



U.S. Department of Health & Human Services

Food and Drug Administration

SAVE REQUEST

USER: (cwf)
FOLDER: K955300 - 93 pages
COMPANY: DATA MEDICAL ASSOCIATES, INC. (DATAMEDI)
PRODUCT: DIAZO COLORIMETRY, BILIRUBIN (CIG)
SUMMARY: Product: TOTAL BILIRUBIN PROCEDURE

DATE REQUESTED: Aug 26, 2016

DATE PRINTED: Aug 26, 2016

Note: Printed





Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

10-20-10

510(k) Summary

This Summary of Safety and Effectiveness is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.82.

Submitter: Data Medical Associates, Incorporated (DMA)
Contact Person: C. H. Morris, Ph.D., Vice President, Scientific and Government Affairs

The assigned 510(k) number is : K-955302

Device: DMA Total Bilirubin Procedure
75CIG Bilirubin (total or direct), Test System

Class: II

Predicate Device: Total Bilirubin Plus Procedure, Data Medical Associates, Inc., Arlington, Texas.

Description and Intended Use: DMA's Total Bilirubin Procedure is intended for in-vitro diagnostic use for the quantitative determination of total bilirubin in human serum, and plasma.

Technological Characteristics: Both DMA procedures are based on the following principle; Total bilirubin, both conjugated and free, is measured using 3,5-dichlorophenyl diazonium tetrafluoroborate which reacts with bilirubin to form azobilirubin. The concentration of bilirubin is directly proportional to the absorbance of the azobilirubin measured spectrophotometrically at 540 nm.



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Comparison of Performance:

| | <u>DMA NEW</u> 0.1 to 20 mg/dL | <u>DMA Predicate</u> to 25 mg/dL |
|--|-----------------------------------|-------------------------------------|
| Linearity | | |
| Precision Within-Run | | |
| Within Normal Range %C.V. Hitachi 704 ^R | 0.0 | 5.5 |
| Above Normal Range %C.V. Hitachi 704 ^R | 0.85, 0.66 | 2.0, 2.3 |
| Within Normal Range Manual | 5.0 | --- |
| Above Normal Range Manual | 2.2, 1.56 | --- |
| Precision Run-to-Run | | |
| Within Normal Range %C.V. | 1.11 | 3.6 |
| Above Normal Range %C.V. | 1.2, 1.2 | 1.6, 2.2 |
| Within Normal Range Manual | 6.4 | --- |
| Above Normal Range Manual | 0.83, 2.1 | --- |
| Shelf-life at 2-8°C | 14 months | 12 months |
| Sensitivity (0.001A) | 0.07 mg/dL | 0.026 |
| Analytical | 0.1 mg/dL | NA |
| Interferences | | |
| Hemoglobin | Significant above 83 mg/dL | Gross hemolysis interferes |
| Lipemia | Not significant to 1335 mg/dL | Interferes |
| Expected Values | Hitachi 704 ^R 0.2-1.5 | 0.0-1.5 |
| | Manual 0.4-1.7 | |

Statement of Equivalency: Based on the comparison of the technological characteristics of DMA's device with the predicate device, and the performance characteristics, DMA proposes that the DMA device is substantially equivalent to the predicate device.


 C. H. Morris, Ph.D.
 December 7, 1995

IN TEXAS: 800/633-5338

OUTSIDE TEXAS: 800/433-7224

FAX: 817/649-2461



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

K955300/A1
Rec-2-22-96
K955302/51

Add to file

RECEIVED
12 DEC 95 11 20
FDA/CDRH/OCE/DWC

December 7, 1995

Ms. Carol Benson
Food and Drug Administration
Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
9200 Corporate Drive
Rockville, MD 20850

Dear Ms. Benson:

Responses to your request for additional information of 12/6/95 are as follows:

- | <u>Request</u> | <u>Response</u> |
|--|--|
| 1. On page 19, under the "Sample Storage" section, provide the temperature for the frozen serum. | Refer to attached revised page 19. |
| 2. On page 21, in the "Expected Values" section, add the word "serum" to define samples. | Refer to attached revised page 21. |
| 3. In the response, provide a reference for the use of plasma. | The use of plasma is referenced in "Clinical Chemistry, Theory, Analysis, and Correlation, 2nd. Ed., Kaplan, L.A., and Pesce, A.J., 1989, p. 1013, The C.V. Mosby Company. |
| 4. Evaluate Within-Run and Run-to-Run % CV on the low sample. Describe how many days the "Run-to-Run" precision study covered. | (b)(4) |
| 5. On page 19 under the "Materials Required But Not Provided" section, list controls. | Refer to attached revised page 19. |

Page 2 of 2
December 7, 1995

Request

Response

6. Provide revision date at end of labeling. Refer to attached revised page 23.

Thank you for your consideration of these responses to your inquiries. Please contact me if you have any questions.

Sincerely,



C. H. Morris, Ph.D.
Vice President, Scientific
and Government Affairs

encl

CHM:led



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

Comparison of Performance:

| | <u>DMA NEW</u> | <u>DMA Predicate</u> |
|--|----------------------------------|----------------------------|
| | 0.1 to 20 mg/dL | to 25 mg/dL |
| Linearity | | |
| Precision Within-Run | | |
| Within Normal Range %C.V. Hitachi 704 ^R | 0.0 | 5.5 |
| Above Normal Range %C.V. Hitachi 704 ^R | 0.85, 0.66 | 2.0, 2.3 |
| Within Normal Range Manual | 5.0 | --- |
| Above Normal Range Manual | 2.2, 1.56 | --- |
| Precision Run-to-Run | | |
| Within Normal Range %C.V. | 1.11 | 3.6 |
| Above Normal Range %C.V. | 1.2, 1.2 | 1.6, 2.2 |
| Within Normal Range Manual | 6.4 | --- |
| Above Normal Range Manual | 0.83, 2.1 | --- |
| Shelf-life at 2-8°C | 14 months | 12 months |
| Sensitivity (0.001A) | 0.07 mg/dL | 0.026 |
| Analytical | 0.1 mg/dL | NA |
| Interferences | | |
| Hemoglobin | Significant above 83 mg/dL | Gross hemolysis interferes |
| Lipemia | Not significant to 1335 mg/dL | Interferes |
| Expected Values | | |
| | Hitachi 704 ^R 0.2-1.5 | 0.0-1.5 |
| | Manual 0.4-1.7 | |

Statement of Equivalency: Based on the comparison of the technological characteristics of DMA's device with the predicate device, and the performance characteristics, DMA proposes that the DMA device is substantially equivalent to the predicate device.


 C. H. Morris, Ph.D.
 December 7, 1995

F. PRECISION (continued)

(b)(4)

Within-Run Manual

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

Run-to-Run with Hitachi 704^R

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

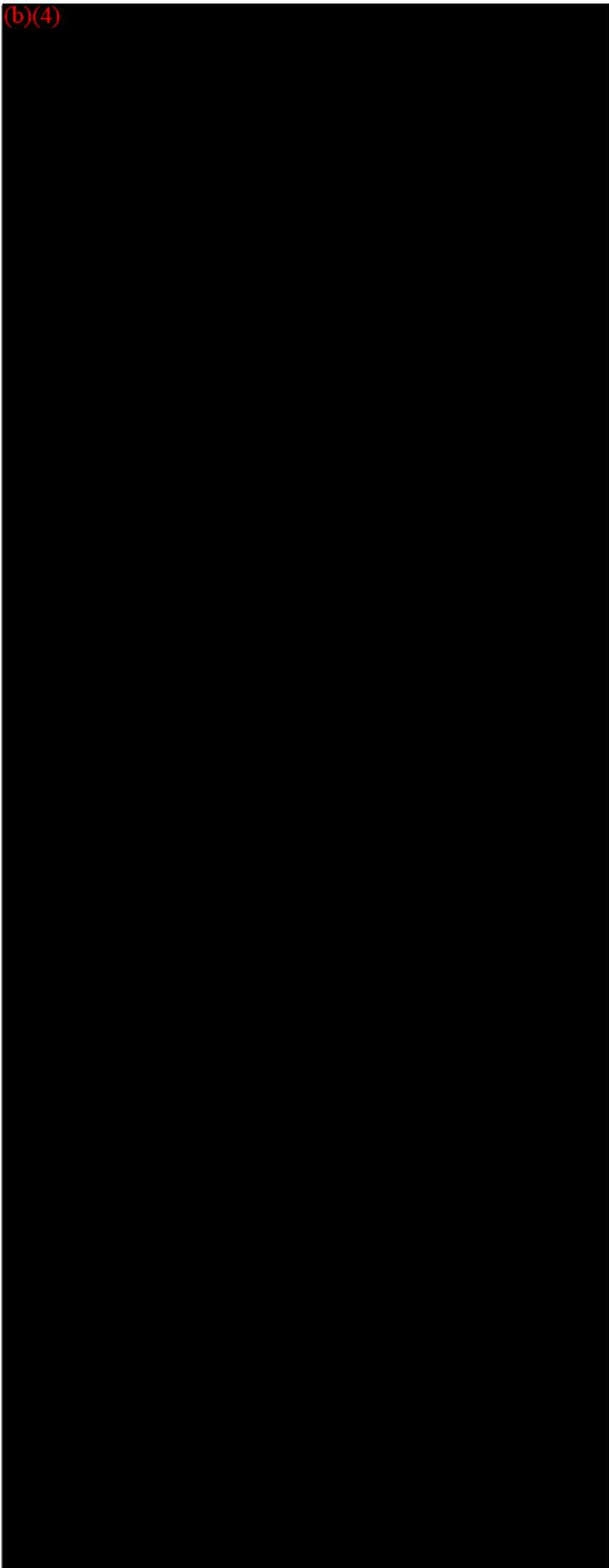
Level 3
mean
std. dev.
CV%

Run-to-Run Manual

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%



DMA Total Bilirubin Procedure

SAMPLE STORAGE

Serum bilirubin is stable up to one week if stored at 2-8°C and for approximately three months if stored frozen at -20°C and protected from light exposure.¹

HITACHI 704^R PROCEDURE

(b)(4)

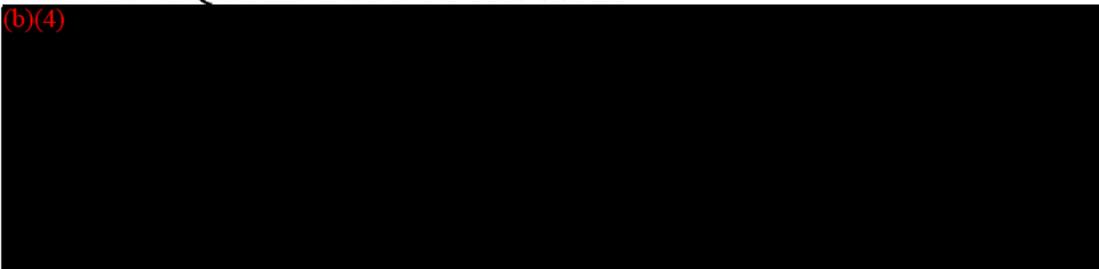


The above parameters should be used when programming the Hitachi 704^R. Consult your instrument manual for further instructions.

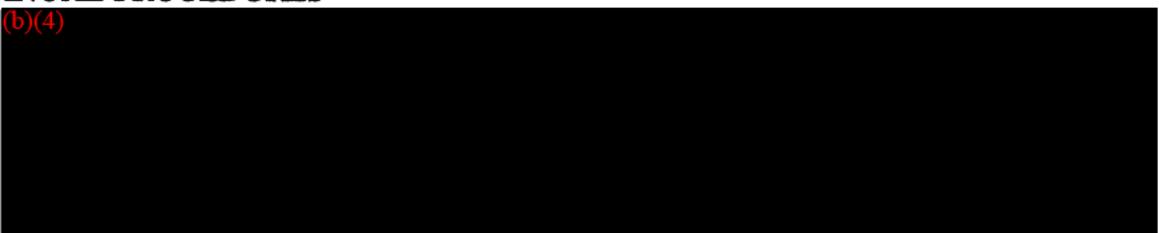
MATERIALS PROVIDED

Total Bilirubin Reagent

MATERIALS REQUIRED BUT NOT PROVIDED

1. (b)(4)
 - 2.
 - 3.
 - 4.
 - 5.
 - 6.
- 

MANUAL PROCEDURES

1. (b)(4)
 - 2.
 - 3.
 - 4.
 - 5.
- 

DMA Total Bilirubin Procedure

Example:



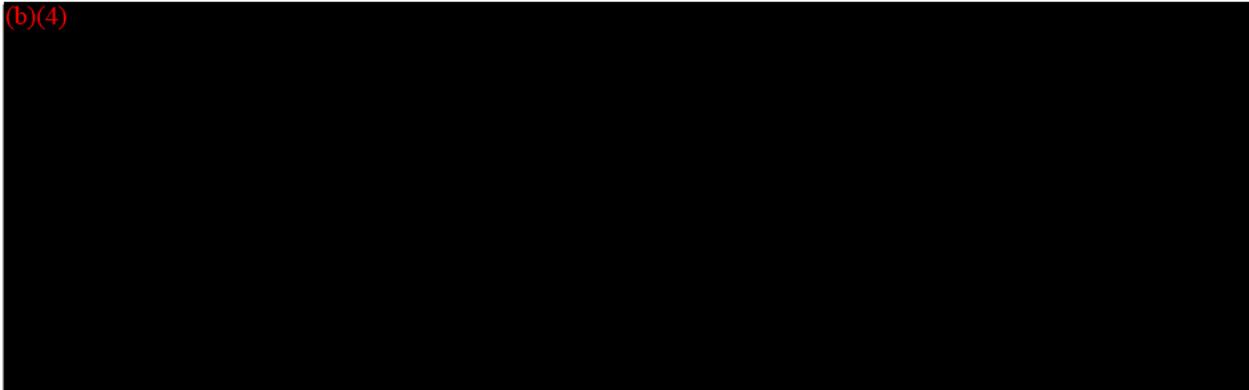
LIMITATIONS

See Storage and Stability, Deterioration, Specimen Collection, Interfering Substances, Sample Storage, Stability of Final Reaction Mixture, and Linearity sections for limitations to this procedure.

Bilirubin calibrators in chloroform may not be used in this procedure since chloroform miscible solvents are not employed.

Bilirubin is extremely light sensitive. Calibrator, control and unknown specimens must be stored protected from light sources for optimal stability.

EXPECTED VALUES⁷



PERFORMANCE CHARACTERISTICS⁷

The Performance Characteristics were established on a Hitachi 704^R analyzer and using the manual procedure. The user should establish performance characteristics if the product is used on another analyzer.

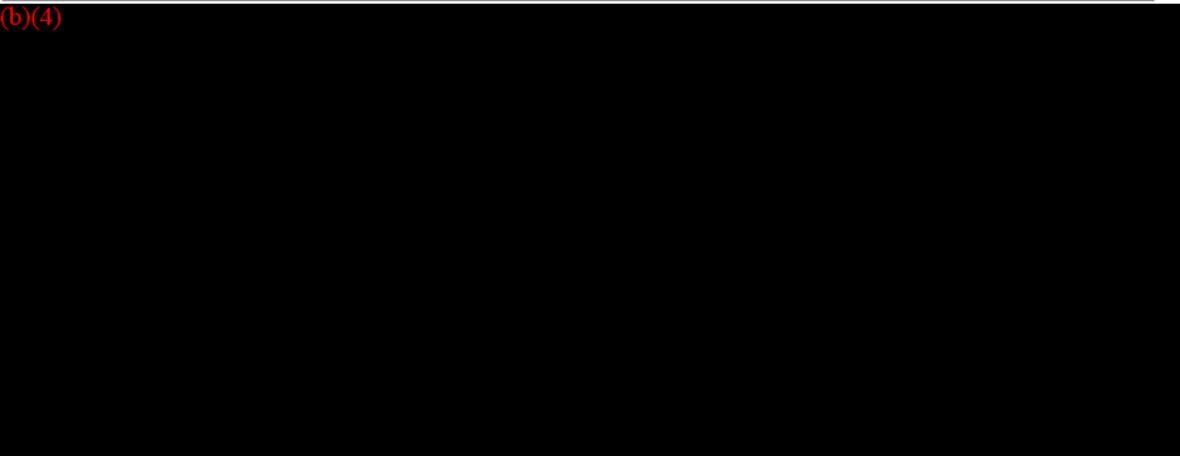
DMA Total Bilirubin Procedure

PRECISION

(b)(4)



(b)(4)



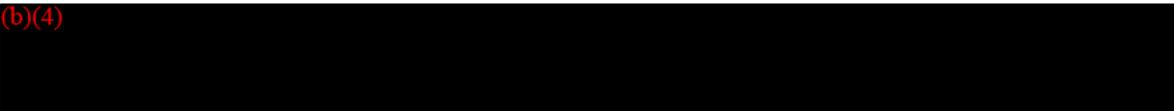
COMPARISON

A comparison of the DMA Total Bilirubin Procedure with the DMA Total Bilirubin Plus Procedure was performed on the Hitachi 704^R on 169 samples in a range of [redacted] (b)(4) [redacted].

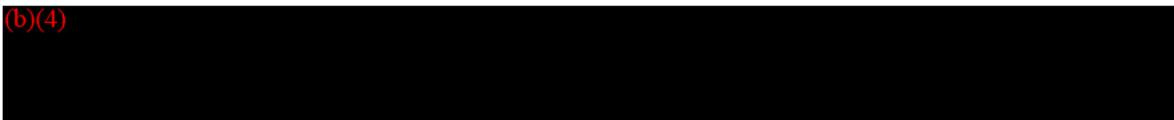
(b)(4)



(b)(4)



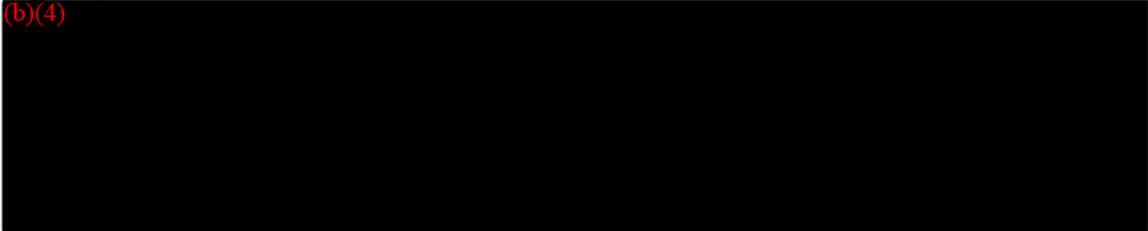
(b)(4)



DMA Total Bilirubin Procedure

SENSITIVITY⁷

(b)(4)



BIBLIOGRAPHY

1. Tietz, N.W., *Fundamentals of Clinical Chemistry*, 2nd Ed., W.B. Saunders, Philadelphia, 1976, p. 1028-1044.
2. Annino, J.S., *Clinical Chemistry Principles and Procedures*, 2nd Ed., Little, Brown and Company, Boston, 1960, p. 203.
3. Van den Bergh, A., and Mueller, P., *Biochem Z.* 77, p. 90, 1916.
4. Young, D.S., *Effects of Drugs on Clinical Laboratory Tests*, 3rd Ed., AACC Press, Washington, D.C., 1990, p. 3-61--3-72.
5. Henry, R.J., Cannon, D.C., and Winkelman, J.W., *Clinical Chemistry Principles and Technics*, 2nd ed., Harper and Row, New York, 1974, p. 1042.
6. NCCLS: Standard Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture (H3), Standard Procedures for the Collection of Diagnostic Blood Specimens by Skin Puncture (H4), Standard Procedures for Blood Specimen Processing (H18), National Committee for Clinical Laboratory Standards, Villanova, PA.
7. Data on file. Data Medical Associates, Inc., Arlington, Texas.

