method is that the position of the tip inside the venous system can be detected by regarding the catheter itself (or a guidewire inside the catheter) as an intracavitary electrode which replaces the 'red' or 'right shoulder' electrode of the standard surface EKG (Figure 1). When the EKG monitor is connected to the intracavitary electrode, the reading of lead II will show a P wave whose shape and height will be a reflection of the closeness of the intracavitary electrode (i.e. the tip) to the seno-atrial nodus. A 'giant' P wave – as high as the QRS – indicates that the tip is inside the right atrium; when the P wave is as small as in the surface EKG, the

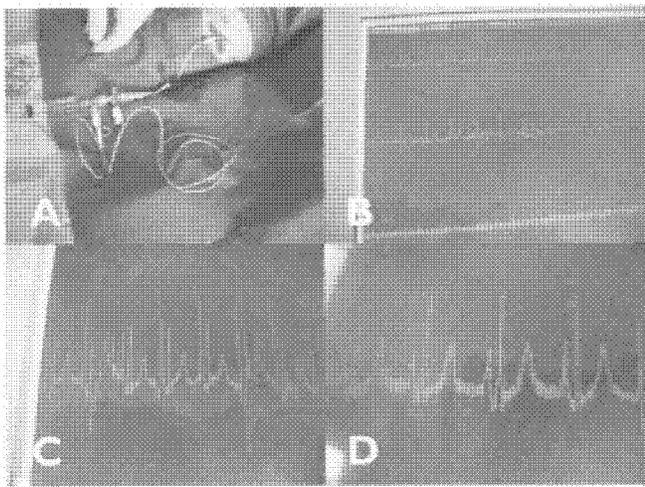


Fig. 3 – EKG method for positioning the tip of an open-ended PICC:
 a – the PICC is inserted for the estimated length (previous anthropometric measurement), filled with normal saline and connected to the EKG monitor through the VygoCard, so to work as intracavitary electrode

- b – standard EKG reading
- c – tip in right atrium (giant P wave)
- d – tip at atrio-caval junction (P wave half of QRS)

tip of the electrode is in the superior vena vein or above; a P wave whose height is half of the QRS is considered indicative of the atrio-caval junction. When the tip is in the lower part of the right atrium, the P wave may appear as bi-phasic or even negative (if close to the inferior vena cava) (Figure 2). Thus, simply by monitoring the height of the P wave, one can determine the location of the tip of the catheter as it travels through the superior vena cava, right atrial junction, and right atrium.

Limiting factors for this technique are in patients where alterations of cardiac rhythm change the presentation of the P wave as in atrial fibrillation, atrial flutter, severe tachycardia, and a pacemaker driven rhythm. The EKG method was first introduced in 1949 (Von Hellerstein et al., 1949) and has been successfully used for central venous catheter placement in Europe (especially Germany) since the '90s (Schummer et al., 2004).

During the last two decades, many clinical papers have demonstrated – with a few exceptions (Schummer et al., 2003; Schummer et al., 2004) – the accuracy of the EKG method, compared to the standard radiological assessment. Quite recently, other Authors (Gebhard et al., 2007) provided substantial research that has proven the EKG method is more specific and more precise when compared to conventional methods (i.e.: methods based on anthropometric measurements or standard formulas for estimating depth of catheter insertion, as available in the literature). In this clinical randomized study, all tips checked with the EKG method were in the superior vena cava or above, in contrast with other methods which showed 16% of those tips in the right atrium or in the right ventricle; also, only 3% of the tips checked by the EKG method were located above the superior vena cava (axillary, subclavian, internal jugular vein, innominate vein) versus

