Application Integrity Policy

The Application Integrity Policy (AIP) focuses on the integrity of data and information in applications submitted for FDA review and approval. On September 10, 1991, the FDA published the Notice of this policy formally entitled, "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities; Final Policy" (Federal Register, 56 FR 46191). The AIP described the Agency's approach regarding the review of applications that may be affected by an applicant’s wrongful acts that raise significant questions about data reliability.

Applied Biotech Inc.’s Application(s) Subject to Application Integrity Policy

On March 9, 2005, FDA notified Applied Biotech Inc. (ABI), San Diego, California, that they had been added to the Application Integrity Policy (AIP) list-signifying that FDA is deferring substantive scientific review of one or more of a firm’s applications and/or is proceeding to withdraw approved applications. FDA had conducted a number of inspections and had identified numerous deficiencies, which raised data integrity issues. In response to the AIP notification, ABI voluntarily withdrew the applications that FDA had specifically questioned, and the cleared premarket notifications (510(k)) associated with those applications.

Bioreserarch Monitoring

Overview of Bioreserarch Monitoring Program at the Center for Devices and Radiological Health

- Of the 175 clinical investigator inspections classified in Fiscal Year (FY) 2005, 19 resulted in the issuance of Warning Letters.
- Of the 76 sponsor inspections classified in FY 2005, 8 resulted in the issuance of Warning Letters.
- Of the 42 Institutional Review Board (IRB) inspections classified in FY 2005, three resulted in Warning Letters. Two of those three Institutional Review Boards had been inspected as a follow-up to a previous Warning Letter and were given further sanctions until corrective actions were taken.

- Of the 76 sponsor inspections classified during FY 2005, one resulted in the invocation of the Application Integrity Policy against the firm.

Warning Letter Issued to Clinical Investigator

On April 11, 2005, CDRH issued a Warning Letter to Dr. Kenneth J. Rosenthal, Great Neck, New York. The Warning Letter was issued following FDA’s inspection on December 29, 2004-January 19, 2005. The inspection revealed that Dr. Rosenthal's activities as a Clinical Investigator in human research studies failed to comply with applicable FDA regulations.

The Warning Letter included the following serious violations:

- Failure to maintain accurate and complete records relating to his participation in the study.

- Failure to maintain accurate and complete records for each subject’s case history and exposure to the device.

- Failure to ensure that the investigation is conducted according to the signed agreement, Investigational plan and applicable regulations.

- Failure to ensure submission of complete and accurate progress reports as required by the reviewing Institutional Review Board (IRB).

The Warning Letter requested that Dr. Rosenthal take action to promptly correct the violations and prevent similar violations from occurring in the future.

Warning Letter Issued to ReGen Biologics for Violations of FDA Regulations In the Conduct of Investigational Studies

On September 16, 2005, CDRH issued a Warning Letter to ReGen Biologics, Franklin Lakes, New Jersey. The Warning Letter was based on FDA’s inspection on April 21-May 18, 2005, by an investigator from the FDA's New Jersey District Office. The inspection revealed serious violations from FDA regulations applicable to sponsors of investigational studies of FDA-
regulated products. The inspection was conducted under a program designed to ensure that information contained in applications for Investigational Device Exemptions (IDEs) are scientifically valid and accurate, and that human subjects are protected from undue hazard or risk during the course of scientific investigations.

The Warning Letter identified the following serious violations:

- Failure to provide clinical investigators with information they needed to conduct the investigation properly.
- Failure to secure the compliance of an investigator who was not complying with the investigational plan.
- Failure to obtain approval from an Institutional Review Board (IRB) prior to the initiation of an investigation.
- Failure to maintain complete records of investigational devices.

The Warning Letter requested that ReGen Biologics promptly correct these violations and describe the actions they have taken or will take to prevent the recurrence of similar violations in other studies.

**Warning Letter Issued to Institutional Review Board**

On August 1, 2005, CDRH issued a Warning Letter to Huntsville Hospital's Institutional Review Committee, Huntsville, Alabama, for their continuing failure to comply with FDA regulations applicable to Institutional Review Boards (IRBs). The Warning Letter was issued following FDA’s inspection on February 10-11, 2005, by an investigator with the FDA's New Orleans District Office. The purpose of the inspection was to determine if the Institutional Review Committee had implemented corrective actions assured in their response to FDA's April 11, 2003 Warning Letter. The inspection was also conducted to determine if the IRB was presently functioning in compliance with applicable FDA regulations.

The IRB was cited for the following violations:

- Failure to follow written procedures for IRB functions and operations.
- Failure to require that informed consent be given to subjects in accordance with the regulations.
The Warning Letter requested that the IRB take immediate action to correct the violations. The Warning Letter also notified the IRB that, as a result of their continued noncompliance, FDA would withhold approval of new studies reviewed by the IRB, and that no new subjects could be admitted to ongoing studies that were currently under review by the IRB. The Warning Letter informed the IRB that these restrictions would remain in effect until FDA notified them in writing that their corrective actions were satisfactory.

Cardiovascular

Boston Scientific Agreed to Pay $74 Million Civil Settlement

On June 24, 2005, the U.S. Department of Justice (DOJ) issued a Press Release announcing that Natick-based Boston Scientific Corporation (BSC), agreed to pay $74 million to the United States to resolve an ongoing investigation concerning its 1998 distribution and subsequent recall of one of its coronary stent delivery systems.

The U.S. Attorney's Office announced that a civil complaint was filed in federal district court charging BSC with distributing in interstate commerce 34,589 medical devices that were adulterated and misbranded between August 12, 1998 through October 5, 1998. To resolve the allegations in the civil complaint, BSC, without admitting liability, agreed to pay $74 million to the United States. To read the full text of DOJ's extensive Press Release go to: http://boston.fbi.gov/dojpressrel/pressrel05/bostonscientificcivset.pdf.