^RHitachi 704 is a registered trademark of Boehringer Mannheim Diagnostics, Inc., Indianapolis, Indiana, 46250

DMA, Inc. 845 Avenue "G" East, Arlington, TX 76011 U.S.A.

DMA 1995 Revision No. ____



Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

REC 20 1995

C. H. Morris, Ph.D.
• Vice President, Scientific
and Government Affairs
Data Medical Associates, Inc.
845 Avenue G East
Arlington, Texas 76011

Re: K955300
Total Bilirubin
Regulatory Class: II
Product Code: CIG
Dated: November 17, 1995
Received: November 20 1995

Dear Dr. Morris:

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 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 (Pre-market 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

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity reclassification. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification immediately. An FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in any way represent your device or its labeling as being approved by FDA. 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), promotion, or advertising please contact the Office of Compliance, Promotion and Advertising Policy Staff (HFZ-302) at (301) 594-4639. 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 at (301) 443-6597.

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory
Device
Office of Device Evaluation
Center for Devices and
Radiological Health

0002

510 (K) ROUTE SLIP

CCB
11/22
✓R-11-27

510 (K) NUMBER K955300 PANEL CH DIVISION DCLD BRANCH CLCB
TRADE NAME TOTAL BILIRUBIN PROCEDURE
COMMON NAME BILIRUBIN (TOTAL OR DIRECT) TEST SYSTEM
PRODUCT CODE _____

APPLICANT DATA MEDICAL ASSOCIATES, INC.
SHORT NAME DATAMEDI
CONTACT C. H. MORRIS
DIVISION _____
ADDRESS 845 AVENUE "G" EAST
ARLINGTON, TX 76011
PHONE NO. (817) 640-0965 FAX NO. (817) 649-2461

MANUFACTURER DATA MEDICAL ASSOCIATES, INC. REGISTRATION NO. 1650060

DATE ON SUBMISSION 17-NOV-95 DATE DUE TO 510(K) STAFF 03-FEB-96
DATE RECEIVED IN ODE 20-NOV-95 DATE DECISION DUE 18-FEB-96
DECISION SE DECISION DATE _____
12-11-95

Is this 510(k) identified as a Class I device _____ YES

~~NO~~

0003



Memorandum

12-11-95

From REVIEWER(S) - NAME(S) Carol C Benson

Subject 510(k) NUMBER K955300

To THE RECORD -- It is my recommendation that the subject 510(k) Notification:

- Is substantially equivalent to marketed devices *21 CFR 862.1100
Diags, Colorimetry, Bilirubin*
- Requires premarket approval. NOT substantially equivalent to marketed devices.
- Requires more data.
- Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Postmarket Surveillance? YES NO

Is this device subject to the Tracking Regulation? YES NO

Was clinical data necessary to support the review of this 510(k)? YES NO

This 510(k) contains: Truthful and Accurate Statement Requested Enclosed -
(required for originals received 3-14-95 and after)

- A 510(k) summary OR A 510(k) statement
- The required certification and summary for class III devices

The submitter requests under 21 CFR 807.95: No Confidentiality

Confidentiality for 90 days Continued Confidentiality exceeding 90 days

Predicate Product Code with panel and class:
75 CIG Class II

Additional Product Code(s) with panel (optional):

REVIEW: [Signature]
(BRANCH CHIEF)

CLCB
(BRANCH CODE)

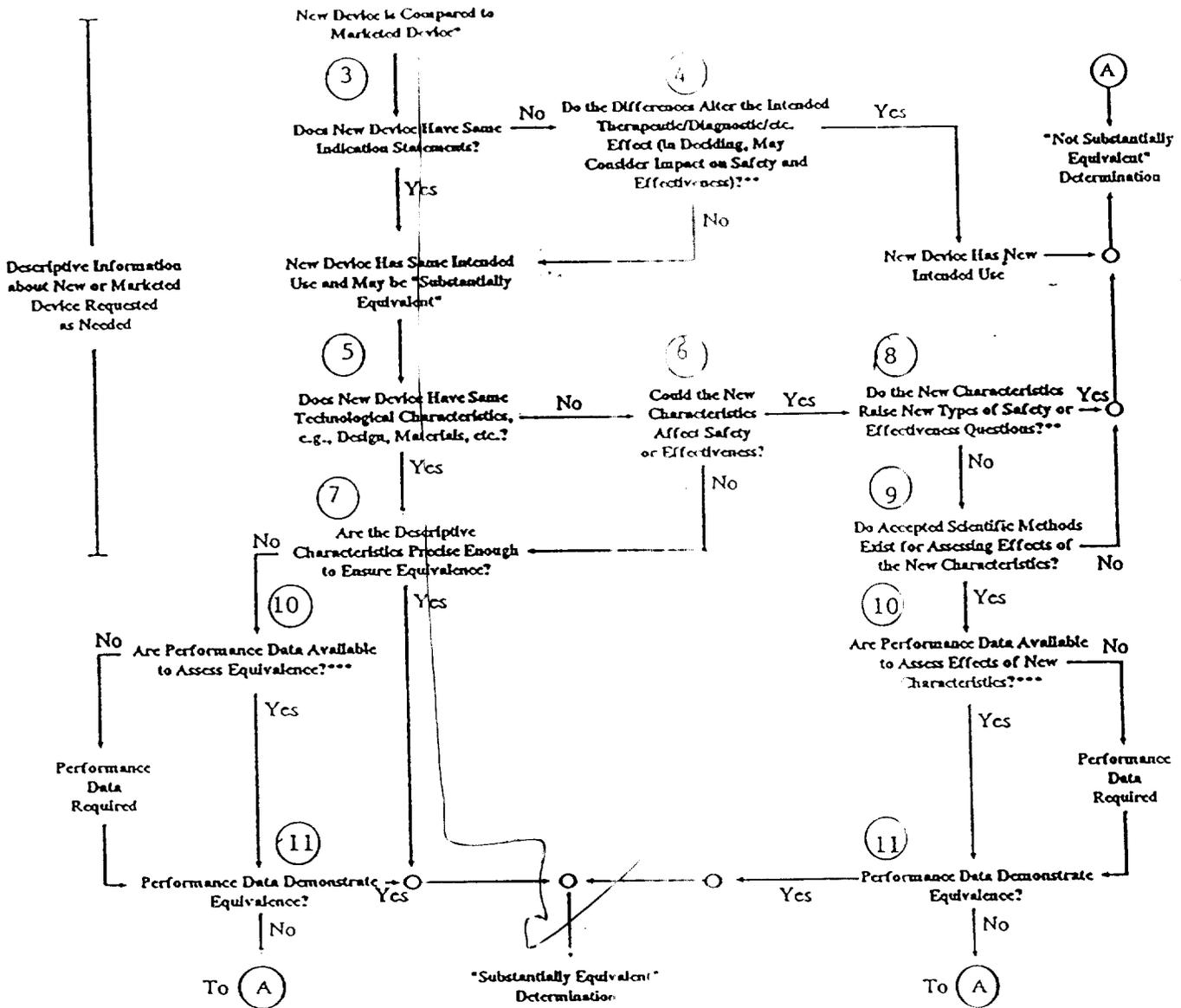
12/12/95
(DATE)

FINAL REVIEW: [Signature]
(DIVISION DIRECTOR)

12/17/95
(DATE)

Revised 3/8/95

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS (DETAILED)



* 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. 0005

*** Data may be in the 510(k), other 510(k)s, the Center's classification files, or the literature.

REVISED:3/14/95

THE 510(K) DOCUMENTATION FORMS ARE AVAILABLE ON THE LAN UNDER 510(K) BOILERPLATES TITLED "DOCUMENTATION" AND MUST BE FILLED OUT WITH EVERY FINAL DECISION (SE, NSE, NOT A DEVICE, ETC.).

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION MAKING DOCUMENTATION

k- 955300

Reviewer: Carol C. Benson

Division/Branch: DCLD/CLCB

Device Name:Total Bilirubin Procedure

Product To Which Compared (510(K) Number If Known):DMA's Total Bilirubin Plus Procedure (k-861413)

| | YES | NO | |
|--|-----|----|---|
| 1. Is Product A Device? | X | | If NO = Stop |
| 2. Is Device Subject To 510(k)? | X | | If NO = Stop |
| 3. Same Indication Statement? | X | | If YES=Go To 5 |
| 4. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness? | | | If YES = Stop NE |
| 5. Same Technological Characteristics? | X | | If YES = Go To 7 |
| 6. Could The New Characteristics Affect Safety Or Effectiveness? | | | If YES = Go To 8 |
| 7. Descriptive Characteristics Precise Enough? | X | | If NO = Go To 10 If YES = Stop SE |
| 8. New Types Of Safety Or Effectiveness Questions? | | | If YES = Stop NE |
| 9. Accepted Scientific Methods Exist? | | | If NO = Stop NE |
| 10. Performance Data Available? | | | If NO = Request Data |
| 11. Data Demonstrate Equivalence? | | | Final Decision: |

0006

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 5, 8, and 11, and every "no" response requires an explanation.

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION-MAKING DOCUMENTATION

NARRATIVE DEVICE DESCRIPTION k-95530

1. INTENDED USE:

The Total Bilirubin Procedure is for the quantitative determination of total bilirubin in serum and plasma.

2. DEVICE SUMMARY:

The Total Bilirubin Procedure is an in vitro diagnostic device consisting of 200 ml bottle of 3,5-dichlorophenyl diazonium liquid reagent (0.36 mmol/L).

The principle of the method is a variation of the classical method of Van den Bergh and Mueller. Total bilirubin, both conjugated and free, is measured by using a stabilized diazonium

(b)(4)

(b)(4)

A claim of substantial equivalence is made to the DMA's Total Bilirubin Plus Procedure (k-861439). Both an automated (Hitachi 704) and a manual sample comparison were performed. The Hitachi

(b)(4)

This device is substantially equivalent to 21 CFR 862.1100, Diazo Colorimetry, Bilirubin, 75CIG, Class II.

0007



K955302/A1

ata Medical Associates • Avenue C East • Arlington, TX 76011 • 817/640-0965

December 11, 1995

Food and Drug Administration
Document Mail Center, HFZ-401
Center for Devices and Radiological Health
9200 Corporate Drive
Rockville, MD 20850

Dear Sirs:

Please find enclosed two copies of additional information to be added to our 510(k) submission for DMA Total Bilirubin Procedure.

All inquiries should be directed to C. H. Morris, Ph.D.

Respectfully yours,

C. H. Morris, Ph.D.
Vice President, Scientific
and Government Affairs

enclosures

CHM:led

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0008



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

December 7, 1995

Ms. Carol Benson
Food and Drug Administration
Document Mail Center (HFZ-401)
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Dear Ms. Benson:

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- | <u>Request</u> | <u>Response</u> |
|--|--|
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| 3. In the response, provide a reference for the use of plasma. | The use of plasma is referenced in "Clinical Chemistry, Theory, Analysis, and Correlation, 2nd. Ed., Kaplan, L.A., and Pesce, A.J., 1989, p. 1013, The C.V. Mosby Company. |
| 4. Evaluate Within-Run and Run-to-Run % CV on the low sample. Describe how many days the "Run-to-Run" precision study covered. | (b)(4) |
| 5. On page 19 under the "Materials Required But Not Provided" section, list controls. | Refer to attached revised page 19. |

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FDA/CDRH/OCE/DMC

0009

Page 2 of 2
December 7, 1995

Request

Response

6. Provide revision date at end of labeling. Refer to attached revised page 23.

Thank you for your consideration of these responses to your inquiries. Please contact me if you have any questions.

Sincerely,



C. H. Morris, Ph.D.
Vice President, Scientific
and Government Affairs

encl

CHM:led

0010



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

Comparison of Performance:

Linearity

Precision Within-Run

Within Normal Range %C.V. Hitachi 704^R

Above Normal Range %C.V. Hitachi 704^R

Within Normal Range Manual

Above Normal Range Manual

Precision Run-to-Run

Within Normal Range %C.V.

Above Normal Range %C.V.

Within Normal Range Manual

Above Normal Range Manual

Shelf-life at 2-8°C

Sensitivity (0.001A)

Analytical

Interferences

Hemoglobin

Lipemia

Expected Values

(b)(4)

(b)(4)

Statement of Equivalency: Based on the comparison of the technological characteristics of DMA's device with the predicate device, and the performance characteristics, DMA proposes that the DMA device is substantially equivalent to the predicate device.

C. H. Morris, Ph.D.

December 7, 1995

0011

F. **PRECISION** (continued)

Within-Run Manual

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

Run-to-Run with Hitachi 704^R

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

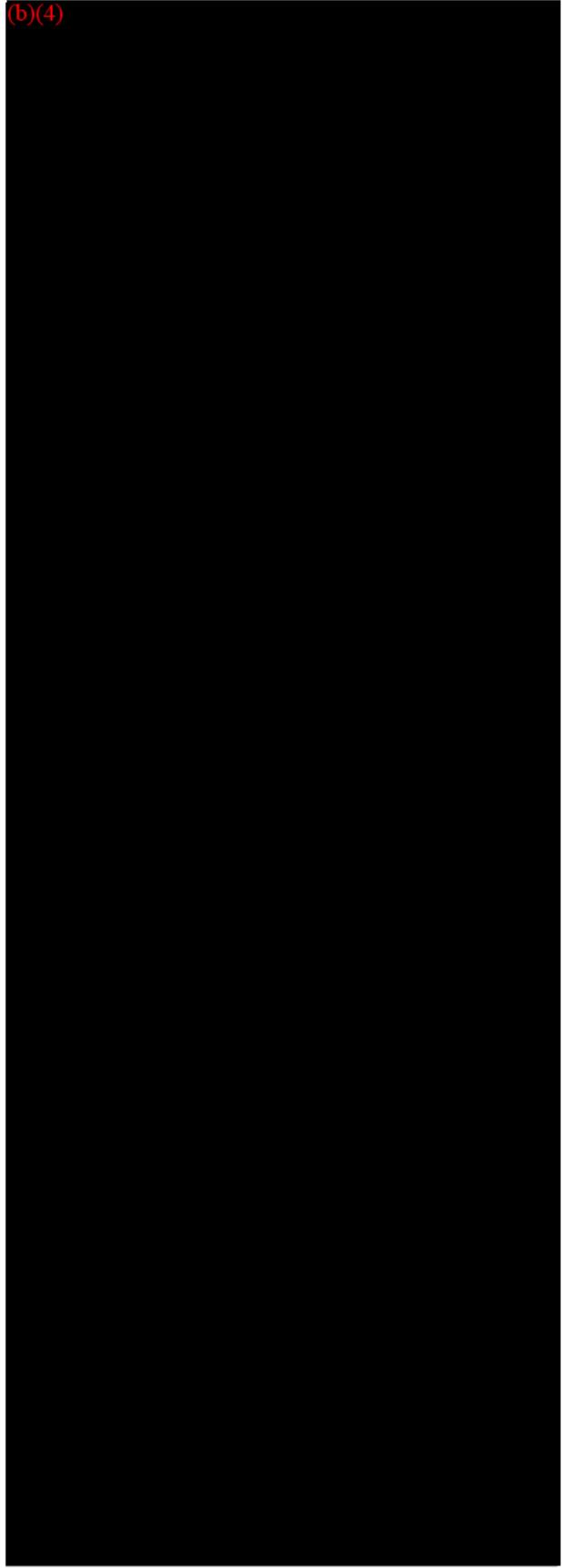
Run-to-Run Manual

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

(b)(4)



DMA Total Bilirubin Procedure

SAMPLE STORAGE

(b)(4)

HITACHI 704^R PROCEDURE

(b)(4)

MATERIALS PROVIDED

Total Bilirubin Reagent

MATERIALS REQUIRED BUT NOT PROVIDED

1. DMA's Bilirubin Calibrators (Cat. No. 2241-151 or 2241-152) or equivalent.
2. DMA's Normal and Abnormal controls (Cat. Nos. 1901-605 and 1902-605) or equivalent.
3. Pipettes for accurately dispensing 1.0 mL volumes.
4. Micropipettes for dispensing 0.05 mL volumes.
5. Suitable manual instrument calibrated to read at 540 nm.
6. Hitachi 704^R Analyzer, or equivalent, with manual and accessories.

MANUAL PROCEDURES

1. (b)(4)

2.

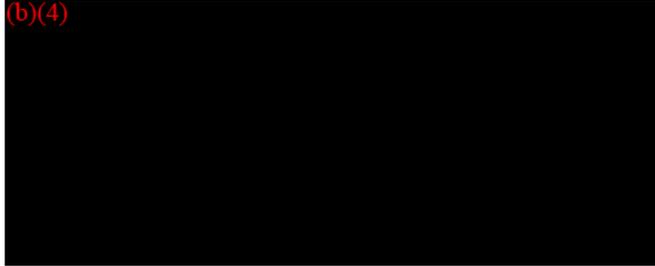
3.

4.

5.