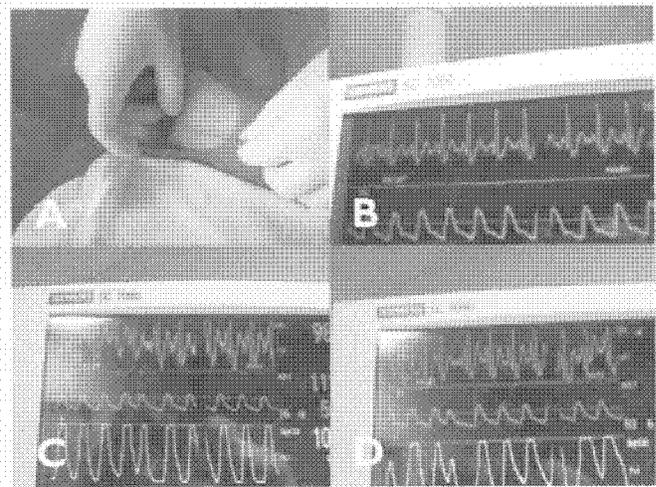


Fig. 4 – EKG method for positioning the tip of a closed-ended PICC:
 a – the PICC is inserted for the estimated length, filled with normal saline and connected to the EKG monitor through the VygoCard; to make the catheter work as intracavitary electrode, it must be flushed continuously with saline so keep the valve open

- b – standard EKG reading
- c – tip in right atrium (giant P wave)
- d – tip at atrio-caval junction (P wave half of QRS)

15% of the tips positioned with other methods.

This same clinical trial has shown that the EKG method did not significantly increase the length of time required to perform the procedure, and actually saved time by avoiding the need to reposition the catheter and get a second chest x-ray.

Many clinical trials have shown that the EKG method has clear advantages in terms of accuracy, cost-effectiveness and feasibility in conditions where X-ray control can be difficult or expensive to obtain (Corsten et al., 1994; Francis et al., 1992; Gebhard et al., 2007; Antonaglia et al., 2008; David et al., 2005). The method is quite simple, easy to learn and to teach, non-invasive, easy to reproduce, safe, and apt to minimize both malpositions due to failure of entering the superior vena cava (tip in internal jugular or subclavian or innominate vein) as well as malpositions due to error in the length of the catheter (catheter too short or too long). Though a thorough computation of the actual costs may differ, depending on the choice of technique and clinical setting, overall costs of the EKG method are consistently lower if compared to the standard check of the tip position by post-procedural X-ray. In fact, (a) the technique is inexpensive (the additional materials needed for the manoeuvre cost less than twenty dollars), (b) it can be performed at bedside, (c) the costs related to performing and interpreting chest X-ray are avoided, and (d) intra-procedural check of the tip position protects from expensive and timely repositioning manoeuvres sometimes needed after chest x-ray.

The trials concerning testing EKG have taken into consideration short term and long term central venous access devices inserted by puncture of the subclavian or the internal jugular vein (Chu et al., 2004; Cheng et al., 2002); in a few cases, the method

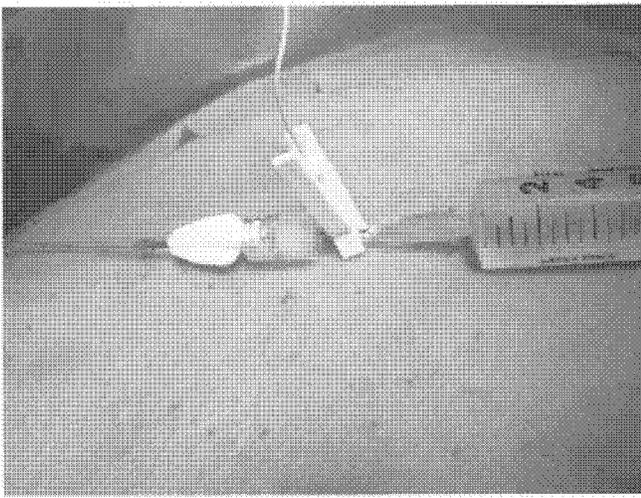


Fig. 5 – Alternative method for using the PICC as intracavitary electrode: electrode with alligator clip attached to a needle inserted in an injectable cap