Guidant Corporation Recalled Cardiac Implantable Defibrillators and Pacemakers; FDA Classified Recalls as Class I or Class II

Defibrillators

Recall of Implantable Defibrillators and Cardiac Resynchronization Therapy Defibrillators

On June 17, 2005, FDA issued a Press Release stating that the Agency was notifying health care providers and patients that Guidant Corporation (Guidant), Indianapolis, Indiana, was recalling certain of its implantable defibrillators and cardiac resynchronization therapy defibrillators. The
recall was based on the fact that these devices could develop an internal short circuit without warning, resulting in failure to deliver a shock when needed.

The devices affected by this notification are:

- PRIZM 2 DR, Model 1861, manufactured on or before April 16, 2002
- CONTAK RENEWAL, Model H135, manufactured on or before August 26, 2004
- CONTAK RENEWAL 2, Model H155, manufactured on or before August 26, 2004

The devices are surgically implanted in persons who have a type of heart disease that creates the risk of a life-threatening heart arrhythmia (abnormal rhythm). The devices deliver an electrical shock to the heart to restore normal heart rhythm. The PRIZM 2 and RENEWAL devices are subject to different failures, resulting in the devices' inability to deliver an electrical shock during episodes of arrhythmia, which could lead to a serious, life-threatening event for a patient. FDA advised that there have been two deaths reported to the Agency suspected to be associated with this malfunction.


FDA Classified Recalls - Provides Additional Information on Risks

On July 1, 2005, FDA issued a Press Release providing additional information on the recall of certain implantable defibrillators manufactured by Guidant. In the Press Release, FDA provided information on the recall classification of each type of defibrillator, either a Class I recall or a Class II recall. In addition, FDA provided information on the relative risks associated with each type of device.

Below is a full list of the devices affected by this recall classification:

- **Class I Recall of Defibrillators**
  - Prizm 2DR
  - Contak Renewal
  - Contak Renewal Defibrillator

FDA classified the action taken by Guidant for the above defibrillators as a Class I recall. In a Class I recall, there is a reasonable probability that if a particular device is malfunctioning, the malfunctioning device will cause serious adverse health consequences or death.
Guidant's investigation determined these devices can develop an internal short circuit when attempting to deliver an electrical shock to the heart, preventing the treatment of abnormal heart rhythms. The problem is caused by deterioration of electrical insulation in the device and can only be detected after the device has already malfunctioned. The device does not give any sign of impending failure and there is no test that predicts whether the device will fail.

Two deaths associated with these 42,000 affected devices worldwide (20,600 are still implanted) have been reported to FDA.

To read more about FDA’s actions and Guidant’s recommendations, go to: [http://www.fda.gov/bbs/topics/NEWS/2005/NEW01210.html](http://www.fda.gov/bbs/topics/NEWS/2005/NEW01210.html).

- **Class II Recall of Defibrillators (Memory Error):**
  - Ventak Prism AVT
  - Vitality AVT
  - Renewal AVT

FDA classified the action taken by Guidant for the devices listed above as a Class II recall. For a Class II recall, the malfunctioning product may cause temporary or medically reversible adverse health consequences, however, the probability of serious adverse health consequences is remote.

These devices are subject to a memory error which, in rare cases, may limit available therapy. Of the 21,000 devices implanted worldwide (18,000 in the U.S.), two incidents have been confirmed, neither of which resulted in death or injury.

- **Class II Recall of Defibrillators (Magnetic Switch May Become Stuck):**
  - Contak Renewal 3 and 4
  - Renewal 3 and 4 AVT and
  - Renewal RF

FDA classified the action taken by Guidant for the devices listed above as a Class II recall.

These devices are subject to a component failure that, in rare cases, may limit available therapy. A magnetic switch in these devices may become stuck in the closed position, which in some cases inhibits the device’s ability to treat ventricular or atrial tachyarrhythmias (abnormally fast heart rhythms) and also accelerates battery depletion.
Four occurrences have been confirmed out of approximately 46,000 devices; a fifth occurrence is suspected but cannot be confirmed. In the four confirmed cases, patients and/or physicians were alerted to the condition by audible device tones signaling that the magnetic switch was closed. Based on this information, it is important that patients who hear tones from their device immediately contact their physician or go to the hospital emergency room.

FDA advised that if you are a physician or a patient who has experienced a problem with any of the affected defibrillator models, please send a report to FDA's MedWatch program and to Guidant. See http://www.fda.gov/medwatch/index.html for filing information or call 1-800-FDA-1088 (1-800-332-1088).

Guidant has posted information for patients and physicians on its web site at http://guidant.com/physician_communications/, and provided a telephone number: (1-866-484-3268).


UPDATE: Class I Recall of Implantable Cardioverter Defibrillator

On July 14, 2005, FDA issued an update to provide clinicians with current information and guidance concerning malfunctions occurring with Guidant’s PRIZM® 2 and CONTAK RENEWAL® implantable cardioverter defibrillator (ICD) devices, which were the subject of a Class I recall announced by FDA on July 1, 2005.

- **Class I Recall of Implantable Cardioverter Defibrillator (Problem with Device Circuitry)**

  The affected devices are:

  > VENTAK PRIZM® 2 DR, Model 1861, manufactured on or before April 16, 2002
  > CONTAK RENEWAL®, Model H135, manufactured on or before August 26, 2004
  > CONTAK RENEWAL® 2, Model H155, manufactured on or before August 26, 2004.

Each device’s malfunction causes damage to the device’s circuitry, potentially resulting in the inability to deliver the required shock during episodes of arrhythmia. This malfunction could lead to a serious, life-threatening event. Importantly, the device does not give any sign of impending failure, and there is no test that predicts whether any particular device
will fail. At this time it is not possible to provide accurate estimates of the failure rate for these devices, but at least two deaths attributable to this failure mode have been reported.