DMA Total Bilirubin Procedure

Example:



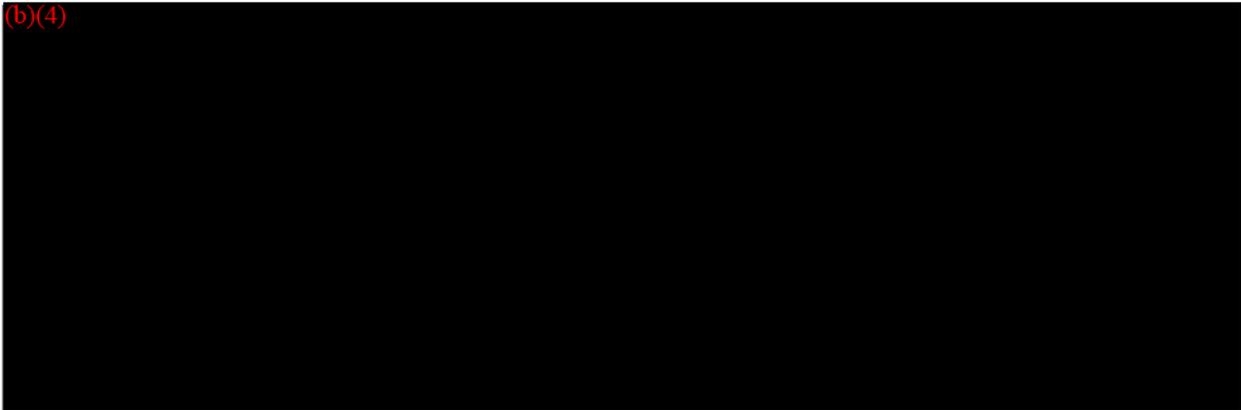
LIMITATIONS

See Storage and Stability, Deterioration, Specimen Collection, Interfering Substances, Sample Storage, Stability of Final Reaction Mixture, and Linearity sections for limitations to this procedure.

Bilirubin calibrators in chloroform may not be used in this procedure since chloroform miscible solvents are not employed.

Bilirubin is extremely light sensitive. Calibrator, control and unknown specimens must be stored protected from light sources for optimal stability.

EXPECTED VALUES⁷



PERFORMANCE CHARACTERISTICS⁷

The Performance Characteristics were established on a Hitachi 704^R analyzer and using the manual procedure. The user should establish performance characteristics if the product is used on another analyzer.

0014

DMA Total Bilirubin Procedure

PRECISION

Within-run reproducibility was determined by assaying three levels of control sera (b)(4).

Within-Run on the Hitachi 704^R

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

Within-Run, Manual Procedure

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

Run-to-run reproducibility was determined by assaying three levels of control sera as single points for (b)(4), (b)(4), (b)(4).

Run-to-Run on the Hitachi 704^R

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

Run-to-Run, Manual Procedure

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

COMPARISON

A comparison of the DMA Total Bilirubin Procedure with the DMA Total Bilirubin Plus Procedure was performed on the Hitachi 704^R on (b)(4).

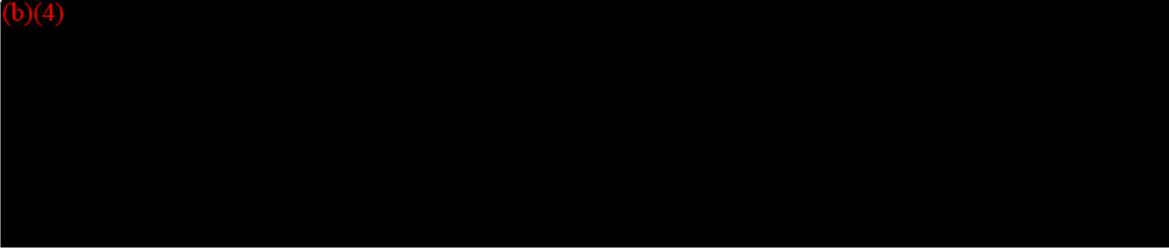
(b)(4)

5

DMA Total Bilirubin Procedure

SENSITIVITY⁷

(b)(4)



BIBLIOGRAPHY

1. Tietz, N.W., *Fundamentals of Clinical Chemistry*, 2nd Ed., W.B. Saunders, Philadelphia, 1976, p. 1028-1044.
2. Annino, J.S., *Clinical Chemistry Principles and Procedures*, 2nd Ed., Little, Brown and Company, Boston, 1960, p. 203.
3. Van den Bergh, A., and Mueller, P., *Biochem Z.* 77, p. 90, 1916.
4. Young, D.S., *Effects of Drugs on Clinical Laboratory Tests*, 3rd Ed., AACC Press, Washington, D.C., 1990, p. 3-61--3-72.
5. Henry, R.J., Cannon, D.C., and Winkelman, J.W., *Clinical Chemistry Principles and Technics*, 2nd ed., Harper and Row, New York, 1974, p. 1042.
6. NCCLS: Standard Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture (H3), Standard Procedures for the Collection of Diagnostic Blood Specimens by Skin Puncture (H4), Standard Procedures for Blood Specimen Processing (H18), National Committee for Clinical Laboratory Standards, Villanova, PA.
7. Data on file. Data Medical Associates, Inc., Arlington, Texas.

⁸Hitachi 704 is a registered trademark of Boehringer Mannheim Diagnostics, Inc., Indianapolis, Indiana, 46250

DMA, Inc. 845 Avenue "G" East, Arlington, TX 76011 U.S.A.

DMA 1995 Revision No. ___

0016



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

| | | |
|--|----------------------|----------------|
| Post-It™ brand fax transmittal memo 7671 | | # of pages ▶ 8 |
| To Carol Benson | From Dr. C.H. Morris | |
| Co. FDA | Co. DMA, Inc | |
| Dept. Clin. Lab. Devices | Phone # 817 640 0965 | |
| Fax # 301 594 5940 | Fax # 817 649 2461 | |

December 7, 1995

Ms. Carol Benson
 Food and Drug Administration
 Document Mail Center (HFZ-401)
 Center for Devices and Radiological Health
 9200 Corporate Drive
 Rockville, MD 20850

*12-11-95
 He'll send the hard copy
 of this fax to DMC today.
 CMB*

Dear Ms. Benson:

Responses to your request for additional information of 12/6/95 are as follows:

Request

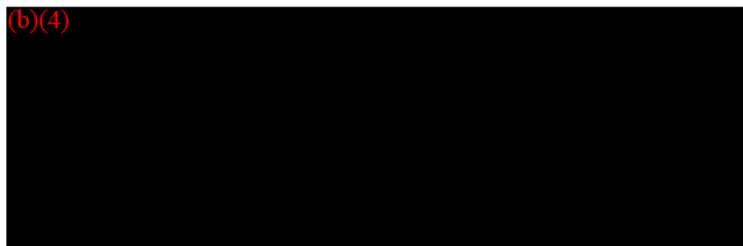
Response

1. On page 19, under the "Sample Storage" section, provide the temperature for the frozen serum.
2. On page 21, in the "Expected Values" section, add the word "serum" to define samples.
3. In the response, provide a reference for the use of plasma.
4. Evaluate Within-Run and Run-to-Run % CV on the low sample. Describe how many days the "Run-to-Run" precision study covered.
5. On page 19 under the "Materials Required But Not Provided" section, list controls.

Refer to attached revised page 19.

Refer to attached revised page 21.

The use of plasma is referenced in "Clinical Chemistry, Theory, Analysis, and Correlation, 2nd. Ed., Kaplan, L.A., and Pesce, A.J., 1989, p. 1013, The C.V. Mosby Company.



Refer to attached revised page 19.

0017

Page 2 of 2
December 7, 1995

Request

Response

- | | | |
|----|---|------------------------------------|
| 6. | Provide revision date at end of labeling. | Refer to attached revised page 23. |
|----|---|------------------------------------|

Thank you for your consideration of these responses to your inquiries. Please contact me if you have any questions.

Sincerely,



C. H. Morris, Ph.D.
Vice President, Scientific
and Government Affairs

encl

CHM:led

0018

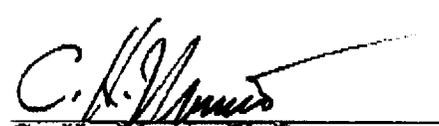


Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

Comparison of Performance:

| | <u>DMA NEW</u> 0.1 to 20 mg/dL | <u>DMA Predicate</u> to 25 mg/dL |
|--|-----------------------------------|-------------------------------------|
| Linearity | | |
| Precision Within-Run | | |
| Within Normal Range %C.V. Hitachi 704 ^R | 0.0 | 5.5 |
| Above Normal Range %C.V. Hitachi 704 ^R | 0.85, 0.66 | 2.0, 2.3 |
| Within Normal Range Manual | 5.0 | --- |
| Above Normal Range Manual | 2.2, 1.56 | --- |
| Precision Run-to-Run | | |
| Within Normal Range %C.V. | 1.11 | 3.6 |
| Above Normal Range %C.V. | 1.2, 1.2 | 1.6, 2.2 |
| Within Normal Range Manual | 6.4 | --- |
| Above Normal Range Manual | 0.83, 2.1 | --- |
| Shelf-life at 2-8°C | 14 months | 12 months |
| Sensitivity (0.001A) | 0.07 mg/dL | 0.026 |
| Analytical | 0.1 mg/dL | NA |
| Interferences | | |
| Hemoglobin | Significant above 83 mg/dL | Gross hemolysis interferes |
| Lipemia | Not significant to 1335 mg/dL | Interferes |
| Expected Values | Hitachi 704 ^R 0.2-1.5 | 0.0-1.5 |
| | Manual 0.4-1.7 | |

Statement of Equivalency: Based on the comparison of the technological characteristics of DMA's device with the predicate device, and the performance characteristics, DMA proposes that the DMA device is substantially equivalent to the predicate device.


 C. H. Morris, Ph.D.
 December 7, 1995

0019

F. PRECISION (continued)

Within-Run Manual

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

Run-to-Run with Hitachi 704^R

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

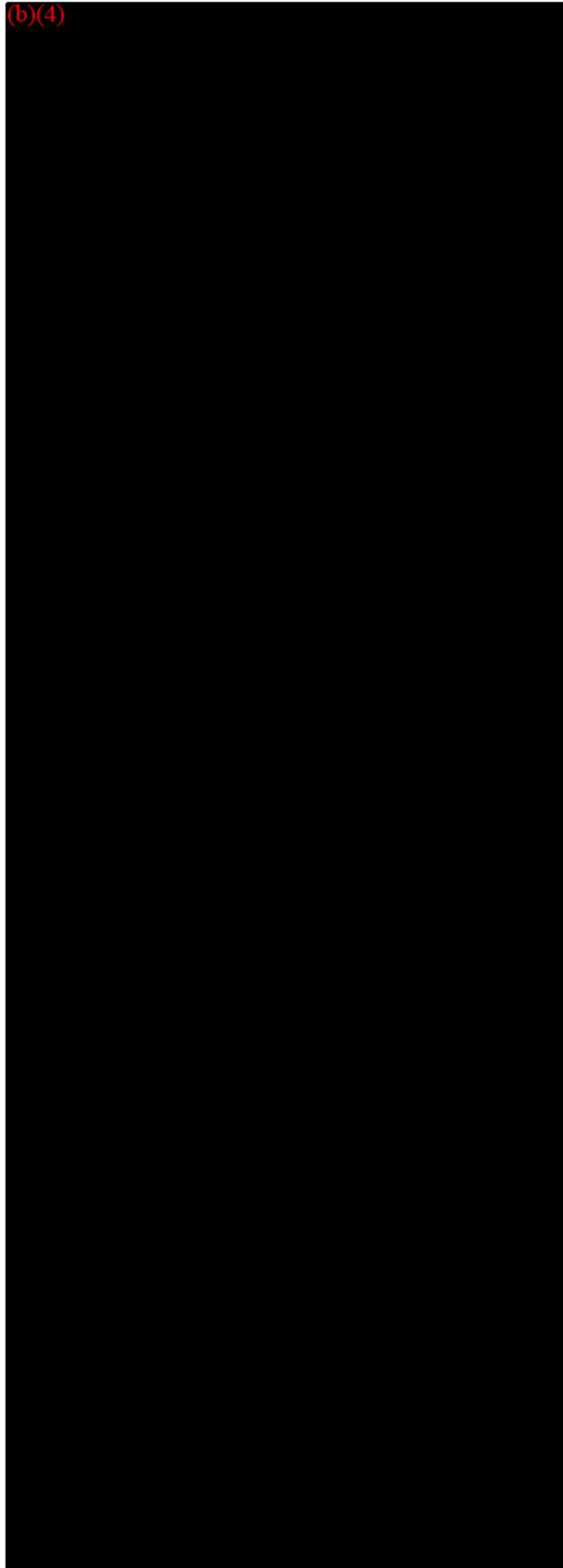
Run-to-Run Manual

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

(b)(4)



DMA Total Bilirubin Procedure

SAMPLE STORAGE

(b)(4)

HITACHI 704^R PROCEDURE

(b)(4)

MATERIALS PROVIDED

Total Bilirubin Reagent

MATERIALS REQUIRED BUT NOT PROVIDED

1. DMA's Bilirubin Calibrators (Cat. No. 2241-151 or 2241-152) or equivalent.
2. DMA's Normal and Abnormal controls (Cat. Nos. 1901-605 and 1902-605) or equivalent.
3. Pipettes for accurately dispensing 1.0 mL volumes.
4. Micropipettes for dispensing 0.05 mL volumes.
5. Suitable manual instrument calibrated to read at 540 nm.
6. Hitachi 704^R Analyzer, or equivalent, with manual and accessories.

MANUAL PROCEDURES

1. (b)(4)
- 2.
- 3.
- 4.
- 5.

DMA Total Bilirubin Procedure

Example:

(b)(4)

LIMITATIONS

See Storage and Stability, Deterioration, Specimen Collection, Interfering Substances, Sample Storage, Stability of Final Reaction Mixture, and Linearity sections for limitations to this procedure.

Bilirubin calibrators in chloroform may not be used in this procedure since chloroform miscible solvents are not employed.

Bilirubin is extremely light sensitive. Calibrator, control and unknown specimens must be stored protected from light sources for optimal stability.

EXPECTED VALUES⁷

(b)(4)

The published normal range is 0.0 to 1.5.⁵

These ranges should serve only as guidelines. It is recommended that each laboratory establish its own range of expected values, since differences may exist between instruments, laboratories and local populations.

PERFORMANCE CHARACTERISTICS⁷

The Performance Characteristics were established on a Hitachi 704^R analyzer and using the manual procedure. The user should establish performance characteristics if the product is used on another analyzer.

0022

DMA Total Bilirubin Procedure

PRECISION

Within-run reproducibility was determined by assaying three levels of control sera

(b)(4)

Within-Run on the Hitachi 704^R

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
|---------------|-------------|------------------|------------|

| | | | |
|----------|--------|--|--|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

Within-Run, Manual Procedure

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
|---------------|-------------|------------------|------------|

| | | | |
|----------|--------|--|--|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

Run-to-run reproducibility was determined by assaying three levels of control sera as single points for 10 runs, over a 4 day period.

Run-to-Run on the Hitachi 704^R

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
|---------------|-------------|------------------|------------|

| | | | |
|----------|--------|--|--|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

Run-to-Run, Manual Procedure

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
|---------------|-------------|------------------|------------|

| | | | |
|----------|--------|--|--|
| Low | (b)(4) | | |
| Moderate | | | |
| High | | | |

COMPARISON

A comparison of the DMA Total Bilirubin Procedure with the DMA Total Bilirubin Plus Procedure was performed on the Hitachi 704^R on (b) samples in a range of (b)(4)

(b)(4)

A comparison of the DMA Total Bilirubin Procedure with the DMA Total Bilirubin Plus Procedure was performed manually on (b) samples in a range of

(b)(4)

(b)(4)

DMA Total Bilirubin Procedure**SENSITIVITY⁷**

(b)(4)

BIBLIOGRAPHY

1. Tietz, N.W., *Fundamentals of Clinical Chemistry*, 2nd Ed., W.B. Saunders, Philadelphia, 1976, p. 1028-1044.
2. Annino, J.S., *Clinical Chemistry Principles and Procedures*, 2nd Ed., Little, Brown and Company, Boston, 1960, p. 203.
3. Van den Bergh, A., and Mueller, P., *Biochem Z.* 77, p. 90, 1916.
4. Young, D.S., *Effects of Drugs on Clinical Laboratory Tests*, 3rd Ed., AACC Press, Washington, D.C., 1990, p. 3-61--3-72.
5. Henry, R.J., Cannon, D.C., and Winkelman, J.W., *Clinical Chemistry Principles and Technics*, 2nd ed., Harper and Row, New York, 1974, p. 1042.
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7. Data on file. Data Medical Associates, Inc., Arlington, Texas.

⁷Hitachi 704 is a registered trademark of Boehringer Mannheim Diagnostics, Inc., Indianapolis, Indiana, 46250

DMA, Inc. 845 Avenue "G" East, Arlington, TX 76011 U.S.A.

DMA 1995 Revision No. _____ ✓

0024



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SECOND EDITION

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II. Pesce, Amadeo J.