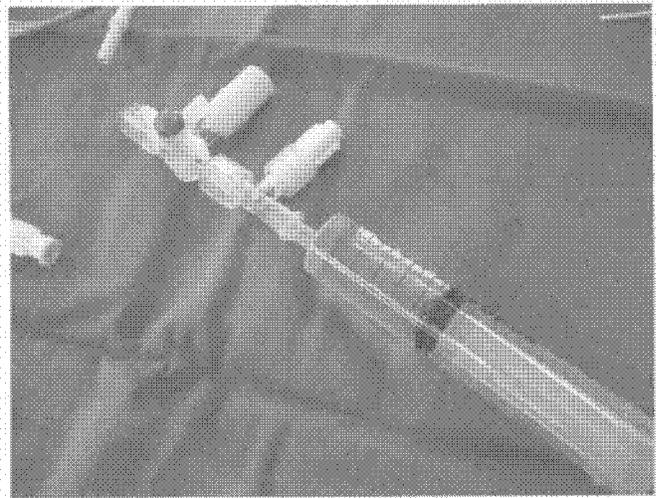


Fig. 6 – VygoCard (manufactured by Vygon)

has also been tested in neonates (Biban et al., 2000; Tierney et al., 2000), with umbilical catheters and epicutaneo-caval catheters.

Considering demonstration of safety and cost-effectiveness of the EKG trial results carried out with central venous catheters within the past few years, we decided to apply this method, which appears so safe and cost-effective, to PICC placement.

The EKG Method for Positioning PICCs

In our 1200 bed University Hospital, PICCs are inserted by members of a dedicated team. The team consists of four physicians (two surgeons, two infectious disease practitioners) and ten nurses. Our team inserts approximately 1000 PICCs and 700 long term central venous access devices per year, and is committed to several clinical tasks, including monitoring VAD related complications, counselling in VAD indications and maintenance, education and training of nurses in our institution, and, most importantly, teaching on a national level. We provided more than 40 courses in 19 different Italian hospitals training clinicians to use ultrasound guided placement of PICCs.

Our experience with the EKG method for standard short term and long term central venous access devices began many years ago. In our hands, the method has proven to be safe and cost-effective, and it has dramatically reduced the number of chest x-rays necessary to check the position of the tip.

Recently, we began a project for verifying the feasibility of applying this method to PICC. Until 2006, our standard protocol for PICC positioning consisted (Pittiruti et al., 2005) of (a) anthropometric estimate of the desired length of the PICC by anatomical landmarks (from the site of puncture to the third intercostal space on the right sternal border); (b) ruling out the presence of the catheter in the internal jugular vein by direct ultrasound examination during the procedure; and (c) postoperative, chest x-ray.

After a few preliminary clinical experiments carried out in 2007, whose goal was to define the technical aspects of the meth-

od, in the first months of 2008 we performed two pilot studies, one on open ended PICCs and one on closed ended (Groshong) PICCs. The details of these studies are listed below.

First study: Open Ended PICCs*

The aim of the first study was to verify the feasibility of the EKG method to open-ended PICCs. After approval of the Ethical Committee of our University, twelve consecutive patients requiring PICC lines were enrolled in this study. Exclusion criteria were: atrial fibrillation or other supra-ventricular arrhythmias; presence of a pace-maker. Desired catheter length was pre-operatively estimated by means of anthropometric parameters. We used the VygoCard device (Vygon) as the electrical transducer between the catheter (filled with standard 0.9% saline solution) and the EKG cable. The VygoCard transducer is part of a 3-way stopcock connected with the catheter and with a cable going to lead III of a standard EKG monitor. The catheter acts as an intracavitary electrode which replaces the traditional 'red' electrode on the right shoulder. The PICCs were inserted in the basilic (first choice) or brachial (second choice) vein at mid-arm under direct ultrasound guidance. Then, the catheter was slowly advanced in the venous system while observing the morphological intracavitary EKG changes until the P wave reached the desired shape and amplitude (one-half of the QRS complex), corresponding to the atrio-caval junction (Fig. 3). The catheter was then secured to the skin by means of a sutureless device. All patients underwent a post-operative chest x-ray (postero-anterior and lateral views). X-ray films were evaluated by an independent radiologist not involved in the insertion procedure; the atrio-caval junction was radiologically identified as 2 cm below the carina.