FDA posted advice about these devices at:
http://www.fda.gov/cdrh/medicaldevicesafety/atp/071405-guidant.html

FDA Reported Six Additional Clinical Occurrences of Failure of Defibrillators Involved in the July 1, 2005 Class I Recall

On October 13, 2005, FDA issued an update of the July 14, 2005 Preliminary Public Health Notification (PPHN) about malfunctions occurring with Guidant’s PRIZM® 2 and CONTAK RENEWAL® implantable cardioverter defibrillator (ICD) devices, which were the subjects of a Class I recall announced by FDA on July 1, 2005.

FDA provided this update because Guidant informed the Agency that 6 additional clinical occurrences (of which FDA has 4 confirmed reports) exhibiting this failure mode worldwide had been reported for the Contak Renewal® and Renewal® 2 devices since FDA's July 14, 2005 PPHN, for a total of 21 clinical failures, including 3 patient deaths, worldwide as of October 7, 2005.

The affected devices are:

> VENTAK PRIZM® 2 DR, Model 1861, manufactured on or before April 16, 2002
> CONTAK RENEWAL®, Model H135, manufactured on or before August 26, 2004
> CONTAK RENEWAL® 2, Model H155, manufactured on or before August 26, 2004.

No additional clinical failures have been reported for the Ventak Prizm® 2DR since FDA's July 14, 2005 PPHN. Guidant informed FDA and the clinical community that there were a total of 28 clinical failures, including 1 patient death, worldwide as of June 17, 2005, with no new reports since that date. Therefore, previous recommendations remained unchanged for patients implanted with the Prizm® 2 DR.

In addition to design changes previously instituted by Guidant, FDA approved a modification to the Prizm 2 DR and Contak Renewal devices that should further reduce the likelihood of this failure mode occurring in newly manufactured devices.

The full text of the Press Release is available at:
Pacemakers

FDA Announced Guidant’s Class I Pacemaker Recall

On July 22, 2005, FDA notified health care providers and patients that Guidant was voluntarily recalling certain pacemakers. The recall was initiated because a seal within the devices could leak, allowing moisture to affect the electronic circuits. This defect could cause the pacemakers to fail to provide pacing or could cause a rapid heart rate. Other unexpected device behaviors were also possible. The problems could occur without warning and could lead to loss of consciousness, and possibly heart failure and death.

Only the following models were affected by this recall. All were manufactured from November 25, 1997-October 26, 2000.

- PULSAR® MAX Models 1170, 1171, 1270
- PULSAR Models 0470, 0870, 0970, 0972, 1172, 1272
- DISCOVERY® Models 1174, 1175, 1273, 1274, 1275
- MERIDIAN® Models 0476, 0976, 1176, 1276
- PULSAR MAX II Models 1180, 1181, 1280
- DISCOVERY II Models 0481, 0981, 1184, 1186, 1187, 1283, 1284, 1285, 1286
- CONTAK TR® Model 1241
- VIRTUS PLUS® II* Models 1380, 1480
- INTELIS II Models 1483, 1484, 1485, 1384, 1385, 1349, 1499

* VIRTUS PLUS II and INTELIS II models available only outside the U.S.

Guidant announced the initiation of the voluntary recall on July 18, 2005.

For patients who depend on these pacemakers to maintain an adequate heart rate, failure of the device to provide pacing output can cause sudden faintness or loss of consciousness, and can result in death. The leakage defect can also cause a sustained rapid heart rate, which can cause heart failure and result in death.

While the failures can occur without warning, sometimes a leak-related malfunction can be detected by a physician before the malfunction causes serious problems. Guidant provided information to physicians about ways to identify a leak-related malfunction. However, Guidant advised that they are not aware of any test that will show if a normally functioning pacemaker is likely to fail in the future.

As of July 11, 2005, Guidant had received reports that 69 pacemakers may have failed because of the leakage. Twenty of the devices were confirmed to have stopped providing pacing output, resulting in loss of consciousness in five patients. Guidant also received reports of two patients who had sustained pacing at a rapid rate. A patient whose device exhibited sustained pacing at a
rapid rate was admitted to the hospital and later died. The device problem could not be confirmed as leakage since the device was not returned.

Approximately 18,000 of the affected devices remain in service in the U.S. and an additional 10,000 are in service in other countries. Guidant estimated that the failure rate from the leakage defect will be between 0.17% and 0.51% (i.e., between 1.7 per one thousand and 5.1 per one thousand) over the remaining lifetime of the devices. It is possible that the actual failure rate will be greater than this, in part, because some past failures may not have been reported to Guidant.

**FDA Inspected Guidant Corporation**

On August 22-September 1, 2005, FDA conducted an inspection of Guidant Corporation's main plant located in St. Paul, Minnesota. Following the inspection, FDA provided Guidant with FDA Form 483, noting observations related to deviations from the Quality System Regulation for medical devices.

FDA documented fifteen observations primarily related to quality control procedures, unapproved processes, and document control procedures.

The full text of the FDA 483 issued to Guidant Corporation is available on FDA's website at: [http://www.fda.gov/ora/frequent/483s/2124215_guidant/guidant_rptFDA483_cfm1.html](http://www.fda.gov/ora/frequent/483s/2124215_guidant/guidant_rptFDA483_cfm1.html).

**UPDATE:** On December 22, 2005, FDA's Minneapolis District Office issued a Warning Letter to the Chairman and CEO of Guidant Corporation, Indianapolis, Indiana. The December 2005 Warning Letter listed eight deviations from FDA regulations, including violations of the Quality System Regulation and the Medical Device Reporting regulations. In addition to advising the firm of the violations, the Warning Letter stated,

"Additionally, no premarket approval applications for Class III devices to which the Quality System regulation deficiencies are reasonably related will be approved until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be granted until the violations related to the subject devices have been corrected."