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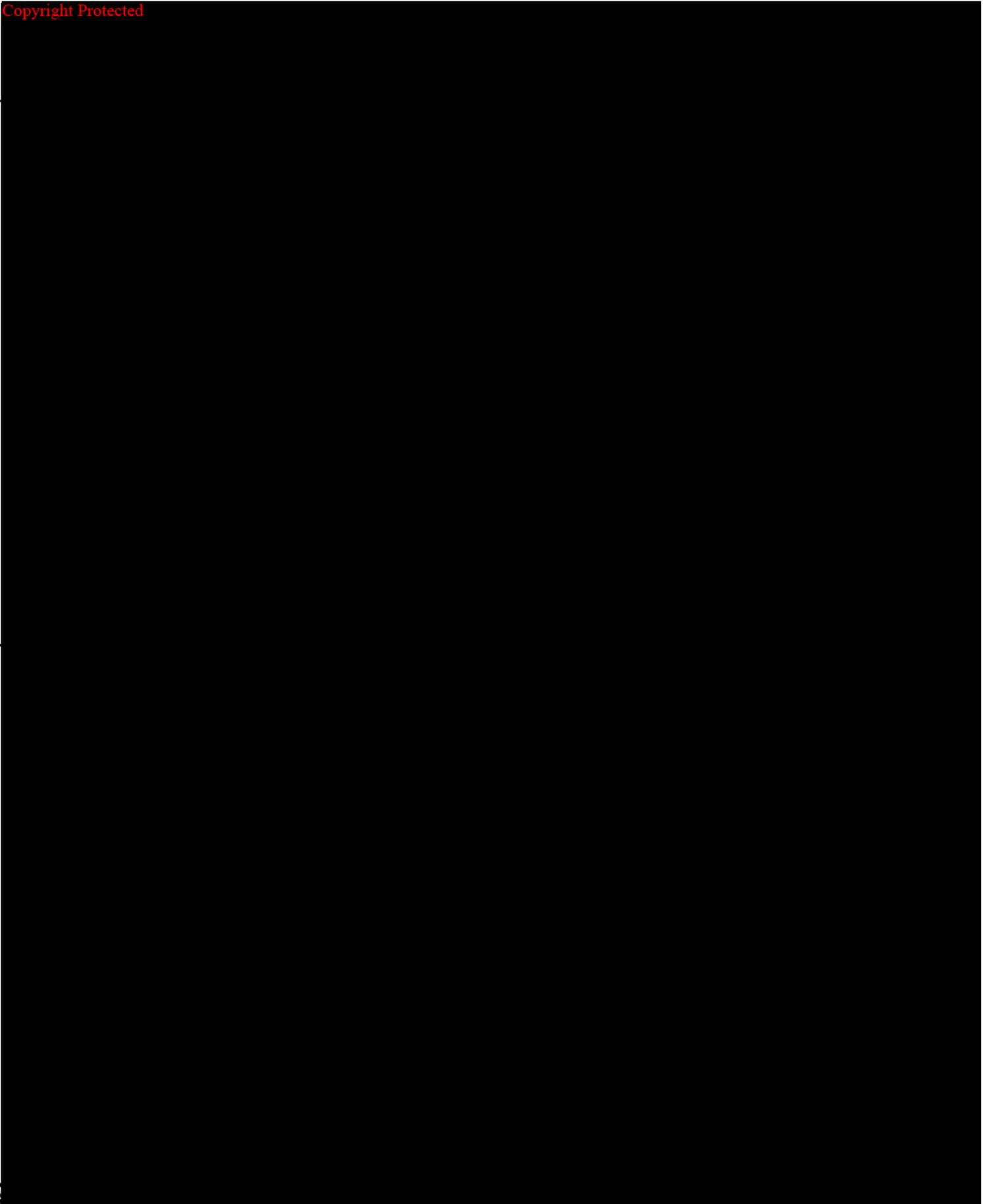
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MEMO RECORD

FROM: Carol C. Benson DATE: December 4, 1995

TO: Branch Chief/The Record OFFICE: ODE/DCLD/CLCB

SUBJECT: Telephone contact with firm 510(k): k-955300

Phone: 1-817-640-0965, FAX 1-817-649-2461; TX

Date: December 7, 1995 (with concurrence from Branch Chief: 12/7/95)

I spoke with C. H. Morris, Ph.D., Vice President, Scientific and Government Affairs, Data Medical Associates, Inc. (DMA), for more information/clarification as follows:

- 1. ✓ Provide a temperature for frozen sample storage.
- 2. ✓ Provide the data to support the use of plasma (heparin and EDTA) as stated in the intended use. *Wants to use a recent literature source.*
- 3. ✓ State the type of samples (serum or plasma) used to determine the reference interval.
- 4. ✓ Explain a 0% CV for the imprecision study.
- 5. ✓ Provide 510(k) for the recommended DMA's calibrator.
- 6. ✓ Clarify your recommended controls as the Corning controls. State controls under materials needed but not provided.
- 7. ✓ Provide a revision date on the labeling.

Send the requested information and revised labeling to the DMC. A FAX maybe sent to CLCB with follow up hard copies to the DMC.

Calibrator - Verichem's Bilirubin Calibrator - k-882059
Controls - Corning's preamendment
Predicate - DMA's Total Bilirubin Procedure - k-861413

| SIGNATURE | Reg | Code | Class | DOCUMENT NO. |
|------------------------|----------|-------|----------|--------------|
| <i>Carol C. Benson</i> | 862.1100 | 75CIG | Class II | k-955300 |

0027

PREMARKET NOTIFICATION (510(K)) CHECKLIST FOR ACCEPTANCE DECISION

I. 19255300 Device Name Total Bilirubin Procedure
Division/Branch DEVD/CLCB
Administrative Reviewer Signature Carol C. Benson Date 11-27-95
Supervisory Signature [Signature] Date 12/11/95

Did the firm request expedited review? Yes No
Did we grant expedited review? Yes No
Truthful and accurate statement enclosed? Yes No
(If Not Enclosed, Must Be A Refuse To Accept Letter)
Required For Originals Received 3/14/95 And After

Without reviewing this 510(k), do you believe this device type may be a preamendments class III device? Yes No (IF YES, NOTIFY POS IMMEDIATELY IF THE OUTSIDE OF THE 510(k) HAS NOT BEEN STAMPED CLASS III SO THAT THE GMP INSPECTION CAN BE SCHEDULED AS SOON AS POSSIBLE). Class III devices can not receive a determination of substantial equivalence until the GMP inspection process has been completed.

Is this a file that was determined to be substantially equivalent by ODE, but placed on hold due to GMP violations and deleted after 12 months on hold? If so, a new ODE review not required, please forward to POS.

Yes No
 Accepted Refuse To Accept

0028

| I. CRITICAL ELEMENTS: | YES PRESENT OMISSION JUSTIFIED | NO INADEQUATE OMITTED |
|--|--|---|
| A. Is The Product A Device? | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| B. Is The Device Exempt From 510(k) By Regulation Or Policy? | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| C. Is Device Subject To Review By CDRH? | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| D. (i) Are You Aware That This Device Has Been The Subject Of A Previous NSE Decision? (ii) If Yes, Does This New 510(k) Address The NSE Issue(s) (E.G., Performance Data)? | <input type="checkbox"/> <input type="checkbox"/> | <input checked="" type="checkbox"/> <input type="checkbox"/> |
| E. (i) Are You Aware Of The Submitter Being The Subject Of An Integrity Investigation? If Yes, Consult The ODE Integrity Officer. (ii) Has The ODE Integrity Officer Given Permission To Proceed With The Review? (Blue Book Memo #I91-2 And Federal Register 90N-0332, September 10, 1991.) | <input type="checkbox"/> <input type="checkbox"/> | <input checked="" type="checkbox"/> <input type="checkbox"/> |
| F. Does The Submission Contain The Information Required Under Sections 510(k), 513(f), And 513(i) Of The Federal Food, Drug, and Cosmetic Act (Act) And Subpart E Of Part 807 In Title 21 Of The Code Of Federal Regulations?: | <input type="checkbox"/> | <input type="checkbox"/> |
| 1. Device Trade Or Proprietary Name | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 2. Device Common Or Usual Name Or Classification Name | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 3. Establishment Registration Number (Only Applies If Establishment Is Registered) | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 4. Class Into Which The Device Is Classified Under (21 CFR Parts 862 to 892) | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 5. Classification Panel | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 6. Action Taken To Comply With Section 514 Of The Act | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 7. Proposed Labels, Labeling And Advertisements (If Available) That Describe The Device, Its Intended Use, And Directions For Use (Blue Book Memo #G91-1) | <input checked="" type="checkbox"/> | <input type="checkbox"/> 0029 |

| | | |
|--|-------------------------------------|--------------------------|
| 8. A 510(k) <u>Summary</u> Of Safety And Effectiveness Or A 510(k) Statement That Safety And Effectiveness Information Will Be Made Available To Any Person Upon Request | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 9. For Class III Devices Only, A Class III Certification And A Class III Summary | NA <input type="checkbox"/> | <input type="checkbox"/> |
| 10. Photographs Of The Device | <input type="checkbox"/> | <input type="checkbox"/> |
| 11. Engineering Drawings For The Device With Dimensions And Tolerances | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 12. The Marketed Device(s) To Which Equivalence Is Claimed Including Labeling And Description Of The Device | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 13. Statement Of Similarities And/Or Differences With Marketed Device(s) | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 14. Data To Show Consequences And Effects Of A Modified Device(s) | NA <input type="checkbox"/> | <input type="checkbox"/> |
| 15. Truthful And Accurate Statement | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| II. Additional Information That <u>Is</u> Necessary Under 21 CFR 807.87(h): | <input type="checkbox"/> | <input type="checkbox"/> |
| A. Submitter's Name And Address | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| B. Contact Person, Telephone Number And Fax Number | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| C. Representative/Consultant If Applicable | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| D. Table Of Contents With Pagination | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| E. Address Of Manufacturing Facility/Facilities And, If Appropriate, Sterilization Site(s) | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| III. Additional Information That <u>May Be</u> Necessary Under 21 CFR 807.87(h): | <input type="checkbox"/> | <input type="checkbox"/> |
| A. Comparison Table Of The New Device To The Marketed Device(s) | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| B. Action Taken To Comply With Voluntary Standards | NA <input type="checkbox"/> | <input type="checkbox"/> |
| C. Performance Data | <input type="checkbox"/> | <input type="checkbox"/> |
| MARKETED DEVICE: | <input type="checkbox"/> | <input type="checkbox"/> |
| Bench Testing | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| Animal Testing | <input type="checkbox"/> | <input type="checkbox"/> |
| Clinical Data | <input type="checkbox"/> | <input type="checkbox"/> |
| NEW DEVICE: | <input type="checkbox"/> | <input type="checkbox"/> |
| Bench Testing | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| Animal Testing | <input type="checkbox"/> | <input type="checkbox"/> |

8/30

| | | |
|--|-------------------------------------|-------------------------------------|
| Clinical Data | <input type="checkbox"/> | <input type="checkbox"/> |
| D. Sterilization Information | NA <input type="checkbox"/> | <input type="checkbox"/> |
| E. Software Information | <input type="checkbox"/> | <input type="checkbox"/> |
| F. Hardware Information | <input type="checkbox"/> | <input type="checkbox"/> |
| G. If This 510(k) Is For A Kit, Has The Kit Certification Statement Been Provided? | <input type="checkbox"/> | <input type="checkbox"/> |
| H. Is This Device Subject To Issues That Have Been Addressed In Specific Guidance Document(s)? | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| If Yes, Continue Review With Checklist From Any Appropriate Guidance Documents. | NA <input type="checkbox"/> | <input type="checkbox"/> |
| If No, Is 510(k) Sufficiently Complete To Allow Substantive Review? | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| I. Other (Specify) | <input type="checkbox"/> | <input type="checkbox"/> |

0031

REVISED: 3/14/95

THE 510(K) DOCUMENTATION FORMS ARE AVAILABLE ON THE LAN UNDER 510(K) BOILERPLATES TITLED "DOCUMENTATION" AND MUST BE FILLED OUT WITH EVERY FINAL DECISION (SE, NSE, NOT A DEVICE, ETC.).

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION MAKING DOCUMENTATION

K _____

Reviewer: _____

Division/Branch: _____

Device Name: _____

Product To Which Compared (510(K) Number If Known): _____

YES NO

| | YES | NO | |
|--|-----|----|--------------------------------------|
| 1. Is Product A Device | | | If NO = Stop |
| 2. Is Device Subject To 510(k)? | | | If NO = Stop |
| 3. Same Indication Statement? | | | If YES = Go To 5 |
| 4. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness? | | | If YES = Stop NE |
| 5. Same Technological Characteristics? | | | If YES = Go To 7 |
| 6. Could The New Characteristics Affect Safety Or Effectiveness? | | | If YES = Go To 8 |
| 7. Descriptive Characteristics Precise Enough? | | | If NO = Go To 10 If YES = Stop SE |
| 8. New Types Of Safety Or Effectiveness Questions? | | | If YES = Stop NE |
| 9. Accepted Scientific Methods Exist? | | | If NO = Stop NE |
| 10. Performance Data Available? | | | If NO = Request Data |
| 11. Data Demonstrate Equivalence? | | | Final Decision: |

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 6, 8, and 11, and every "no" response requires an explanation.

1. Intended Use:
2. Device Description: Provide a statement of how the device is either similar to and/or different from other marketed devices, plus data (if necessary) to support the statement. Is the device life-supporting or life sustaining? Is the device implanted (short-term or long-term)? Does the device design use software? Is the device sterile? Is the device for single use? Is the device product as a component? Is this device a kit? Provide a summary about the devices design, materials, physical properties and toxicology profile if important.

EXPLANATIONS TO "YES" AND "NO" ANSWERS TO QUESTIONS ON PAGE 1 AS NEEDED

1. Explain why not a device:
2. Explain why not subject to 510(k):
3. How does the new indication differ from the predicate device's indication:
4. Explain why there is or is not a new effect or safety or effectiveness issue:
5. Describe the new technological characteristics:
6. Explain how new characteristics could or could not affect safety or effectiveness:
7. Explain how descriptive characteristics are not precise enough:
8. Explain new types of safety or effectiveness questions raised or why the questions are not new:
9. Explain why existing scientific methods can not be used:
10. Explain what performance data is needed:
11. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

ATTACH ADDITIONAL SUPPORTING INFORMATION

0033

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
 Center for Devices and
 Radiological Health
 Office of Device Evaluation
 Document Mail Center (HFZ-401)
 9200 Corporate Blvd.
 Rockville, Maryland 20850

November 21, 1995

DATA MEDICAL ASSOCIATES, INC.
 845 AVENUE "G" EAST
 ARLINGTON, TX 76011
 ATTN: C. H. MORRIS

510(k) Number: K955300
 Received: 20-NOV-95
 Product: TOTAL BILIRUBIN
 PROCEDURE

The Center for Devices and Radiological Health (CDRH), Office of Device Evaluation (ODE), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in any future correspondence that relates to this submission. We will notify you when the processing of your premarket notification 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.

On December 14, 1994, FDA published a regulation entitled "Medical Devices; Substantial Equivalence; 510(k) Summaries and 510(k) Statements; Class III Summaries; Confidentiality of Information." The regulation took effect March 14, 1995. Please note that this regulation includes a requirement that all submitters provide a statement that the submitter believes, to the best of his or her knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted. There may be other regulations or requirements affecting your device such as Postmarket Surveillance (Section 522(a)(1) of the Act) and the Device Tracking regulation (21 CFR Part 821). Please contact the Division of Small Manufacturers Assistance at the number below for more information.

With regard to the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) which became effective September 1, 1992, the Center for Disease Control (CDC) and Prevention is currently handling complexity category/assignments concurrent with FDA's 510(k) review. To determine if your device requires a CLIA complexity categorization, contact CDC at (770)488-7655.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the Document Mail Center will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations, we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official. Any telefaxed material must be followed by a hard copy to the Document Mail Center (HFZ-401).

If you have procedural or policy questions, or want information on how to check on the status of your submission (after 90 days from the receipt date), please contact the Division of Small Manufacturers Assistance at (301) 443-6597 or their toll-free number (800) 638-2041, or call me at (301) 594-1190. 0034

Sincerely yours,

Marjorie Shulman
 Consumer Safety Officer
 Premarket Notification Staff

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

Premarket Submission Cover Sheet

Date of Submission:
November 17, 1995

FDA Document Number: **K955308**

Section A Type of Submission

- | | | | |
|---|---|--|---|
| <input checked="" type="checkbox"/> 510(k) | <input type="checkbox"/> IDE | <input type="checkbox"/> PMA | <input type="checkbox"/> PMA Supplement - Regular |
| <input type="checkbox"/> 510(k) Add'l information | <input type="checkbox"/> IDE Amendment | <input type="checkbox"/> PMA Amendment | <input type="checkbox"/> PMA Supplement - Special |
| | <input type="checkbox"/> IDE Supplement | <input type="checkbox"/> PMA Report | <input type="checkbox"/> PMA Supplement - 30 day |
| | <input type="checkbox"/> IDE Report | | <input type="checkbox"/> PMA Supplement - Panel Track |

Section B1 Reason for Submission — 510(k)s Only

- | | | |
|--|---|--|
| <input checked="" type="checkbox"/> New device | <input type="checkbox"/> Additional or expanded indications | <input type="checkbox"/> Change in technology, design, materials, or manufacturing process |
| <input type="checkbox"/> Other reason (specify): | | |

Section B2 Reason for Submission — PMAs Only

- | | | |
|---|---|--|
| <input type="checkbox"/> New device | <input type="checkbox"/> Change in design, component, or specification: | <input type="checkbox"/> Location change: |
| <input type="checkbox"/> Withdrawal | <input type="checkbox"/> Software | <input type="checkbox"/> Manufacturer |
| <input type="checkbox"/> Additional or expanded indications | <input type="checkbox"/> Color Additive | <input type="checkbox"/> Sterilizer |
| <input type="checkbox"/> Licensing agreement | <input type="checkbox"/> Other (specify below) | <input type="checkbox"/> Packager |
| <input type="checkbox"/> Labeling change: | | <input type="checkbox"/> Distributor |
| <input type="checkbox"/> Indications | <input type="checkbox"/> Process change: | <input type="checkbox"/> Report submission: |
| <input type="checkbox"/> Instructions | <input type="checkbox"/> Manufacturer | <input type="checkbox"/> Annual or periodic |
| <input type="checkbox"/> Performance Characteristics | <input type="checkbox"/> Sterilizer | <input type="checkbox"/> Post-approval study |
| <input type="checkbox"/> Shelf life | <input type="checkbox"/> Packager | <input type="checkbox"/> Adverse reaction |
| <input type="checkbox"/> Trade name | | <input type="checkbox"/> Device defect |
| <input type="checkbox"/> Other (specify below) | <input type="checkbox"/> Response to FDA correspondence (specify below) | <input type="checkbox"/> Amendment |
| <input type="checkbox"/> Change in ownership | <input type="checkbox"/> Request for applicant hold | |
| <input type="checkbox"/> Change in correspondent | <input type="checkbox"/> Request for removal of applicant hold | |
| <input type="checkbox"/> Other reason (specify): | <input type="checkbox"/> Request for extension | |
| | <input type="checkbox"/> Request to remove or add manufacturing site | |

Section B3 Reason for Submission — IDEs Only

- | | | |
|---|--|--|
| <input type="checkbox"/> New device | <input type="checkbox"/> Change in: | <input type="checkbox"/> Response to FDA letter concerning: |
| <input type="checkbox"/> Addition of institution | <input type="checkbox"/> Correspondent | <input type="checkbox"/> Conditional approval |
| <input type="checkbox"/> Expansion / extension of study | <input type="checkbox"/> Design | <input type="checkbox"/> Deemed approved |
| <input type="checkbox"/> IRB certification | <input type="checkbox"/> Informed consent | <input type="checkbox"/> Deficient final report |
| <input type="checkbox"/> Request hearing | <input type="checkbox"/> Manufacturer | <input type="checkbox"/> Deficient progress report |
| <input type="checkbox"/> Request waiver | <input type="checkbox"/> Manufacturing | <input type="checkbox"/> Deficient investigator report |
| <input type="checkbox"/> Termination of study | <input type="checkbox"/> Protocol - feasibility | <input type="checkbox"/> Disapproval |
| <input type="checkbox"/> Withdrawal of application | <input type="checkbox"/> Protocol- other | <input type="checkbox"/> Request extension of time to respond to FDA |
| <input type="checkbox"/> Unanticipated adverse effect | <input type="checkbox"/> Sponsor | <input type="checkbox"/> Request meeting |
| <input type="checkbox"/> Emergency use: | <input type="checkbox"/> Report submission: | <input type="checkbox"/> IOL submissions only: |
| <input type="checkbox"/> Notification of emergency use | <input type="checkbox"/> Current investigator | <input type="checkbox"/> Change in IOL style |
| <input type="checkbox"/> Additional information | <input type="checkbox"/> Annual progress | <input type="checkbox"/> Request for protocol waiver |
| <input type="checkbox"/> Other reason (specify): | <input type="checkbox"/> Site waiver limit reached | |
| | <input type="checkbox"/> Final | |

0035

Section C Product Classification

| | | | |
|---|-----------------------------|---|---|
| Product code: 75CIG | C.F.R. Section: 862.1110 | Device class: <input type="checkbox"/> Class I <input type="checkbox"/> Class III | <input checked="" type="checkbox"/> Class II <input type="checkbox"/> Unclassified |
| Classification panel: Clinical Chemistry | | | |

Section D Information on 510(k) Submissions

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

Information on devices to which substantial equivalence is claimed:

| 510(k) Number | Trade or proprietary or model name | Manufacturer |
|---------------|------------------------------------|-----------------------------|
| 1 K861413 ✓ | 1 Total Bilirubin Plus Procedure | 1 Medical Analysis Systems, |
| 2 | 2 | 2 Inc. |
| 3 | 3 | 3 |
| 4 | 4 | 4 |
| 5 | 5 | 5 |
| 6 | 8 | 8 |

Section E Product Information — Applicable to All Applications

Common or usual name or classification name: Bilirubin (total or direct) test system, 75CIG

| Trade or proprietary or model name | Model number |
|------------------------------------|--------------------|
| 1 Total Bilirubin Procedure | 1 Not yet assigned |
| 2 | 2 |
| 3 | 3 |
| 4 | 4 |
| 5 | 5 |
| 6 | 6 |

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

Indications (from labeling):

For the quantitative determination of total bilirubin in serum and plasma.