In this study, all twelve PICCs were successfully inserted. The "atrio-caval junction p-wave" was observed in all cases, in one patient after withdrawing and re-introducing the catheter. Final position at the atrio-caval junction was confirmed by postoperative intracavitary EKG control and chest x-ray in all

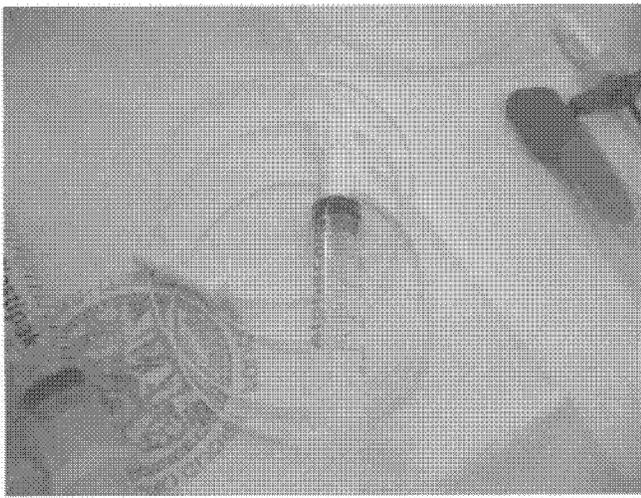


Fig. 7 – AlphaCard (manufactured by BBraun)

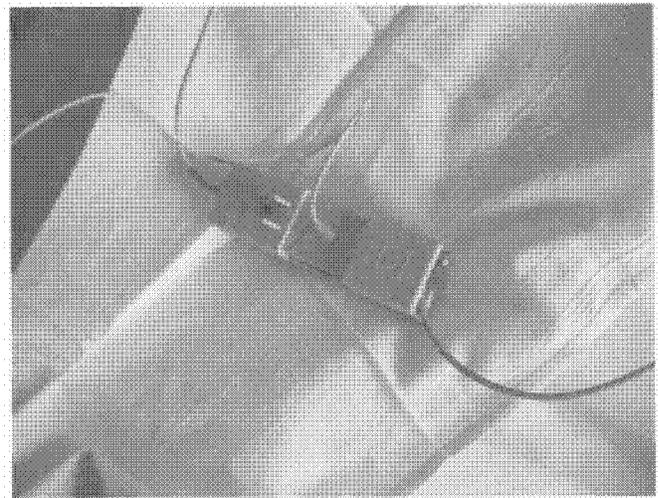


Fig. 8 – Certodyn (manufactured by BBraun)

patients. Consistently, no primary malpositions were observed on chest X-ray and all catheter tips appeared to be at the atrio-caval junction on X-ray films. In 3 cases the catheter length, as preoperatively estimated by anthropometric measurement, was significantly different (> 2 cm) from the length measured by the atrio-caval junction P wave; though, the final tip position was chosen according to the EKG measurement, and chest X-ray films were consistent with the EKG data.

***This study has been presented at the 2008 Meeting of the Infusion Nursing Society (Pittiruti, LaGreca, Scoppettuolo et al., 2008).*

Second study: Groshong PICCs**

In the second pilot study, six consecutive ICU patients requiring PICC lines were studied. The aim of this study was to verify the feasibility of the EKG method during the insertion of closed ended PICCs. Exclusion criteria were atrial fibrillation or other supra-ventricular arrhythmias, and/or the presence of a pace-maker. We used the Vygonard device (Vygon) as the electrical transducer between the catheter (filled with standard 0.9% saline solution) and the EKG cable. After ultrasound guided insertion in the basilic (first choice) or brachial (second choice) vein at mid-arm, each catheter was connected to an infusion line and a continuous saline infusion was started to keep the distal valve open. Baseline EKG rhythm was visualized. Then the catheter was slowly advanced in the venous system while observing the morphological changes of the P wave until the P wave reached the desired amplitude (one-half of the QRS complex), corresponding to the atrio-caval junction (Fig. 4). All patients underwent a post-operative chest x-ray (posterior-anterior and lateral views): the atrio-caval junction was radiologically identified as 2 cm below the carina. All x-rays confirmed EKG results of atrio-caval placement.

In this study, all six Groshong PICCs were successfully inserted. The "atrio-caval junction P wave" was observed in 5 patients.