To view the full text of the Warning Letter go to: [http://www.fda.gov/foi/warning_letters/g5657d.htm](http://www.fda.gov/foi/warning_letters/g5657d.htm).
Class I Medical Device Recall - Laerdal Medical Corporation Recall
100 HeartStart Automatic External Defibrillator (AED) Adapter Cables

On April 28, 2005, Laerdal Medical Corporation issued a press release followed by a letter notification to customers to announce that it was recalling the CM 100 HeartStart® Adapter Cable, Cat. No. 920650, all lots. Over 3,000 Adapter Cables were distributed in the U.S. since 1996. The adapter cables were sold in a clear plastic bag with a white stick on label that read “PART # 920650 ADAPTER CM100/LMC ELECTRODE.” The products could also be identified by the number 281-132-00 displayed on a white label affixed to one of the cable leads.

On April 29, 2005, FDA issued a press release about this recall.

The affected AED adapter cables were susceptible to breakage which may, in some cases, prevented the AED from delivering a shock, which could result in a delay in treatment or death of a viable patient. This recall was initiated after receipt of several user complaints of malfunction during clinical use that resulted in deaths in the U.S.

The adapter cable allows the use of the Laerdal Heartstart multifunction defibrillator pads to be used with the Heartstart 4000 series defibrillators and Philips Medical Systems CodeMaster 100 and XL series defibrillators. Automatic external defibrillators are intended to be used for the treatment of cardiac arrest. The defibrillators are intended to deliver a shock to the heart to restore normal heart rhythm. Prior to delivering the shock, the device analyzes the patient’s heart rhythm to determine if a shock is appropriate.

General Hospital and Personal Use

Consent Decree of Injunction - HDC Corporation,
Carey E. Bolden, Leonard O. Ross

On January 6, 2005, a Consent Decree of Permanent Injunction was signed by the Judge and entered in the U.S. District Court for the Northern District of California in the case of U.S. v. HDC Corporation, Carey E. Bolden, and Leonard O. Ross (Defendants).

During FDA’s inspection of HDC Corporation (HDC), Milpitas, California, on February 6 to March 16, 2004, an investigator collected information that revealed serious regulatory problems involving the manufacture of V-Cath Catheters. This resulted in an injunction against HDC and
the above-named individuals.

This Consent Decree was negotiated after numerous violative inspections found both Quality System (QS) regulation and Medical Device Reporting (MDR) regulation violations. The Decree enjoins the Defendants' from manufacturing, packing, and distributing any device unless and until: HDC retained an independent expert to perform a comprehensive inspection of Defendants' facilities and certify in writing to FDA when Defendants have successfully implemented corrective actions to address all violations found during all previous FDA inspections. After receipt of the certification, the FDA's San Francisco District inspected the facilities to confirm that the Defendants were operating in conformity with the QS and MDR regulations.

Following an April 8 – 13, 2005 FDA inspection, on April 27, 2005, FDA notified HDC that it may resume its manufacturing operations for certain sizes and types of Peripherally Inserted Central Catheters (PICC) and Midline catheters. On August 24, 2005, FDA notified HDC that it may resume manufacturing its NeutroTrace needle products following third party certification.

Order of Condemnation and Injunction - Vail Products, Inc.

On August 23, 2005, U.S. District Judge David Katz entered an Order of Condemnation and Injunction against seized enclosed bed systems owned by Vail Products, Inc. (Vail), Toledo, Ohio.

FDA initiated a seizure against the goods in March 2005, after determining that they were adulterated and misbranded. Vail shut down its manufacturing operations and went out of business. As a result of the order, Vail was enjoined from restarting manufacturing as another company until the firm satisfied FDA that it was in compliance with the Quality System (QS) regulation. For a complete list of violations of the QS and Medical Device Reporting (MDR) regulations, see the article below entitled, "Seizure of Enclosed Bed Systems at Vail Products, Inc."

Seizure of Enclosed Bed Systems at Vail Products, Inc.

The U.S. Marshals Office also seized welded in-process components and all labeling and promotional materials for the Vail 500, 1000, and 2000 enclosed bed systems. FDA determined that the Vail products seized did not comply with the Quality System (QS) and Medical Device Reporting (MDR) regulations to carry out the Federal Food, Drug, and Cosmetic Act (the Act) and posed significant health risks for consumers.

The most recent FDA inspection in January/February 2005, revealed that the firm's enclosed bed systems were associated with approximately thirty patient entrapments and eight deaths since 2002. FDA considered these enclosed bed systems to be dangerous to health when used in the manner or with the frequency or duration prescribed, recommended, or suggested in the labeling, and were therefore misbranded under the Act.

Vail manufactured enclosed bed systems that were intended to restrain pediatric and adult patients who were behaviorally, physically, or mentally compromised and who presented a risk of nighttime injuries.

FDA conducted four previous inspections in March 1997, March 1998, June 2003, and June 2004, all of which revealed significant violations of the QS regulation. Each time, Vail promised to make necessary corrections. In April 1997, FDA issued a Warning Letter to Vail Products for significant QS violations and lack of MDR procedures. A second Warning Letter was issued to the firm in September 2003, for significant violations of the QS regulation, lack of MDR procedures, and failure to report a recall to FDA as required by the agency’s Corrections and Removals regulation.

FDA’s inspection conducted in January/February 2005, resulted in a Warning Letter that revealed continuing significant violations of the QS regulation including, but not limited to, the following:

- Failure of management to ensure that an adequate and effective quality system was fully implemented and maintained at all levels of the organization.
- Failure to ensure that corrective action and preventive actions are effective and do not adversely affect the finished devices.
- Failure to report serious injuries and deaths associated with Vail beds.
- Failure to provide FDA with information that is incomplete or missing from reports submitted by user facilities and other initial reporters.
- Failure to adequately implement the complaint handling procedure to ensure that all complaints are evaluated to determine whether the complaint should be filed as a Medical Device Report.
- Failure to establish and maintain adequate procedures for the identification, documentation, validation, review, and approval of design changes before their implementation.