0036

FDA Document Number:

| | | | |
|--|---|--|---|
| <input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete | FDA establishment registration number: 1650060 | <input checked="" type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer | <input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager / relabeler |
| Company / Institution name: Data Medical Associates, Inc. | | | |
| Division name (if applicable): | | Phone number (include area code): (817) 640-0965 | |
| Street address: 845 Avenue "G" East | | FAX number (include area code): (817) 649-2461 | |
| City: Arlington | State / Province: TX | Country: USA | ZIP / Postal Code: 76011 |
| Contact name: C. H. Morris, Ph.D. | | | |
| Contact title: Vice President, Scientific and Government Affairs | | | |
| <input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete | FDA establishment registration number: | <input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer | <input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager / relabeler |
| Company / Institution name: | | | |
| Division name (if applicable): | | Phone number (include area code): () | |
| Street address: | | FAX number (include area code): () | |
| City: | State / Province: | Country: | ZIP / Postal Code: |
| Contact name: | | | |
| Contact title: | | | |
| <input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete | FDA establishment registration number: | <input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer | <input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager / relabeler |
| Company / Institution name: | | | |
| Division name (if applicable): | | Phone number (include area code): () | |
| Street address: | | FAX number (include area code): () | |
| City: | State / Province: | Country: | ZIP / Postal Code: |
| Contact name: | | | |
| Contact title: | | | |

0037

| Section G Applicant's Information | | | |
|---|--------------------------------|--|------------------------------------|
| Company / Institution name: Data Medical Associates, Inc. | | FDA establishment registration number: 1650060 | |
| Division name (if applicable): | | Phone number (include area code): (817) 640-0965 | |
| Street address: 845 Avenue "G" East | | FAX number (include area code): (817) 649-2461 | |
| City: Arlington | State / Province: TX | Country: USA | ZIP / Postal Code: 76011 |
| Signature: | | | |
| Name: C. H. Morris, Ph.D. | | | |
| Title: Vice President, Scientific and Government Affairs | | | |
| Section H Submission correspondent (if different from above) | | | |
| Company / Institution name: | | | |
| Division name (if applicable): | | Phone number (include area code): () | |
| Street address: | | FAX number (include area code): () | |
| City: | State / Province: | Country: | ZIP / Postal Code: |
| Contact name: | | | |
| Contact title: | | | |

Your voluntary completion of this Premarket Submission Cover Sheet will not affect any FDA decision concerning your submission, but will help FDA's Center for Devices and Radiological Health process your submission more efficiently. The information you provide should apply only to a single accompanying submission. Please do not send cover sheets for any previous submissions. See the instructions for additional information on completing the cover sheet. If you have a question concerning completion of the cover sheet, please contact the Division of Small Manufacturers Assistance at (800) 638-2041 or (301) 443-6597.

0038



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

NOV 17 10 55 AM '95
FBI - MEMPHIS

November 17, 1995

Food and Drug Administration
Document Mail Center, HFZ-401
Center for Devices and Radiological Health
9200 Corporate Drive
Rockville, MD 20850

Dear Sirs:

Please find enclosed two copies of a 510(k) submission for DMA Total Bilirubin Procedure.

All inquiries should be directed to C. H. Morris, Ph.D.

Respectfully yours,

C. H. Morris, Ph.D.
Vice President, Scientific
and Government Affairs

enclosures

CHM:led

0039

Survey on Costs and Benefits of Premarket Submission Cover Sheet

1. Did use of the Premarket Submission Cover Sheet help you *organize* your submission?

| | | | | | |
|---------|---|---|---|---------|---|
| ←Not | | | | Vary→ | |
| Helpful | | | | Helpful | |
| 1 | 2 | 3 | 4 | 5 | 6 |
| | X | | | | |

2. Did use of the Premarket Submission Cover Sheet help you prepare a *complete* submission?

| | | | | | |
|---------|---|---|---|---------|---|
| ←Not | | | | Vary→ | |
| Helpful | | | | Helpful | |
| 1 | 2 | 3 | 4 | 5 | 6 |
| | | | X | | |

3. Is there any information requested by the Premarket Submission Cover Sheet that you believe is *unnecessary* or *inappropriate*?
If "yes," please provide suggestions on items to remove, and why:

| | |
|-----|----|
| Yes | No |
| X | |

Duplication of information in Sections F and G.

4. Is there any *additional* information you believe should be requested by the Premarket Submission Cover Sheet?
If "yes," please provide your suggestions on items to add:

| | |
|-----|----|
| Yes | No |
| | X |

5. Overall, is the Premarket Submission Cover Sheet organized to make it easy to complete?

| | | | | | |
|---------------|---|---|---|----------|---|
| ←Difficult to | | | | Easy to→ | |
| Complete | | | | Complete | |
| 1 | 2 | 3 | 4 | 5 | 6 |
| | | | | X | |

6. How can the Premarket Submission Cover Sheet be better organized to make it easier to complete?

Combine the information in Section F and G.

FDA USE ONLY Please do not write in this area. 0010

Document number: _____

Data entry control: _____

7. Overall, are the instructions clear and complete?

| | | | | | |
|-------------|---|---|---|--------|---|
| ←Not at all | | | | Fully→ | |
| 1 | 2 | 3 | 4 | 5 | 6 |
| | | | | X | |

8. How can the instructions be improved?

9. Approximately how much time did it take to complete the Premarket Submission Cover Sheet?

15 minutes

10. Approximately how much time did it take to complete the accompanying submission?

10 hours

11. Approximately how much time does it *normally* take to prepare similar submissions?

10 hours

12. What type(s) of personnel will normally complete the Premarket Submission Cover Sheet?

Regulatory Specialists

13. Overall, do you believe the benefits from use of the Premarket Submission Cover Sheet sheet are likely to outweigh the costs of preparing it?

| | | | | | |
|-----------------|---|---|------------------|---|---|
| ←Not Worthwhile | | | Very Beneficial→ | | |
| 1 | 2 | 3 | 4 | 5 | 6 |
| | | X | | | |

14. What is the *total* number of submissions — IDEs, 510(k)s, and PMAs, including Amendments and Supplements of all types — submitted by your firm to FDA in the past 12 months?

| | | | | |
|---|-----|-----|-------|-----|
| 1 | 2-5 | 6-9 | 10-19 | 20+ |
| | | X | | |

15. How many *full-time* employees does your firm have?

| | | | | |
|---|-----|-------|-------|-----|
| 1 | 2-9 | 10-19 | 20-49 | 50+ |
| | | | X | |

16. What types of personal computers and operating systems software do you have?

| | |
|-------------------------------------|---------------------------------------|
| <input type="checkbox"/> | IBM-compatible with DOS only |
| <input checked="" type="checkbox"/> | IBM-compatible with Windows 3.1 or NT |
| <input checked="" type="checkbox"/> | All other |

0041

16. Please provide the name and title of the person who completed this survey:

Name: C. H. Morris, Ph.D.

Title: Visiting Professor, Center for Health and Government Affairs

17. May we contact you if we have questions concerning your responses to this survey?

| | |
|-------------------------------------|--------------------------|
| Yes | No |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> |

If "yes," please provide a phone number: 817 640-0965

18. If you have additional suggestions or comments, please provide them below.

Please include this survey with your premarket submission.
Send all materials to:

Food and Drug Administration
Center for Devices and Radiological Health (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

0042



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

Pursuant to 21 C.F.R. 807. 87(j), I, C. H. Morris, Ph.D., Vice President Scientific and Government Affairs, certify that to the best of my knowledge and belief and based upon the data and information submitted to me in the course of my responsibilities as the Regulatory Officer for DMA, Inc., and in reliance thereupon, the data and information submitted in this premarket notification are truthful and accurate and that no facts material to a review of the substantial equivalence of this device have been knowingly omitted from this submission.



C. H. Morris, Ph.D.
Vice President, Scientific
and Government Affairs

0043



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

510(k) Summary

This Summary of Safety and Effectiveness is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.82.

Submitter: Data Medical Associates, Incorporated (DMA)
Contact Person: C. H. Morris, Ph.D., Vice President, Scientific and
Government Affairs

The assigned 510(k) number is : K-955300

Device: DMA Total Bilirubin Procedure
75CIG Bilirubin (total or direct), Test System

Class: II

Predicate Device: Total Bilirubin Plus Procedure, Data Medical Associates, Inc., Arlington, Texas.

Description and Intended Use: DMA's Total Bilirubin Procedure is intended for in-vitro diagnostic use for the quantitative determination of total bilirubin in human serum, and plasma.

Technological Characteristics: Both DMA procedures are based on the following principle; Total bilirubin, both conjugated and free, is measured using 3,5-dichlorophenyl diazonium tetrafluoroborate which reacts with bilirubin to form azobilirubin. The concentration of bilirubin is directly proportional to the absorbance of the azobilirubin measured spectrophotometrically at 540 nm.

0044



Data Medical Associates, Inc. • 845 Avenue G East • Arlington, TX 76011 • 817/640-0965

Comparison of Performance:

| | <u>DMA NEW</u> | <u>DMA Predicate</u> |
|--|----------------------------------|----------------------------|
| Linearity | 0.1 to 20 mg/dL | to 25 mg/dL |
| Precision Within-Run | | |
| Within Normal Range %C.V. Hitachi 704 ^R | 0.0 | 5.5 |
| Above Normal Range %C.V. Hitachi 704 ^R | 0.85, 0.66 | 2.0, 2.3 |
| Within Normal Range Manual | 5.0 | --- |
| Above Normal Range Manual | 2.2, 1.56 | --- |
| Precision Run-to-Run | | |
| Within Normal Range %C.V. | 0.0 | 3.6 |
| Above Normal Range %C.V. | 1.2, 1.2 | 1.6, 2.2 |
| Within Normal Range Manual | 6.4 | --- |
| Above Normal Range Manual | 0.83, 2.1 | --- |
| Shelf-life at 2-8°C | 14 months | 12 months |
| Sensitivity (0.001A) | 0.07 mg/dL | 0.026 |
| Analytical | 0.1 mg/dL | NA |
| Interferences | | |
| Hemoglobin | Significant above 83 mg/dL | Gross hemolysis interferes |
| Lipemia | Not significant to 1335 mg/dL | Interferes |
| Expected Values | Hitachi 704 ^R 0.2-1.5 | 0.0-1.5 |
| | Manual 0.4-1.7 | |

Statement of Equivalency: Based on the comparison of the technological characteristics of DMA's device with the predicate device, and the performance characteristics, DMA proposes that the DMA device is substantially equivalent to the predicate device.



 C. H. Morris, Ph.D.
 November 17, 1995

0045

Proprietary Information

This submission contains proprietary information.

0046

DMA Total Bilirubin Procedure

**A Pre-market Notification Under Section
510(k) of the Food, Drug, and Cosmetic Act**

0047

DMA Total Bilirubin Procedure

CONTENTS

| | |
|--|--------|
| Pre-Market Notification, 510(k)..... | 1 |
| Comparison Run Data (Hitachi 704 ^R)..... | 5-8 |
| Comparison Run Data (Manual)..... | 10-13 |
| Linear Regression Graph..... | 9, 14 |
| Combined Linearity Data..... | 15, 16 |
| Sample Package Insert..... | 17 |
| Sample Box Labeling..... | 24 |
| Sample Bottle Labeling..... | 25 |

0048

DEVICE NAME: DMA Total Bilirubin Procedure

ESTABLISHMENT REGISTRATION: 1650060

CLASS: II

DEVICE: DMA Total Bilirubin Procedure
75CIG Bilirubin (total or direct) Test System

STATEMENT OF ACTION: Data Medical Associates, Inc., hereafter referred to as DMA, proposes this Total Bilirubin Procedure for the quantitative determination of total bilirubin in serum or plasma.

The principle of this assay is found in the scientific literature (1,2). Analytical parameters, stability, and expected values for the procedure were established under expected operation conditions.

LABELING: Sample labels and labeling are attached.

STATEMENT OF EQUIVALENCY: This section compares the reagent contents, stability, and performance characteristics of DMA proposed Total Bilirubin Procedure, hereafter referred to as DMAP, to a Total Bilirubin Procedure marketed by DMA, hereafter referred to as DMAM. A copy of the labeling for DMAM Total Bilirubin Procedure is attached.

A. PRINCIPLE

Both methods are based on the following principle:

Total Bilirubin, both conjugated and free, is measured by using 3,5-dichlorophenyl diazonium tetrafluoroborate which reacts with bilirubin to form azobilirubin. Sodium dodecyl sulfate (SDS) and Lipocol accelerate the reaction. The concentration of bilirubin is directly proportional to the absorbance of the azobilirubin measured spectrophotometrically at 540 nm.

B. COMPARISON OF INGREDIENTS

3,5-dichlorophenyl diazonium tetrafluoroborate
Caffeine
SDS
Lipocol 20%
Buffer
Surfactant
Preservative

DMAP

DMAM



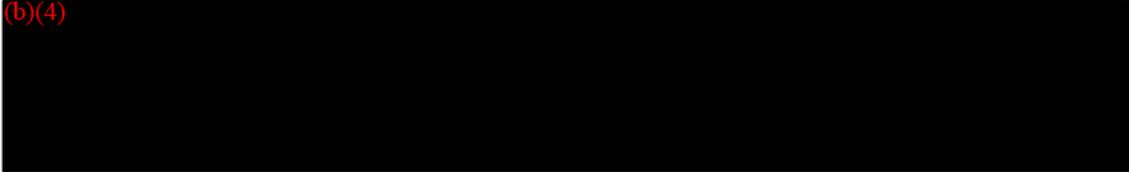
0049

C. STABILITY AT 2-8 C

| Reagent | <u>DMAP</u> exp. date | <u>DMAM</u> exp. date |
|---------|--------------------------|--------------------------|
|---------|--------------------------|--------------------------|

Stability Study Design:

(b)(4)



D. EXPECTED VALUES/NORMAL RANGES

[Redacted]

[Redacted] (b)(4)

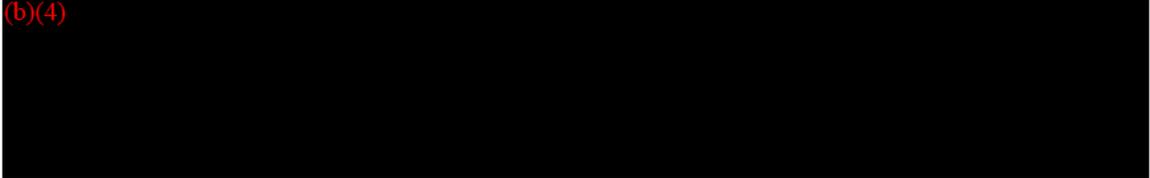
E. LINEARITY

(b)(4)

[Redacted]

Linearity Study Design:

(b)(4)



F. PRECISION

Within-Run with Hitachi 704^R

(n=20)

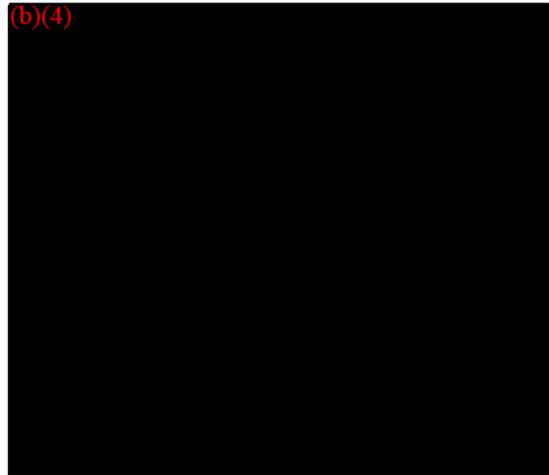
(n=30)

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

(b)(4)



0050

F. PRECISION (continued)

DMAP

DMAM

Within-Run Manual

(n=20)

(n=30)