In one case, the baseline cardiac signal was disturbed by electrical artefacts and the patient was excluded from the protocol. No primary malpositions were observed on chest x-ray and all catheter tips appeared to be at the atrio-caval junction on x-ray films.

**This study has been presented at the 2008 Meeting of the European Society of Intensive Care Medicine (Pittiruti, LaGreca, Brutti et al., 2008)*

Discussion

At present, the most common technique utilized for checking the position of the tip of CVCs by the EKG method employs the use of a guidewire inserted in the catheter as an intracavitary electrode, with the tip of the guidewire free in the bloodstream.

To adapt the EKG method to PICC insertion, we chose the alternative technique (already described for dialysis catheters and umbilical catheters), where the intracavitary electrode is the column of saline contained in the catheter itself (Pawlik et al., 2004; Madias, 2003; Madias, 2004). This is made possible by two different options: (a) With the first option, the PICC is closed proximally with a needle-injectable cap; a blunt needle or blunt ended connector is partially inserted in the cap, and an extension cable is connected to the access (Fig. 5); (b) The second option is more simply done with the proximal end of the PICC connected to a special device consisting of a 3-way stopcock with a transducer (VygoCard, Vygon, Fig. 6) or in a transducer directly attached to a syringe (AlphaCard, BBraun, Fig. 7); the transducer has an extension cable which connects to the EKG monitor.

The manoeuvre is further simplified by utilizing a specific commutator (Certodyn, BBraun, Fig. 8) connected to both the standard 'red' surface electrode on the right shoulder of the patient and to the intracavitary electrode. Changing the position of the switch, it is possible to read the EKG either as standard surface EKG or as intracavitary EKG. The changing morphology of the P wave is best appreciated reading D II.

Before reading the P wave change but after removal of the internal stylet, the PICC is filled with normal saline. If the PICC has a closed end, in order to maintain a column of fluid which may act as continuous intracavitary electrode, it is necessary to have a continuous infusion of saline through the system. Open ended PICCs have not additional requirements other than connection and saline flushing.

The best way to precisely locate the atrio-caval junction is to advance the PICC inside the venous system downward to the superior vena cava and beyond, until the typical 'giant' P wave (as high as the QRS) appears. This full sized P wave indicates that the right atrium has been reached. Once the P wave reaches full height, the PICC is slowly drawn backward until the P wave progressively reduces its height to ½ of the QRS: this corresponds to the atrio-caval junction. The PICC can then be secured to the skin in this position with the knowledge that the terminal end is at the caval-atrial junction.

Disadvantages of this method for checking the position of the tip of PICCs are:

- The method assumes the presence of a P wave on the standard EKG; in situations where the P wave is not present or not readable (atrial fibrillation, atrial flutter, marked tachycardia, pacemaker-driven rhythm), the method cannot be used;
- In some cases of closed ended PICCs, the Groshong valve may not open easily or continuously; intermittent flow across the valve may be consistent with a good infusion, but it causes intermittent EKG reading because the column of saline is interrupted.

Advantages of the EKG method:

- The method is accurate, safe, simple, non-invasive, easy to perform, easy to learn and easy to teach;
- It is inexpensive since it only requires an EKG monitor and a disposable sterile transducer (either Vygoncard or Alphacard) with the extension cable;
- The manoeuvre can be performed at bedside, like most PICC insertions, and can easily be carried out by a nurse after minimal training;
- The method gives definitive information about the position of the tip directly during the procedure, thus saving time and resources;
- The costs as well the x-ray exposure associated with the radiological assessment are avoided in most cases;
- The correct position of the tip can be documented in the medical chart by appropriate printing of the EKG track.

Conclusion

The EKG method for determining caval-atrial junction terminal tip location is well documented in Europe and, through this study, has demonstrated accurate and safe use with PICCs. Though more studies are needed to standardize the procedure and to evaluate the accuracy of the method in different clinical situations and for different types of PICCs, we think these two pilot studies are very promising. This research suggests that the EKG method may strongly improve both the cost-effectiveness and the safety of the procedure for terminal tip interpretation on insertion and potentially, any time evaluation is desired.

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