The Vail enclosed bed systems were also misbranded as follows: 1) because they failed to bear adequate directions for use for their intended purposes; 2) because they failed to bear adequate warnings, thereby placing patients at an increased risk of entrapment and asphyxiation; and 3) because the firm failed to furnish FDA with information regarding MDR reportable adverse events.

**Warning Letters Issued to Patient Lift Manufacturers**

*Arjo Med AB Ltd.*

On January 10, 2005, CDRH issued a Warning Letter with Detention Without Physical Examination to Arjo Med. AB Ltd. (Arjo), a patient lift manufacturer located in Gloucester, United Kingdom. Patient lifts are intended to lift and transport patients from one location to another, as from a bed to a bath. Several of Arjo’s patient lifts were the subject of several Class I recalls due to manufacturing and component failures resulting in two deaths.

FDA issued a Warning Letter after FDA’s inspection revealed significant violations of the Quality System (QS) regulation. Arjo failed to provide validation reports for welding processes and failed to provide scientific rationale for testing criteria on critical components. FDA also found significant QS deviations in Arjo’s corrective and preventive action procedures, calibration program, and purchasing controls.

*Faaborg Rehab Technic*

On January 10, 2005, CDRH issued a Warning Letter with Detention Without Physical Examination to Faaborg Rehab Technic ApS (Faaborg), a patient lift manufacturer located in Faaborg, Denmark.

Faaborg’s patient lifts were the subject of a Class I recall due to component failures resulting in a death and serious injuries. Twenty-six of Faaborg’s patient lifts were also seized in Illinois on June 25, 2004.

FDA issued a Warning Letter to Faaborg because the firm was operating with significant Quality System regulation deviations including, but not limited to, the following:

- Failure to validate critical welding processes.
- Failure to establish procedures for corrective and preventive actions, complaint handling procedures, or production processes.

- Failure to calibrate equipment.

- Failure to conduct internal audits.

The Warning Letter also included deviations from the Medical Device Reporting (MDR) regulation in that the firm failed to report MDR reportable events.

**Class I Recall: Baxter Healthcare Recalled Colleague Volumetric Infusion Pumps**

On March 15, 2005, Baxter Healthcare Corporation (Baxter), Deerfield, Illinois, initiated a worldwide recall of **all models** of its Colleague Volumetric Infusion Pumps because they can shut down while delivering critical medication and fluids to patients. Baxter received six reports of serious injury and three reports of death associated with this shut-down problem. The affected are: Models 2M8151, 2M8151R, 2M8161, 2M8161R, 2M8153, 2M8153R, 2M8163, and 2M8163R.

On July 21, 2005, FDA issued a press release about this recall.

Based on information from FDA’s inspection and independent analysis of the failure modes, as well as a comprehensive review of adverse event reports in FDA's database, FDA determined that this action was a Class I recall. Class I recalls are the most serious type of recall and involve situations in which there is a reasonable probability that use of the affected product will cause serious injury or death.

The firm notified customers that it had voluntarily stopped shipping Colleague Volumetric Infusion Pumps until the problems were resolved. Baxter also advised customers on March 15, 2005, to stop using any pumps that exhibited a failure code beginning with 402, 403, 533, 535, or 599, related to these electronic problems. Additionally, Baxter advised customers to take out of service any pumps that exhibit failure codes 810:04 and 810:11 related to air-in-line sensor problems, until they were inspected by authorized service personnel.

The device may exhibit two additional failure modes related to a shut-down problem:

1. Users may inadvertently press the on/off key instead of the start key when attempting to start an infusion.
2. Disconnecting or connecting the pump from the hospital monitoring system while the pump is powered "on" can result in a failure code, requiring the infusion to be restarted. The firm noted that these failures may occur during the infusion of therapy, so it is imperative that health care institutions have a contingency plan to mitigate any disruptions of infusions of life-sustaining drugs or fluids.

At the time of recall, approximately 255,000 Colleague Volumetric Infusion Pumps were in use, including 206,000 distributed in the U.S. They have been sold to physicians, hospitals, pharmacies, and a variety of other medical facilities.

In Vitro Diagnostic Devices

Seizure of Unapproved In Vitro Test Kits at Prestige Fulfillment, Inc.

On April 22, 2005, FDA investigators from the Los Angeles District Office accompanied the U.S. Marshals Service in a seizure of in vitro test kits located at Prestige Fulfillment, Inc., Vista, California. The kits tested for Rapid HIV, Syphilis, Dengue Fever, Cocaine, Amphetamine, and THC (Marijuana). The State of California Food and Drug Section had embargoed the articles.

The test kits were intended for home use as screening tests to detect HIV antibodies, diagnose Syphilis and Dengue Fever, and screen urine for the presence of drugs of abuse [cocaine, THC (Marijuana), and amphetamines].

The devices were adulterated because they were Class III devices and had no approved applications for premarket approval and no investigational device exemptions in effect. In addition, the devices were misbranded because they were in package form and failed to bear labels containing the name and place of business of the manufacturer, packer, or distributor. The test kits for Rapid HIV, Syphilis, and Dengue Fever were misbranded because a notice or other information about the devices was not provided to FDA.
Seizure of Blood Glucose Test Strips at H & H Wholesale Services, Inc., and EZ Storage

On September 2, 2005, FDA investigators assisted the U.S. Marshals Service in a seizure of blood glucose test strips located at H & H Wholesale Services, Inc., Troy, Michigan, and at EZ Storage, Centerline, Michigan.

These devices are intended for use as diagnostic test kits for use by human diabetic patients for the in vitro determination of blood glucose levels. Once a patient has determined his or her blood glucose level using a diagnostic test kit, he or she uses this information to comply with the physician’s instructions concerning the need for medical intervention, e.g., whether or not to administer insulin and whether or not to adjust their diet.