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

Run-to-Run with Hitachi 704^R

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

Run-to-Run Manual

Level 1
mean
std. dev.
CV%

Level 2
mean
std. dev.
CV%

Level 3
mean
std. dev.
CV%

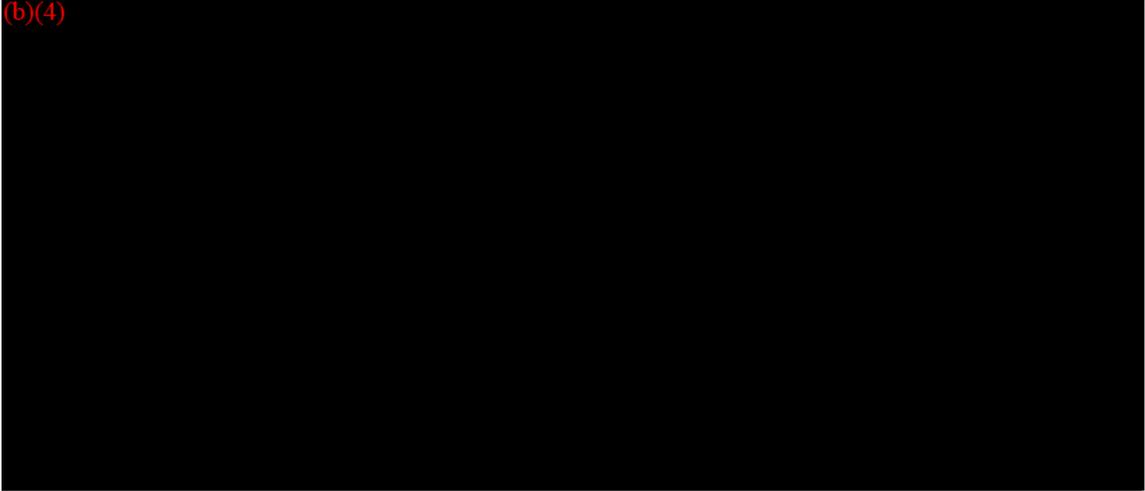
(b)(4)

(b)(4)

51

Precision Study Design:

(b)(4)



G. SENSITIVITY (b)(4)



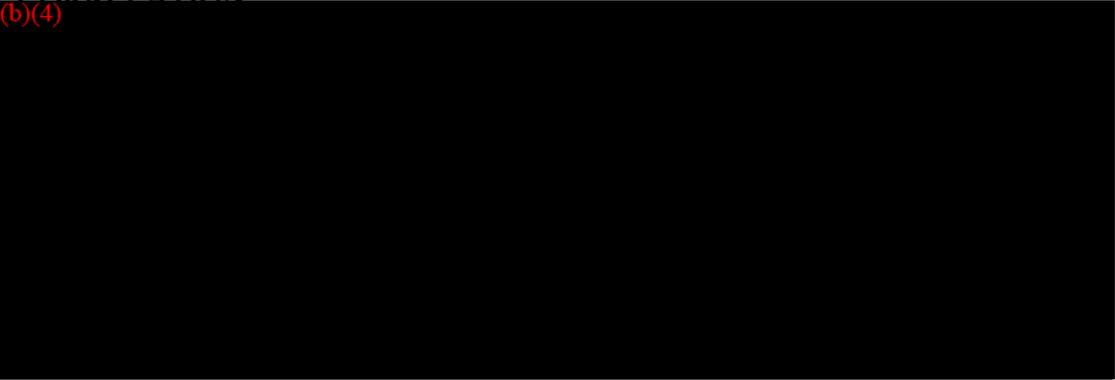
Analytical Study Design:

The analytical sensitivity was determined by assaying dilutions of a primary standard.

*Based on an instrument resolution of (b)(4) Absorbance Units

H. CORRELATION

(b)(4)



REFERENCES:

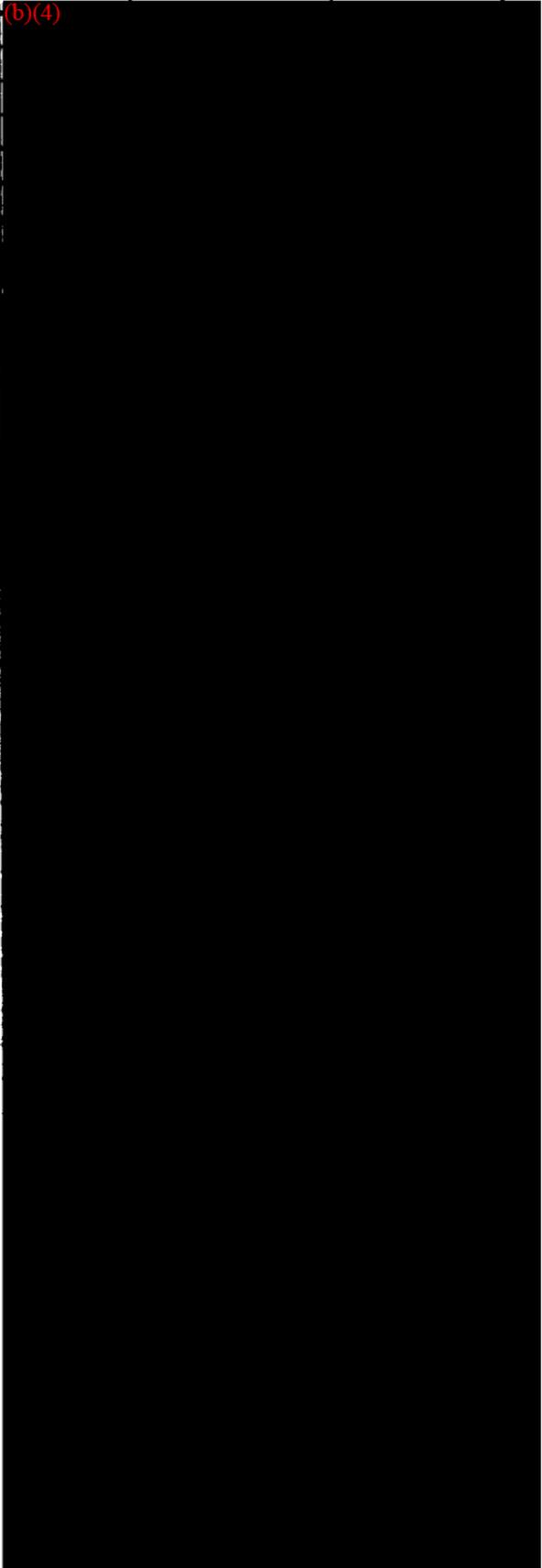
1. Tietz, N.W., *Tietz Textbook of Clinical Chemistry*, 2nd Ed., W.B. Saunders Co., Philadelphia, PA, 1994, p. 1466.
2. Van den Bergh, A., and Mueller, P., *Biochem Z.* 77, p. 90, 1916.

0052

Comparison Run Data, Hitachi 704

| Sample | DMAP | DMAM |
|--------|------|------|
|--------|------|------|

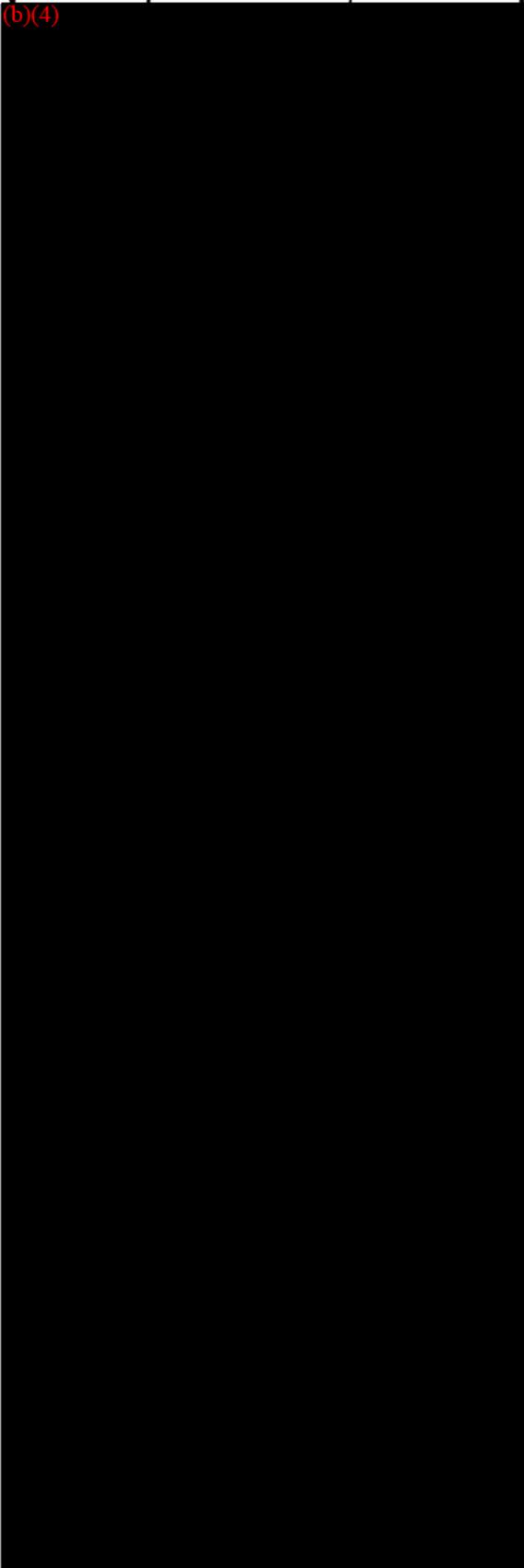
(b)(4)



0053

Comparison Run Data, Hitachi 704

| Sample | DMAP | DMAM |
|--------|------|------|
| (b)(4) | | |



0054

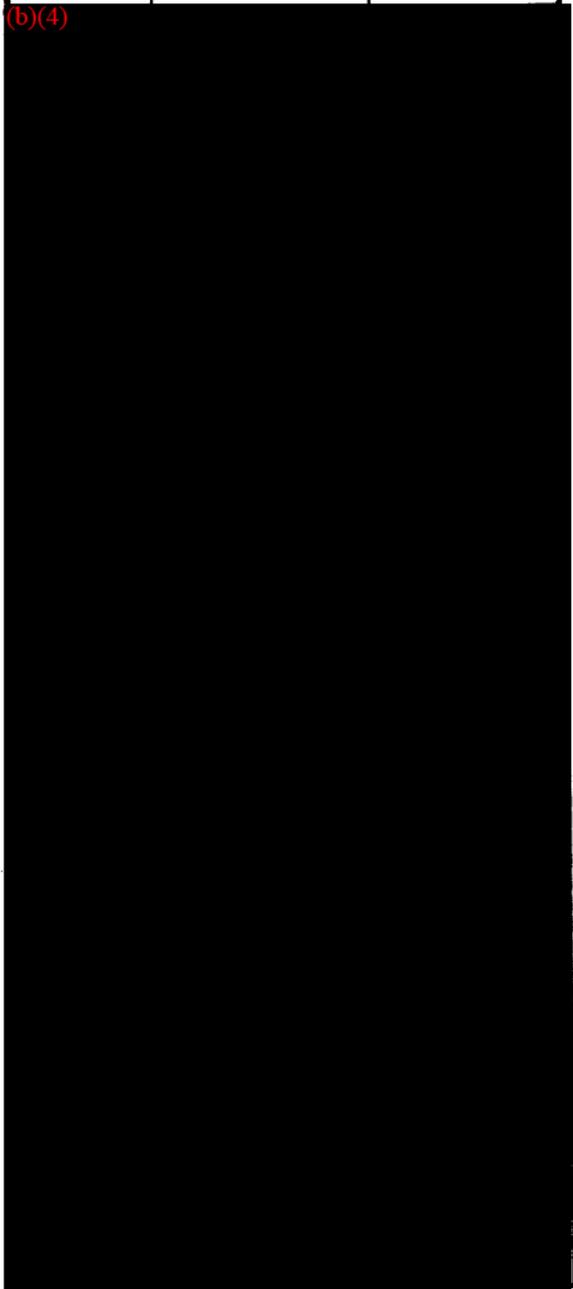
Comparison Run Data, Hitachi 704

| Sample | DMAP | DMAM |
|--------|------|------|
| (b)(4) | | |

0055

Comparison Run Data, Hitachi 704

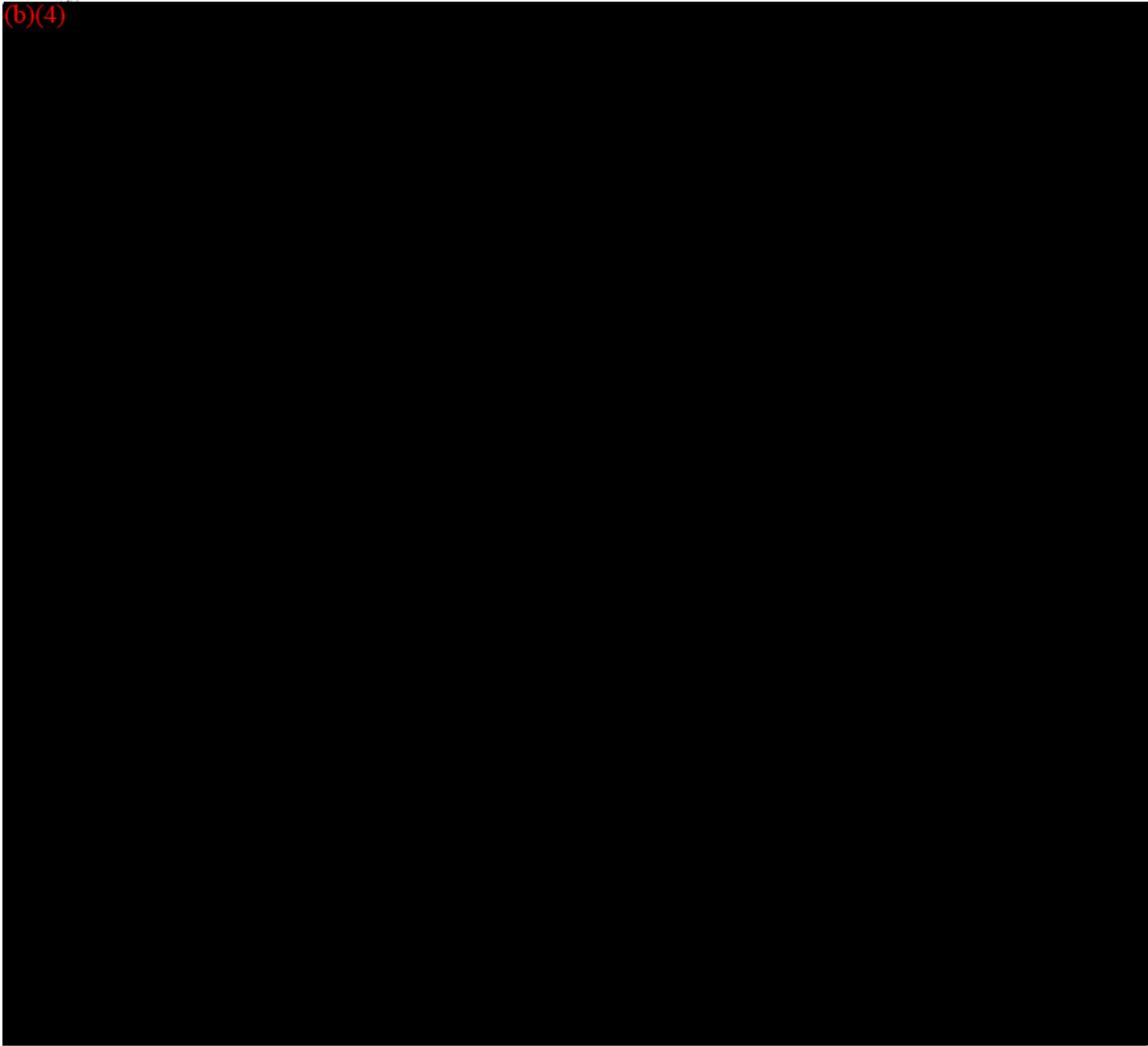
| Sample | DMAP | DMAM |
|--------|------|------|
| (b)(4) | | |



0056

Linear Regression Graph

(b)(4)



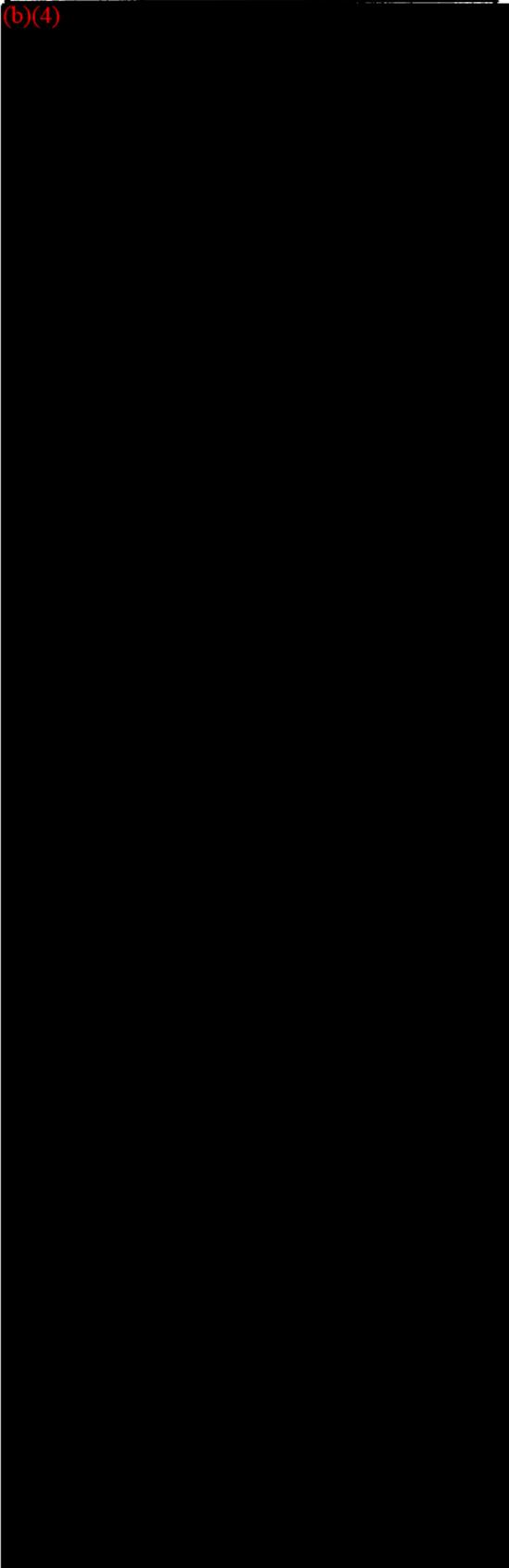
Comparison Run Data, Manual

| Sample | DMAP | DMAM |
|--------|------|------|
| (b)(4) | | |

0058

| Sample | DMAP | DMAM |
|--------|------|------|
| | | |

Comparison Run Data, Manual



(b)(4)

0059

| Sample | DMAP | DMAM |
|--------|------|------|
| (b)(4) | | |

Comparison Run Data, Manual

0060

Comparison Run Data, Manual

| Sample | DMAP | DMAM |
|--------|------|------|
| (b)(4) | | |

0061

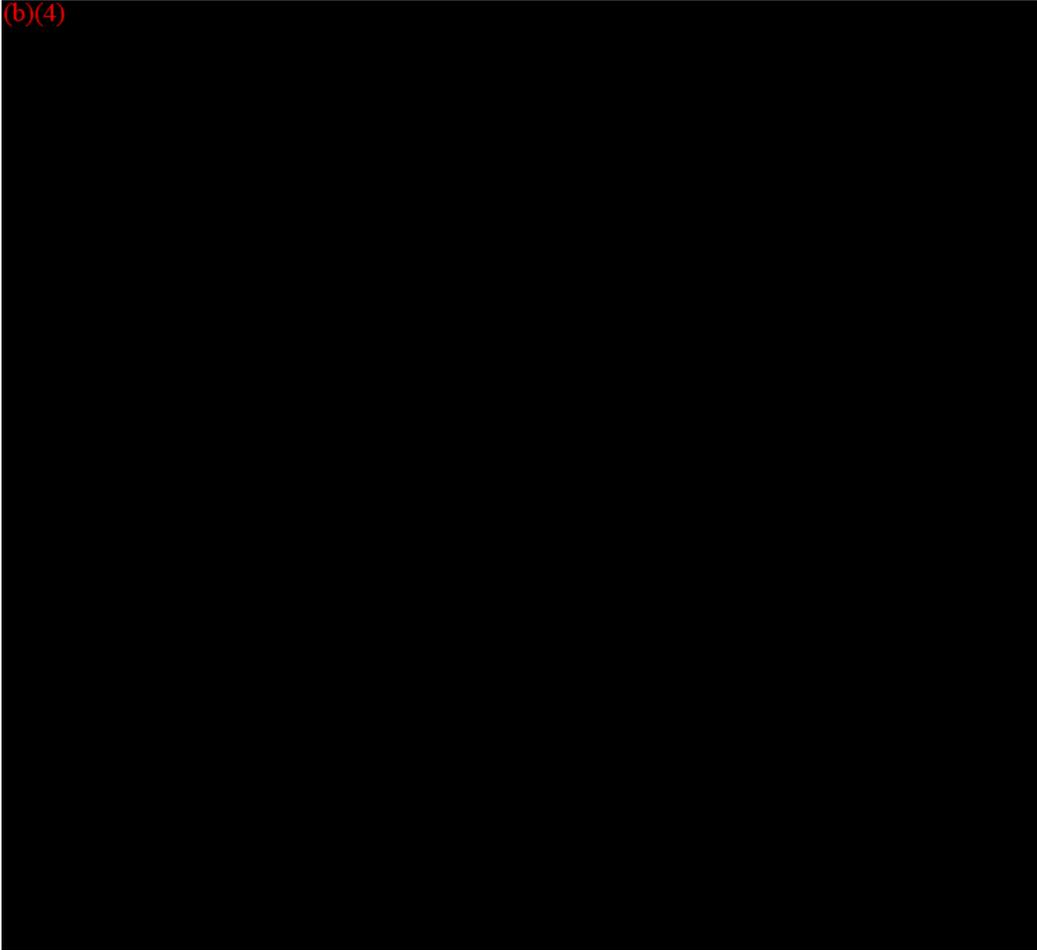
Linear Regression Graph



0062

Hitachi 704: Combined Linearity Data

(b)(4)



0063

Milton Roy 1201: Combined Linearity Data



0064

Sample Procedure/Package Insert

TOTAL BILIRUBIN PROCEDURE

Cat. No. _____

INTENDED USE

For in vitro diagnostic use. For the quantitative determination of total bilirubin in serum and plasma.

SUMMARY AND EXPLANATION

Bilirubin, a product of red blood cell destruction, is a bile pigment normally found in the blood. The average life expectancy of red blood cells is 120 days. Approximately 6 gm of hemoglobin is released per day due to their disintegration. Reticuloendothelial cells from the spleen, liver, and bone marrow phagocytize aged red cells and convert the released hemoglobin to bilirubin.¹ Serum albumin links to bilirubin and transports it to the liver where it is metabolized.

Elevated serum bilirubin can indicate impairment of liver excretory function, excessive hemolysis, or biliary tract obstruction.² Hyperbilirubinemia can also be associated with obstructive jaundice, hemolytic and hepatic jaundice, infectious hepatitis, and pernicious anemia.

PRINCIPLE

This reagent is a variation of the classical method of Van den Bergh and Mueller.³ Total bilirubin, both conjugated and free, is measured by using a stabilized diazonium salt of 3,5-dichloroaniline which reacts with bilirubin to form azobilirubin with maximum absorbance at 540 nm. Surfactants are used as accelerators. The concentration of bilirubin present is directly proportional to the absorbance of the azobilirubin measured spectrophotometrically at 540 nm.

REAGENTS PROVIDED

(for in vitro diagnostic use)

REACTIVE INGREDIENTS

| | |
|--|-------------|
| 3,5-dichlorophenyl diazonium tetrafluoroborate | 0.36 mmol/L |
| surfactants | |

PRECAUTIONS

Do not ingest. Toxicity has not been established. Acidic solution. Avoid contact with eyes and skin.

0065

DMA Total Bilirubin Procedure

REAGENT PREPARATION

Reagent is ready to use as supplied.

STORAGE AND STABILITY

The reagent is stable until the expiration date as stated on the label if stored at 2°-8°C and kept tightly capped. Protect reagent from light.

DETERIORATION

1. The working reagent should be clear, colorless to pale yellow.
2. Turbidity or failure to achieve assigned values on assayed control sera could indicate deterioration.
3. If the reagent absorbance when determined manually is greater than 0.100 at 540 nm, the reagent may have deteriorated and should not be used.
4. If a precipitate is observed, warm reagent to 37°C and mix thoroughly to dissolve.

INSTRUMENTS

The procedure may be performed on a Hitachi 704^R or on a suitable chemistry analyzer, calibrated to read at 540 nm.

SPECIMEN COLLECTION⁶

1. Fresh, unhemolyzed serum is the recommended sample.¹
2. Separate serum from cells promptly to minimize the hemolysis.
3. If plasma is used, the recommended anticoagulants are EDTA and heparin.³
4. Serum samples should be protected from light. Direct sunlight or white light exposure may cause a 50% decrease in bilirubin within one hour.¹

INTERFERING SUBSTANCES⁷

1. Lipemia does not interfere with this procedure when used on the Hitachi 704^R or with a manual instrument up to 1335 mg/dL of triglyceride.
2. When used with the Hitachi 704^R, hemoglobin levels of 83 mg/dL or above cause significant interference at a bilirubin level of 1.1 mg/dL. A hemoglobin level of up to 398 mg/dL does not significantly interfere at a bilirubin level of 5.1 mg/dL.

When used manually, hemoglobin levels of 83 mg/dL or above cause significant interference at a bilirubin level of 1.3 mg/dL. A hemoglobin level up to 204 mg/dL does not significantly interfere at a bilirubin level of 5.3 mg/dL.

3. Young has reviewed drug effects on serum bilirubin levels.⁴

0066

DMA Total Bilirubin Procedure**SAMPLE STORAGE**

Serum bilirubin is stable up to one week if stored at 2-8°C and for approximately three months if stored frozen and protected from light exposure.¹

HITACHI 704^R PROCEDURE**Hitachi 704^R Instrument Parameters**

| | |
|---------------------|-------------|
| TEST | TBil |
| ASSAY | 1 POINT:6-0 |
| SAMPLE VOLUME | 20 |
| R1 VOLUME | 400-20-NO |
| R2 VOLUME | 0-20-NO |
| WAVELENGTH | 660/546 |
| CALIB. METHOD | LINEAR-0 |
| STD (1) CONC.-POS. | 0-1 |
| STD (2) CONC.-POS. | ()-2 |
| STD (3) CONC.-POS. | ()-3 |
| STD (4) CONC.-POS. | ()-4 |
| STD (5) CONC.-POS. | ()-5 |
| STD (6) CONC.-POS. | ()-6 |
| UNIT | MG/DL |
| SD LIMIT | 0.1 |
| DUPLICATE LIMIT | 200 |
| SENSITIVITY LIMIT | 0 |
| ABS LIMIT (INC.DEC) | 0 (INC) |
| PROZONE LIMIT | 0 (LOWER) |
| EXPECTED VALUE | 0.0-1.5 |
| INSTRUMENT FACTOR | 1.00 |

The above parameters should be used when programming the Hitachi 704^R. Consult your instrument manual for further instructions.

MATERIALS PROVIDED

Total Bilirubin Reagent

MATERIALS REQUIRED BUT NOT PROVIDED

1. DMA's Bilirubin Calibrators (Cat. No. 2241-151 or 2241-152) or equivalent.
2. Pipettes for accurately dispensing 1.0 mL volumes.
3. Micropipettes for dispensing 0.05 mL volumes.
4. Suitable manual instrument calibrated to read at 540 nm.
5. Hitachi 704^R Analyzer, or equivalent, with manual and accessories.

MANUAL PROCEDURES

1. For each sample, dispense 1.0 mL of Total Bilirubin Reagent into labeled test tubes.
2. Add 0.05 mL of calibrator, control, and sample to its respective tube. Mix immediately. Use 0.05 mL of deionized water as sample for reagent blank. 0067
3. Incubate at reaction temperature for 5 minutes.
4. Set the wavelength of the instrument at 540 nm. Zero with reagent blank.
5. Read and record absorbance of samples.

DMA Total Bilirubin Procedure

SAMPLE BLANK

Sample blanks are required for all turbid, icteric and hemolyzed samples. This includes many control sera and calibrators.

1. For each sample to be blanked, dispense 1.0 mL normal saline into labeled test tubes.
2. Add 0.05 mL of each sample to be blanked. Mix and incubate for 5 minutes at the reaction temperature.
3. Set the wavelength of the instrument at 540 nm. Zero with normal saline.
4. Read and record absorbance of blank. Subtract this absorbance from Step 5 in the Manual Procedure Section. The corrected absorbance is used in the calculation of results.

STABILITY OF FINAL REACTION MIXTURE

The final colored product is stable for 60 minutes at controlled room temperature (15-30°C). The Hitachi 704^R reads each standard and sample at the same time.

CALIBRATION

It is not necessary to determine a standard curve with this procedure, since the reaction is linear to 20.0 mg/dL. However, a reagent blank and calibrator should be employed with each set of unknowns assayed.

LINEARITY

Linearity extends to 20.0 mg/dL. Samples exceeding linearity should be diluted with normal saline and repeated. Multiply the concentration by the dilution factor when calculating the unknown.

QUALITY CONTROL

Normal and abnormal control sera of known concentrations of total bilirubin should be analyzed routinely with each group of unknown samples. DMA Data-Trol N and Data-Trol A (Cat. No. 1902-605 and 1901-605) are recommended for this purpose.

CALCULATION OF RESULTS

The Hitachi 704^R analyzer automatically calculates the results.

Use the equation below to calculate the total bilirubin concentration of a sample when using the manual procedure.

$$\frac{\text{Abs. of Unknown}}{\text{Abs. of Calibrator}} \times \text{Conc. of Calibrator} = \text{Total Bilirubin mg/dL}$$

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DMA Total Bilirubin Procedure

Example: Absorbance of Unknown = 0.052
Absorbance of calibrator = 0.180
Concentration of Calibrator = 5.2 mg/dL

$$\frac{0.052}{0.180} \times 5.2 = 1.5 \text{ mg/dL}$$

LIMITATIONS

See Storage and Stability, Deterioration, Specimen Collection, Interfering Substances, Sample Storage, Stability of Final Reaction Mixture, and Linearity sections for limitations to this procedure.

Bilirubin calibrators in chloroform may not be used in this procedure since chloroform miscible solvents are not employed.

Bilirubin is extremely light sensitive. Calibrator, control and unknown specimens must be stored protected from light sources for optimal stability.

EXPECTED VALUES⁷

Normal Range

Samples from 141 individuals, normal with regard to bilirubin levels, were assayed using the Hitachi 704^R. The observed range was 0.2 to 1.5 mg/dL.

Samples from 133 individuals, normal with regard to bilirubin levels, were assayed using the manual procedure. The observed range was 0.4 to 1.7 mg/dL.

The published normal range is 0.0 to 1.5.⁵

These ranges should serve only as guidelines. It is recommended that each laboratory establish its own range of expected values, since differences may exist between instruments, laboratories and local populations.

PERFORMANCE CHARACTERISTICS⁷

The Performance Characteristics were established on a Hitachi 704^R analyzer and using the manual procedure. The user should establish performance characteristics if the product is used on another analyzer.

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DMA Total Bilirubin Procedure

PRECISION

Within-run reproducibility was determined by assaying three levels of control sera 20 times.

Within-Run on the Hitachi 704^R

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | 0.60 mg/dL | 0.00 | 0.0 |
| Moderate | 5.9 mg/dL | 0.05 | 0.85 |
| High | 15.2 mg/dL | 0.10 | 0.66 |

Within-Run, Manual Procedure

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | 1.0 mg/dL | 0.05 | 5.0 |
| Moderate | 5.9 mg/dL | 0.13 | 2.2 |
| High | 14.7 mg/dL | 0.23 | 1.56 |

Run-to-run reproducibility was determined by assaying three levels of control sera as single points for 10 runs.

Run-to-Run on the Hitachi 704^R

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | 0.6 mg/dL | 0.00 | 0.0 |
| Moderate | 5.7 mg/dL | 0.07 | 1.2 |
| High | 14.5 mg/dL | 0.17 | 1.2 |

Run-to-Run, Manual Procedure

| <u>Sample</u> | <u>Mean</u> | <u>Std. Dev.</u> | <u>CV%</u> |
|---------------|-------------|------------------|------------|
| Low | 1.1 mg/dL | 0.07 | 6.4 |
| Moderate | 6.0 mg/dL | 0.05 | 0.83 |
| High | 15.2 mg/dL | 0.32 | 2.1 |

COMPARISON

A comparison of the DMA Total Bilirubin Procedure with the DMA Total Bilirubin Plus Procedure was performed on the Hitachi 704^R on 169 samples in a range of 0.1 mg/dL to 19.5 mg/dL.

The resultant correlation equation is $y = 1.00x - 0.04$ where y = the DMA Total Bilirubin Procedure, and x = the DMA Total Bilirubin Plus Procedure. A correlation coefficient of 0.999 was obtained.

A comparison of the DMA Total Bilirubin Procedure with the DMA Total Bilirubin Plus Procedure was performed manually on 167 samples in a range of 0.2 mg/dL to 21.6 mg/dL.

The resultant correlation equation is $y = 0.99x - 0.01$ where y = the DMA Total Bilirubin Procedure, and x = the DMA Total Bilirubin Plus Procedure. A correlation coefficient of 0.999 was obtained.

DMA Total Bilirubin Procedure

SENSITIVITY⁷

Based on the Hitachi 704^R instrument resolution of $A = 0.001$, the DMA Total Bilirubin Procedure has a sensitivity of 0.07 mg/dL. The analytical sensitivity is 0.1 mg/dL.

Based on a manual instrument resolution of $A = 0.001$, the DMA Total Bilirubin Procedure has a sensitivity of 0.03 mg/dL. The analytical sensitivity is 0.1 mg/dL.

BIBLIOGRAPHY

1. Tietz, N.W., *Fundamentals of Clinical Chemistry*, 2nd Ed., W.B. Saunders, Philadelphia, 1976, p. 1028.
2. Annino, J.S., *Clinical Chemistry Principles and Procedures*, 2nd Ed., Little, Brown and Company, Boston, 1960, p. 203.
3. Van den Bergh, A., and Mueller, P., *Biochem Z.* 77, p. 90, 1916.
4. Young, D.S., *Effects of Drugs on Clinical Laboratory Tests*, 3rd Ed., AACC Press, Washington, D.C., 1990, p. 3-61--3-72.
5. Henry, R.J., Cannon, D.C., and Winkelman, J.W., *Clinical Chemistry Principles and Technics*, 2nd ed., Harper and Row, New York, 1974, p. 1042.
6. NCCLS: Standard Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture (H3), Standard Procedures for the Collection of Diagnostic Blood Specimens by Skin Puncture (H4), Standard Procedures for Blood Specimen Processing (H18), National Committee for Clinical Laboratory Standards, Villanova, PA.
7. Data on file. Data Medical Associates, Inc., Arlington, Texas.

^RHitachi 704 is a registered trademark of Boehringer Mannheim Diagnostics, Inc., Indianapolis, Indiana, 46250

DMA, Inc. 845 Avenue "G" East, Arlington, TX 76011 U.S.A.

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DMA Total Bilirubin Procedure

Sample Box Label

(Logo)

Total Bilirubin Reagent Cat. No. _____ - _____
For the quantitative determination of Total Bilirubin in serum and plasma

For In Vitro Diagnostic Use

Contains: Total Bilirubin Reagent 1 x 200 mL

Reactive Ingredients:
3,5-dichlorophenyl diazonium tetrafluoroborate 0.36 mmol/L, Surfactants.

CAUTION: Do not ingest. Avoid contact with eyes, skin, and clothing.

Store at 2°-8°C.

Lot. No. _____ Expiration Date _____

DMA, Inc., Arlington, Texas 76011 U.S.A

0072

DMA Total Bilirubin Procedure

Sample Bottle Label

(Logo)
Total Bilirubin Reagent

Cat. No. ____ - ____
200 mL

For In Vitro Diagnostic Use
For the quantitative determination of Total Bilirubin in serum and plasma

3,5-dichlorophenyl diazonium tetrafluoroborate 0.36 mmol/L, Surfactants.

CAUTION: Do not ingest. Avoid contact with eyes, skin, and clothing.

Store at 2°-8°C.

Lot. No. _____ Expiration Date _____

DMA, Inc., Arlington, Texas 76011 U.S.A

0073

TOTAL BILIRUBIN PLUS PROCEDURE

(For the Quantitative Determination of Total Bilirubin in Serum)

SUMMARY AND EXPLANATION

Bilirubin, a product of red blood cell destruction, is a bile pigment normally found in the blood. The average life expectancy of red blood cells is 120 days. Approximately 6 gm of hemoglobin is released per day due to their disintegration. Reticuloendothelial cells from the spleen, liver, and bone marrow phagocytize aged red cells and convert the released hemoglobin to bilirubin.¹ Serum albumin links to bilirubin and transports it to the liver where it is metabolized.