FDA was concerned that the wrong measures of units and the incorrect calibration of these devices would result in misinterpretation of glucose level results and/or reporting of incorrect results. The issue of reporting or misunderstanding the correct units of measurement generated both Class 1 and Class 2 device recalls. Patients who undertreat themselves based on incorrect interpretation of results are subject to loss of glucose control and severe hyperglycemia, which can result in injury or death. Patients who overtreat based on incorrect interpretation or generation of results are subject to severe hypoglycemia, which can also lead to severe injury (including coma) and death.

The Federal, Food, Drug, and Cosmetic Act (Act) requires that manufacturers of medical devices obtain marketing clearance or approval from FDA before the devices may be offered for sale in the United States. Certain of the blood glucose test strips (the three lots of ONETOUCH ULTRA and the lot of SureStep) were adulterated because they were class III devices and did not have an approved application for premarket approval in effect or an approved application for an investigational device exemption.

All of the devices were misbranded as follows:

The ACCU-CHEK Active, ACCU-CHEK Compact, the two lots of Prestige Smart System, and the single lot of SureStep were misbranded because words, statements, or other information required by or under the authority of the Act to appear on the label or labeling were not prominently placed thereon with such conspicuousness and in such terms as to render them likely to be read and understood by the ordinary individual under customary conditions of purchase and use because, e.g., performance characteristics are not stated and/or European measurements for glucose levels are used.

The three lots of ONETOUCH ULTRA and the single lot of SureStep were misbranded because there had been no premarket notification submitted to FDA pursuant to Section 510(k).
of the Act, demonstrating that the devices were substantially equivalent to other devices that are legally marketed.

**Mammography**

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**Background**

The Mammography Quality Standards Act (MQSA) was signed into law on October 27, 1992, to establish national quality standards for mammography. The MQSA required that, to perform mammography legally after October 1, 1994, all facilities become certified by FDA (section 900.12, MQSA final regulations) or by an FDA-approved Certifying Agency under the States-As-Certifiers (SAC) program.

**Accreditation**

To become certified, a facility first must be accredited by an Accreditation Body (AB) approved by FDA (section 900.11(b)(1)(ii)). To pass accreditation and subsequently qualify for a MQSA mammography facility certificate, a facility must meet baseline requirements relative to personnel qualifications, equipment performance specifications, quality assurance (QA) and quality control (QC) testing and recordkeeping, and clinical and phantom image reviews.

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**Mammography Facility Statistics**

**September 2005**

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<thead>
<tr>
<th>Description</th>
<th>Count</th>
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<tbody>
<tr>
<td>Certified facilities, as of October 1, 2004</td>
<td>9,011</td>
</tr>
<tr>
<td>Certified statistics as of September 1, 2005</td>
<td>9,011</td>
</tr>
<tr>
<td>Total certified facilities / Total accredited units</td>
<td>8,903 / 13,643</td>
</tr>
<tr>
<td>Certified facilities with FFDM units / Accredited FFDM units</td>
<td>713 / 985</td>
</tr>
</tbody>
</table>

**FY 2005 Inspection Statistics, as of September 1, 2005**

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facilities inspected</td>
<td>7,802</td>
</tr>
<tr>
<td>Total units at inspected facilities</td>
<td>11,973</td>
</tr>
<tr>
<td>Percent of inspections where the highest noncompliance was a:</td>
<td></td>
</tr>
<tr>
<td>Level 1 violation</td>
<td>2.1%</td>
</tr>
<tr>
<td>Level 2 violation</td>
<td>19.5%</td>
</tr>
<tr>
<td>Level 3 violation</td>
<td>8.8%</td>
</tr>
<tr>
<td>Percent of inspections with no violation</td>
<td>69.6%</td>
</tr>
<tr>
<td>Total annual mammography procedures reported, as of September 1, 2005</td>
<td>33,468,030</td>
</tr>
</tbody>
</table>

---
This number is an aggregate of the total number of procedures performed annually as reported by facilities to their accreditation bodies. Facilities are asked to disclose this information at their initial accreditation, and then at the time of their re-accreditation, which takes place once every three years. FDA began collecting these data in 1998. The aggregate does not reflect the current number of procedures performed at these facilities, but only the numbers reported by them during the three-year period prior to the current date. We have aggregated only the numbers reported by certified, non-Veterans Administration facilities.

1 FFDM - Full Field Digital Mammography unit.

The above information is available by month on FDA's Web Site at: http://www.fda.gov/cdrh/mammography/scorecard-statistics.html.

Warning Letter Issued to Kaiser Permanente Medical Center


On July 1, 2004, a representative of the State of California, acting on behalf of FDA, inspected the Kaiser Permanente Medical facility. This inspection revealed a serious problem involving the conduct of mammography at this facility. Under the MQSA which is codified in section 263b of Title 42 of the United States Code, a facility must meet specific requirements for mammography. These requirements help protect the health of women by assuring that a facility can perform quality mammography.

- A Level 1 observation indicates a failure to meet a key MQSA requirement that may compromise the quality of mammography performed at the facility.
- A Level 2 observation indicates that the facility meets all key MQSA requirements but fails to meet a significant mammography quality item.

Examples of the violations documented at Kaiser Permanente Medicare Center, Vallejo, California, included some repeat violations, and involved primarily:

- Repeatedly processing mammograms when the unit was out of limits, e.g., optical density differences outside of allowable limits.
- Failing to take corrective actions prior to conducting exams for reasons such as undocumented Quality Control (QC) failures, failing image scores, and missing QC.
FDA Warned Consumers of the Dangers of Decorative Contact Lenses Without Professional Involvement

On October 28, 2004, FDA issued a warning to consumers about the serious risks of using decorative contact lenses distributed without appropriate involvement by an eye care professional. These decorative lenses can cause permanent eye injury and may potentially lead to blindness. FDA noted that the Agency had received reports of decorative contact lenses being marketed and distributed directly to consumers through sources such as beauty salons, flea markets, convenience stores, beach shops, and the Internet.

FDA received reports of corneal ulcers associated with the wearing of decorative contact lenses in excess of the recommended wearing period. Corneal ulcers can progress rapidly, and, if left untreated, could lead to infection of the eye. Uncontrolled infection can lead to corneal scarring and vision impairment. In the most severe cases, this condition can result in blindness.

Other risks associated with the use of decorative contact lenses include: conjunctivitis (an infection of the eye); corneal edema (swelling); allergic reaction; and corneal abrasion due to poor lens fit. Other problems may include: reduction in visual acuity (sight); contrast sensitivity; and other visual functions, resulting in interference with driving and other activities.

FDA issued an Import Alert for decorative contact lenses presented at U.S. ports of entry that are intended for distribution without the appropriate involvement of an eye care professional. The Agency examined and detained numerous shipments of these lenses. Because there has been no demonstration to FDA's satisfaction that any of these detained products, when distributed without eye care professional involvement, comply with Federal safety standards, these products have not been permitted to enter U.S. commerce.

Domestically, FDA issued several Warning Letters, including a Warning Letter sent to Beauty Supply d/b/a Beauty World, District Heights, Maryland. FDA informed the company that the Agency considered the lenses to be adulterated because they were being distributed to consumers without appropriate eye care professional involvement, and also misbranded because the lenses' labeling failed to warn consumers about the potential injuries that might result from wearing the lenses.

FDA urged consumers not to use decorative contact lenses unless they have seen an eye care professional, and have obtained proper lens fitting and instructions for using the lenses. FDA
requested that consumers report any problems with decorative contact lenses to FDA's district office consumer complaint coordinator in their geographic area. Telephone and TTY contact information for FDA's consumer complaint coordinators is available via FDA's web site at http://www.fda.gov/opacom/backgrounders/complain.html.

**Warning Letter Issued to Diopsys, Inc.,**


FDA’s inspection revealed that these devices were adulterated because the methods used in, or the facilities or controls used for their manufacture, packing, storage, or installation were not in conformance with the Quality System (QS) regulation for medical devices (21 CFR Part 820) as follows:

- Failure of management to assure that an adequate and effective quality system was implemented.
- Failure to establish and maintain procedures for implementing corrective and preventive actions; and to document these required activities and their results.

The Warning Letter also noted that, according to FDA records, the firm had not obtained marketing approval or clearance for the ENFANT™ Vision Testing System. The Warning Letter noted that changes made to the ENFANT™ Vision Testing System, including re-writing the system software, represented a major modification that could significantly affect the safety or effectiveness of the device.

Under FDA regulations any change that could significantly affect the safety or effectiveness of a device, including significant changes to the design, material, chemical composition, energy source, or manufacturing process, requires the submission of a 510(k) in accordance with section 510(k) of the Act.

Because the firm did not submit a 510(k) to FDA prior to introducing the ENFANT™ Vision Testing System into commercial distribution, FDA determined that this device was misbranded. In addition, until the firm submits a 510(k) and FDA reviews it and notifies the firm that their device is substantially equivalent to another legally marketed device, the ENFANT™ Vision Testing System is adulterated.

For a product requiring premarket review before marketing, the notification required by
section 510(k) of the Act is deemed to be satisfied when a Premarket Approval Application is pending before the Agency.

Orthopedics

Warning Letter Issued to Ortek AG, Industrie - Nord S, 5634 Merenschwand, Switzerland. The Warning Letter was issued based on inspectional findings documented during FDA’s inspection on April 13-15, 2004. FDA’s investigator determined that the firm manufactures shoulder, hip, and knee prostheses as well as orthopedic manual surgical instruments.

This inspection revealed that these devices appeared to be adulterated because the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation were not in conformity with the Current Good Manufacturing Practice requirements of the Quality System regulation. The significant violations included, but were not limited to problems with validation of equipment, and failure to establish and maintain adequate quality control procedures.

Warning Letter Issued to Rapid Recovery Health Services, Inc., for Internet Promotion of Unapproved Uses of Orthopedic Device

On March 7, 2005, CDRH issued a Warning Letter to Rapid Recovery Health Services Inc., Westbury, New York. The Warning Letter stated that FDA had reviewed information from the firm's website www.rapidrecoveryinc.com relating to extracorporeal shockwave therapy devices. The website was promoting the Sonocur® and the Epos Ultra for the relief of pain in the elbow, hand/wrist, shoulder, and knee/heel, as well as for other tendon-associated pains.

The Warning Letter noted that this website indicates that the firm will provide the Sonocur® or the Epos Ultra to a practitioner's office, along with a technician trained to use the device. The technician will then administer the device on patient(s) under the practitioner's supervision.
Under the Act, the Sonocur® and the Epos Ultra are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease or to affect the structure or a function of the body.

In a letter dated November 26, 2003, we advised you that the Sonocur was approved only for the treatment of chronic lateral epicondylitis in patients with symptoms for at least six months and a history of unsuccessful conservative treatments. We also advised you that the approved indications for use did not include treatment of pain in the hand/wrist, shoulder, or knee/heel (plantar fasciitis), or other tendon-related problems, like those described on your website.

The Epos Ultra has been approved only for the treatment of chronic plantar fasciitis in patients with symptoms for at least six months and a history of unsuccessful conservative treatments. It has not been approved for treatment of pain in the hand/wrist, shoulder, or elbow, or for other tendon-related pain. PMA approval for the treatment of pain in the aforementioned areas is required before the devices may be marketed or offered for sale for those uses.