Elevated serum bilirubin can indicate impairment of liver excretory function, excessive hemolysis, or biliary tract obstruction.² Hyperbilirubinemia can also be associated with obstructive jaundice, hemolytic and hepatic jaundice, infectious hepatitis, and pernicious anemia.

PRINCIPLE

This reagent is a variation of the classical method of Van den Bergh and Mueller.³ Total bilirubin, both conjugated and free, is measured by using a stabilized diazonium salt of 3,5-dichloroaniline which reacts with bilirubin to form azobilirubin with maximum absorbance at 540 nm. Caffeine and a surfactant are used as reaction accelerators. The concentration of bilirubin present is directly proportional to the absorbance of the azobilirubin measured spectrophotometrically at 540 nm.

REAGENTS PROVIDED

(for in vitro diagnostic use)

REACTIVE INGREDIENTS

| | |
|--|-------------|
| caffeine | 50 mmol/L |
| 3,5-dichlorophenyl diazonium tetrafluoroborate | 0.18 mmol/L |
| surfactant | |
| preservative | |
| stabilizer | |

PRECAUTIONS

Do not ingest. Toxicity has not been established. Avoid contact with eyes and skin.

REAGENT PREPARATION

Reagent is ready to use as supplied.

Questions? Contact FDA/CDRH/OCE/DID at CDRHFOISTATUS@fda.hhs.gov OR 301-796-8118

STORAGE AND STABILITY

The reagent is stable until the expiration date as stated on the label if stored at 2°—8°C and kept tightly capped. Protect reagent from light.

DETERIORATION

1. The reagent should be clear, colorless to pale yellow.
2. Turbidity or failure to achieve assigned values on assayed control sera could indicate deterioration.
3. If the reagent absorbance is greater than 0.100 at 540 nm, the reagent may have deteriorated and should not be used.
4. If a precipitate is observed, warm reagent to 37°C and mix thoroughly to dissolve.

INSTRUMENTS

The procedure may be performed by using a suitable chemistry analyzer, spectrophotometer or colorimeter calibrated to read at 540 nm.

SPECIMEN COLLECTION

1. Fresh unhemolyzed serum is the recommended sample.¹
2. Separate serum from cells promptly to minimize hemolysis.
3. If plasma must be used, the recommended anticoagulants are EDTA and heparin.
4. Serum samples should be protected from light. Direct sunlight or white light exposure may cause a 50% decrease in bilirubin within one hour.¹

INTERFERING SUBSTANCES

1. Gross hemolysis must be avoided since it causes falsely elevated results with this method. Lipemic sera yield falsely elevated results due to turbidity. A serum blank should be used to correct for turbidity in serum samples, control sera and calibrators.
2. Young has reviewed drug effects on serum bilirubin levels.⁴

SAMPLE STORAGE

Serum bilirubin is stable up to one week if stored at 2°—8°C and for approximately three months if stored frozen and protected from light exposure.¹

0074

AUTOMATED PROCEDURE

PROCEDURE PARAMETERS

| | |
|-----------------------|------------------|
| Wavelength | 540 nm |
| Alternate Wavelengths | 500-540 nm |
| Reaction Type | Endpoint |
| Reaction Temperature | 25°, 30° or 37°C |
| Reaction Direction | Increasing |
| Sample/Reagent Ratio | 1:20 |
| Reaction Time | 2 Minutes |
| Low Absorbance Limit | <0.100 |
| Standard Value | Varies |
| Low Normal | 0.0 mg/dL |
| High Normal | 1.5 mg/dL |
| Linearity | 25.0 mg/dL |

The above parameters should be used when programming discrete, photometric, and centrifugal chemistry analyzers for the Total Bilirubin Plus Procedure. Consult your instrument manual for further instructions. Specific programming applications for most popular automated analyzers are available from DMA Customer Service.

MATERIALS PROVIDED

Total Bilirubin Plus Reagent

MATERIALS REQUIRED BUT NOT PROVIDED

1. DMA's Bilirubin Calibrators (Cat. No. 2241-151 or 2241-152) or equivalent.
2. Pipettes for accurately dispensing 1.0 mL volumes.
3. Micropipettes for dispensing 0.05 mL volumes.
4. Suitable instrument calibrated to read at 540 nm.

MANUAL PROCEDURES

1. For each sample, dispense 1.0 mL of Total Bilirubin Plus Reagent into labeled test tubes.
2. Add 0.05 mL of calibrator, control, and sample to its respective tube. Mix immediately. Use 0.05 mL of deionized water as sample for reagent blank.
3. Incubate at reaction temperature for 2 minutes.
4. Set the wavelength of the instrument at 540 nm. Zero with reagent blank.
5. Read and record absorbance of samples.

SAMPLE BLANK

Sample blanks are required for all turbid, icteric, lipemic and hemolyzed samples. This includes many control sera and calibrators.

1. For each sample to be blanked, dispense 1.0 mL normal saline into labeled test tubes.
2. Add 0.05 mL of each sample to be blanked. Mix and incubate for 2 minutes at the reaction temperature.
3. Set wavelength of instrument at 540 nm. Zero with normal saline.
4. Read and record absorbance of blank. Subtract this absorbance from Step 5 in the Manual Procedure Section. The corrected absorbance is used in the calculation of results.

STABILITY OF FINAL REACTION MIXTURE

The final colored product is stable for 30 minutes at controlled room temperature (15°—30°C).

CALIBRATION

It is not necessary to determine a standard curve with this procedure, since the reaction is linear to 25.0 mg/dL. However, a reagent blank and calibrator should be employed with each set of unknowns assayed.

LINEARITY

Linearity extends to 25.0 mg/dL. Samples exceeding linearity should be diluted with normal saline and repeated. Multiply the concentration by the dilution factor when calculating the unknown.

QUALITY CONTROL

Normal and abnormal control sera of known concentration of total bilirubin should be analyzed routinely with each group of unknown samples. DMA's Data-Trol N and Data-Trol A (Cat. No. 1902-605 and 1901-605) are recommended for this purpose.

CALCULATION OF RESULTS

Use the equation below to calculate the total bilirubin concentration of a sample.

$$\frac{\text{Abs. of Unknown}}{\text{Abs. of Calibrator}} \times \text{Conc. of Calibrator} = \text{Total Bili. mg/dL}$$

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Example:

Absorbance of Unknown = 0.052
Absorbance of Calibrator = 0.180
Concentration of Calibrator = 5.2 mg/dL

$$\frac{0.052}{0.180} \times 5.2 = 1.5 \text{ mg/dL}$$

LIMITATIONS

Bilirubin calibrators in chloroform may not be used in this procedure since chloroform miscible solvents are not employed.

Bilirubin is extremely light sensitive. Calibrator, control and unknown specimens must be stored protected from light sources for optimal stability.

EXPECTED VALUES

NORMAL RANGE⁵ 0 - 1.5 mg/dL

This range should serve as a guideline. It is recommended that each laboratory establish its own range of expected values, since differences exist between instruments, laboratories, and local populations.

PERFORMANCE CHARACTERISTICS

PRECISION

Within-run reproducibility was established by assaying three levels of control sera 30 times.

| WITHIN-RUN | MEAN | STD. DEV. | CV % |
|---------------|------|-----------|------|
| LOW..... | 1.1 | 0.06..... | 5.5 |
| MODERATE..... | 6.1 | 0.12..... | 2.0 |
| HIGH..... | 19.3 | 0.45..... | 2.3 |

Run-to-run reproducibility was obtained by assaying three levels of control sera for 10 runs.

| RUN-TO-RUN | MEAN | STD. DEV. | CV % |
|---------------|------|-----------|------|
| LOW..... | 1.1 | 0.04..... | 3.6 |
| MODERATE..... | 6.3 | 0.10..... | 1.6 |
| HIGH..... | 20.2 | 0.44..... | 2.2 |

COMPARISON

A comparison of the DMA Total Bilirubin Plus Procedure with the DMA Auto-Bilirubin/Total Procedure was performed on 67 human serum samples in a range of 0.4 to 14.0 mg/dL. A correlation coefficient of 0.991 was obtained.

SENSITIVITY

Based on an instrument resolution of A=0.001, the DMA Total Bilirubin Plus Procedure has a sensitivity of 0.026 mg/dL.

BIBLIOGRAPHY

1. Tietz, N.W., *Fundamentals of Clinical Chemistry*, 2nd ed., W.B. Saunders Co., Philadelphia, 1976, p. 1028.
2. Annino, J.S., *Clinical Chemistry Principles and Procedures*, 2nd Ed., Little, Brown and Company, Boston, 1960, p. 203.
3. Van den Bergh, A. and Mueller, P., *Biochem. Z.* 77, p. 90, 1916.
4. Young, D.S., *Effects of Drugs on Clinical Laboratory Tests*, 3rd ed., AACC Press, Washington, D.C., 1990, p. 3-61 — 3-72.
5. Henry, R., Cannon, D.C., and Winkelman, J.W., *Clinical Chemistry Principles and Technics*, 2nd ed., Harper and Row, Hagerstown, 1974, p. 1042.

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NOTES:

CUSTOMER SERVICE

TECHNICAL SERVICE

DMA's technical service staff is available to assist you with any questions you may have concerning the use of our products. They are experienced in laboratory methods and are familiar with most automated chemistry analyzers found in today's laboratories.

Please call for assistance with your technical problems.

ORDERING INFORMATION

DMA products are available from local distributors throughout the U.S., Canada, and Puerto Rico. Distributor stocks are further backed by an inventory of all products at DMA's manufacturing facilities. Contact DMA Customer Service for any assistance you may need in obtaining DMA products.

In the continental U.S., Virgin Islands and Puerto Rico, call 800/433-7224

In Texas, call 800/633-5338

In Alaska, Hawaii and Canada, call collect 817/640-0965

Telex Number: 5101012780 DMA TX

Fax Number: 817/649-2461

DMA, Inc. 845 Avenue G East Arlington, Texas 76011

0077

SAMPLE

TOTAL BILIRUBIN Plus
For the quantitative determination of TOTAL BILIRUBIN in serum
STORE AT 2°-8°C
CAT. NO. 1240-200

CAT. NO.
1240-200

TOTAL BILIRUBIN Plus

FOR IN VITRO DIAGNOSTIC USE

SET CONTAINS: Total Bilirubin Plus, 1 x 200 mL

REACTIVE INGREDIENTS: caffeine 50 mmol/L, 3,5-dichlorophenyl diazonium tetrafluoroborate 0.18 mmol/L, surfactant, preservative, stabilizer.

CAUTION: Avoid contact. In case of contact, rinse with water.

STORE AT 2°-8°C

Lot K103 Exp. 15 Jan 96

DMA
Arlington,
TX 76011

CAT. NO. 200 mL

1242-200
TOTAL BILIRUBIN Plus

FOR IN VITRO DIAGNOSTIC USE

For the quantitative determination of Total Bilirubin in serum

REACTIVE INGREDIENTS: caffeine 50 mmol/L, 3,5-dichlorophenyl diazonium tetrafluoroborate 0.18 mmol/L, surfactant, preservative, stabilizer.

CAUTION: Avoid contact. Do not ingest. In case of contact, rinse with water.

STORE AT 2°-8°C

Lot K103 Exp. 15 Jan 96

0078

SAMPLE

STORE AT 2°-8°C

For the quantitative determination of TOTAL BILIRUBIN in serum

TOTAL BILIRUBIN Plus

1240-400

CAT. NO.

Lot K103 Exp. 15 Jan 96

CAT. NO.

1240-400

TOTAL BILIRUBIN Plus

FOR IN VITRO DIAGNOSTIC USE

SET CONTAINS: Total Bilirubin Plus, 2 x 200 mL

REACTIVE INGREDIENTS: caffeine 50 mmol/L, 3,5-dichlorophenyl diazonium tetrafluoroborate 0.18 mmol/L, surfactant, preservative, stabilizer.

CAUTION: Avoid contact. In case of contact, rinse with water.

STORE AT 2°-8°C

DVA
Arlington,
TX 76011

CAT. NO.

200 mL

1242-200

TOTAL BILIRUBIN Plus

FOR IN VITRO DIAGNOSTIC USE

For the quantitative determination of Total Bilirubin in serum

REACTIVE INGREDIENTS: caffeine 50 mmol/L, 3,5-dichlorophenyl diazonium tetrafluoroborate 0.18 mmol/L, surfactant, preservative, stabilizer.

CAUTION: Avoid contact. Do not ingest. In case of contact, rinse with water.

STORE AT 2°-8°C

Lot K103 Exp. 15 Jan 96

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SAMPLE



CAT. NO.

200 mL

1242-200
TOTAL BILIRUBIN Plus

FOR IN VITRO DIAGNOSTIC USE

For the quantitative determination of Total Bilirubin in serum

REACTIVE INGREDIENTS: caffeine 50 mmol/L, 3,5-dichlorophenyl diazonium tetrafluoroborate 0.18 mmol/L, surfactant, preservative, stabilizer.

CAUTION: Avoid contact. Do not ingest. In case of contact, rinse with water.

STORE AT 2°-8°C

Exp. 15 Jan 96

Lot K103

0080

CIBA - CORNING

Records Released under FOIA Request #2016-2065 Released by CDRH on 8/30/2016

Ciba Corning Diagnostics Corp.
17395 Daimler Street
Irvine, CA 92714
Telephone 714-261-3058
Telefax 714-261-2294
Telex No.: 312690

December 19, 1990

Ms. Annette Wells
DMA
845 Ave. G East
Arlington, TX 76011

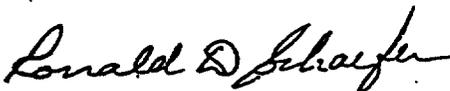
Dear Ms. Well:

The CAP EXCELL product has the same formulation as products that have been in distribution by Ciba Corning (formally Ortho Diagnostics Inc.) prior to May 28, 1976. Therefore, a 510(k) was not obtained. Attached is copy of the original Medical Device Listing.

The product does not meet the requirements of the Hazard Communication Regulation to be classified as hazardous. The product does not require an MSDS.

If you need further information, please contact me.

Sincerely yours,



Ronald D. Schaefer, Ph.D.
Director of Quality Assurance/Regulatory Affairs

0081

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

1st This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2)) and may be a violation of 18 U.S.C. 1001.

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|--|------------------|--|-------------------------------------|--|---------------|--|--------------------------|--|--|--|------------------|--|-----|----------------|-----|--|----|--|----|--|----|--|----|--|
| 1 | | 7 | | 8 | | 14 | | 15 | | 16 | | 21 | | 22 | | 27 | | | | | | | | | |
| 1. DOCUMENT NUMBER | | | | 2. INITIAL DOCUMENT NUMBER | | | | 3. REASON FOR SUBMISSION | | | | 4. ACTIVITY DATE | | | 5. REPORT DATE | | | | | | | | | | |
| A 268142 | | | | | | | | A | | | | MO. DAY YR. | | | MO. DAY YR. | | | | | | | | | | |
| | | | | | | | | | | | | | | | 12 27 77 | | | | | | | | | | |
| 6. OWNER/OPERATOR NAME | | | | | | | | | | 7. OWNER/OPERATOR ID NO. | | | | | | | | | | | | | | | |
| L Ortho Diagnostics Inc. | | | | | | | | | | 2250051 | | | | | | | | | | | | | | | |
| 8. CLASSIFICATION NAME | | | | | | | | | | 9. CLASSIFICATION NO. | | | | | | | | | | | | | | | |
| Multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| 10. PROPRIETARY NAME | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| 184 COMMON OR USUAL NAME | | | | | | | | | | | | | | | | | | | | | | | | | |
| Various clinical chemistry controls | | | | | | | | | | | | | | | | | | | | | | | | | |
| 12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? | | | | | | | | | | 324 | | | | | | | | | | | | | | | |
| | | | | | | | | | | <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO | | | | | | | | | | | | | | | |
| 12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: | | | | | | | | | | 325 | | 326 | | 329 | | 334 | | | | | | | | | |
| | | | | | | | | | | SECTION | | PARA. | | | | | | | | | | | | | |
| 13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? | | | | | | | | | | 335 | | | | | | | | | | | | | | | |
| | | | | | | | | | | <input type="checkbox"/> YES <input type="checkbox"/> NO | | | | | | | | | | | | | | | |
| 13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER: | | | | | | | | | | 336 | | 345 | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | |
| 14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? | | | | | | | | | | 346 | | | | | | | | | | | | | | | |
| | | | | | | | | | | <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO | | | | | | | | | | | | | | | |
| 28 | | 29 | | 31 | | 37 | | 15. | | 16. | | 38 | | 39 | | 40 | | 41 | | 42 | | 43 | | 44 | |
| SEQ | | EST. REG. NUMBER | | ESTABLISHMENT NAME | | 17. EST. TYPE | | | | | | D | | F | | I | | M | | P | | R | | | |
| S01 | | 2250051 | | Ortho Diagnostics Inc., Raritan, NJ | | E | | | | | | | | | | | | | | | | | | | |
| S02 | | | | | | | | | | | | | | | | | | | | | | | | | |
| S03 | | | | | | | | | | | | | | | | | | | | | | | | | |
| S04 | | | | | | | | | | | | | | | | | | | | | | | | | |
| S06 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 18. SIGNATURE | | | | | | | | | | 19. TYPED OR PRINTED NAME | | | | | | | | | | | | | | | |
| | | | | | | | | | | Questions? Contact FDA/CDRH/OCE/DID at CDRHFOISTATUS@fda.hhs.gov OR 301-796-8118 | | | | | | | | | | | | | | | |

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

OCT 25 1988

Verichem Laboratories, Inc.
Attn: Anthony J. Dimonte
90 Narragansett Avenue
Providence, RI 02907

Re: K882059/A
Bilirubin Standard
Dated: August 23, 1988
Received: August 31, 1988
Regulatory Class: II

Dear Mr. Dimonte:

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 to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market the device, subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, and labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Performance Standards) or class III (Pre-market 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. In addition, the Food and Drug Administration (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 the Radiation Control for Health and Safety Act of 1968, or other Federal Laws or Regulations.

This letter immediately will allow you to begin marketing your device as described. An FDA finding of substantial equivalence of your device to a pre-amendments device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in anyway represent your device or its labeling as being approved by FDA. If you desire specific advice on the labeling for your device please contact the Division of Compliance Operations, Regulatory Guidance Branch (HFZ-323) at (301) 427-8040. Other general information on your responsibilities under the Act, may be obtained from the Division of Small Manufacturers Assistance at their toll free number (800) 638-2041 or at (301) 443-6597.

Sincerely yours,

Jerome A. Donlon, M.D. Ph.D.

Jerome A. Donlon, M.D., Ph.D. 0084
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health