The Warning Letter further stated that the firm's promotion and introduction into interstate commerce of the Sonocur® and Epos Ultra devices for these unapproved indications renders them adulterated for failure to obtain FDA premarket approval, and misbranded for failure to notify the Agency of the firm’s intent to introduce the devices into commercial distribution.

For a product requiring premarket approval before marketing, the notification required by section 510(k) of the Act is deemed to be satisfied when a PMA is pending before the Agency.

**Radiology**

**Warning Letter Issued to Hitachi Medical Systems America, Inc.**

On July 13, 2005, FDA's Cincinnati District Office issued a Warning Letter to Hitachi Medical Systems America, Inc. (Hitachi), Twinsburg, Ohio. FDA inspected the medical device manufacturing facilities on March and April 2005. FDA’s inspection revealed that Hitachi is the contracting sales agent, installer and designated complaint handling unit for magnetic resonance imaging (MRI) systems manufactured by Hitachi Medical, Tokyo, Japan.
The above-stated inspection revealed that these devices were misbranded in that the firm failed to furnish material or information as required under section 519 of the Act and the Medical Device Reporting (MDR) regulation.

Specifically, for four separate events, Hitachi failed to submit a MDR to FDA within 30 days of receiving information that the marketed devices may have caused or contributed to a death or serious injury.

FDA received responses, dated April 25, May 25, and June 27, 2005, stating that the firm had filed the four complaints, as well as an additional complaint that was not reviewed by FDA’s investigator, as MDR events. The firm also stated that they had revised their MDR procedure so that a MDR would be submitted if they determined that the device "may have contributed to the death or serious injury."

FDA responded to the firm stating "Your MDR procedure is not adequate…because it does not address several of the factors included in the definition of caused or contributed as defined in 21 CFR 803.3(d). The regulation states that 'caused or contributed' means that a device was or may have been a factor in the death or serious injury, including events occurring as a result of: 1) failure; 2) malfunction; 3) improper or inadequate design; 4) manufacture; 5) labeling; or 6) user error."

The Warning Letter further stated that the firm's devices were adulterated because the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation were not in conformance with the Quality System (QS) regulation. The following deviations from the QS regulation included, but were not limited to, the following:

- Failure to ensure that all complaints are evaluated to determine whether the complaint should be filed as a MDR.

- Failure to verify or validate corrective and preventive actions to ensure that the action is effective and does not adversely affect the finished device.

- Failure to adequately inspect, test, or verify as conforming to specified requirements acceptance activities for incoming components.
Unapproved Devices

Warning Letter Issued to BioImagene, Inc., for Unapproved Device Promoted on the Internet

On May 25, 2005, CDRH issued a Warning Letter to BioImagene, Inc., San Jose, California. The Warning Letter was based on FDA's review of the firm's website http://bioimagene.com. Based on this review, FDA concluded that the firm was marketing PATHIAM without approval or clearance from FDA, in violation of the law.

According to the website, PATHIAM is "a hardware-independent, Web-enabled software allowing pathologists to view and analyze immunohistochemically-stained (IHC-stained) slides from any computer via the Internet." PATHIAM is a device as that term is defined in section 201(h) of the Act because it is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or because it is intended to affect the structure or any function of the body.

The Warning Letter advised the company that the Act requires that manufacturers of medical devices obtain marketing approval or clearance for their products from FDA before they may offer them for sale.

The Warning Letter noted that, based on promotional information, as well as other information available on the firm's website, PATHIAM was being marketed as a device with medical and diagnostic claims.

FDA concluded that the PATHIAM device was adulterated because the firm did not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a) of the Act or an approved application for an Investigational Device Exemption under section 520(g) of the Act.

In addition, the device was also misbranded because the firm did not notify the Agency of their intent to introduce the device into commercial distribution, as required by section 510(k) of the Act. For a device requiring premarket approval, the notification required by section 510(k) of the Act is deemed satisfied when a PMA is pending before the Agency.
Warning Letter Issued to Tepnel Diagnostics Ltd., for Unapproved Genetic Assays Promoted on the Internet

On August 26, 2005, CDRH issued a Warning Letter to Tepnel Diagnostics Ltd., Abingdon, Oxon, United Kingdom. The Warning Letter was issued based on a review of information on the firm's Elucigene™ Brand Internet website http://www.elucigene.com/products.html concerning several devices manufactured by Tepnel Diagnostics.

The devices were marketed as analyte specific reagents—the gel-based ELUCIGENE genetic assays CF-HT, CF29, CF poly-T, CF7, Ashplex 1, Ashplex 2, Gaucher, and TRP. FDA's review revealed serious regulatory problems involving these devices.

CDRH's review indicated that each of these products were devices because they were intended for use in the diagnosis of disease or other conditions, or in the cure, treatment, prevention, or mitigation of disease. According to the instructions for use/methods for use, each of the gel-based ELUCIGENE™ genetic assays was intended for "in vitro diagnostic use" to detect various human genetic mutations.

The Warning Letter noted that statements on the firm's website describing these devices indicated that they were intended for the detection of mutations related to clinical diagnoses of diseases, for example, Cystic Fibrosis, Tay Sachs Disease, and for the risk of venous thromboembolism. In addition, the "Instructions/Methods for Use" supplied for the assays, provided detailed procedures (along with directions and guidelines for the interpretation of results) that were unique for these assays and that constituted analytical and performance claims.

FDA’s review of the Agency's records indicated that there was no clearance or approval for the gel-based ELUCIGENE™ genetic assays or the CF-HT Results Reporter software. The Warning Letter advised that these devices were therefore adulterated, because the firm did not have an approved application for premarket approval in effect, or an approved application for an investigational device exemption.

In addition, the Warning Letter noted that these devices were also misbranded because the firm did not notify FDA of the firm's intent to introduce the device into commercial distribution as required by section 510(k). For a product requiring premarket approval before marketing, the notification required by section 510(k) of the Act is deemed to be satisfied when a Premarket Approval Application is pending before the Agency.