BREAKING NEWS! FDA SOLICITS COMMENTS ON GUIDANCE DOCUMENT Starting on Page 7
FROM THE CHAIR

Allow me to introduce …

… myself:

My name is Jim Stackhouse and I am privileged to begin my term as Chair of COLA’s Board of Directors. I have held several positions on the Board since the ACP appointed me in 2003, most recently serving as Vice-Chair. I have recently completed nine years of service to the ACP as Regent and Treasurer.

I have been in the private practice of internal medicine in Goldsboro, NC for 29 years, where I have been heavily involved in public service and quality improvement activities, including serving as a charter member of the NC Stroke and Heart Disease Task Force since 1996, and as part of the NC Health Quality Alliance.

Serving as COLA’s Chair meshes well with my interests in public service and quality medicine as these are COLA’s values as well. By providing education for your personnel and accreditation for your laboratory, we help you provide your patients with the highest quality medicine possible.

… and this issue of Insights:

We are all familiar with CMS and their oversight of the CLIA regulations, but we may not be aware of the role the FDA plays in laboratory medicine. This issue of Insights will introduce you to the FDA, explain how they are involved with clinical laboratories, and inform you of how to interact with them, when needed.

When you think about it, this issue nicely reflects COLA’s values of education (appraising you of the FDA) and accreditation (the latest Compliance Tip is in this issue) through innovation (the interactive online format) to help you provide quality care to your patients.

W James Stackhouse, MD, MACP
Chair, COLA Board of Directors

COLA INSIGHTS

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The Clinical Laboratory and the FDA

THE FDA?
ISN’T THAT THE FOOD AND DRUG ADMINISTRATION?
WHAT DOES A CLINICAL LAB HAVE TO DO WITH FOOD AND DRUGS?

The FDA plays a major role in laboratory medicine, even though the Centers for Medicare and Medicaid Services (CMS) holds primary responsibility of enforcing CLIA regulations.

It is the responsibility of the FDA to categorize commercially marketed in vitro diagnostic tests. That means that it is the FDA who decides if the test system used in your lab is waived, moderate complexity, or high complexity. The FDA role continues after test systems are marketed since the FDA also tracks adverse events, issues safety communications, and supervises recall notices.

There is a complex process that manufacturers have to follow in order to get test systems to the categorization stage. This process begins when the manufacturer first seeks FDA approval to market the test system in the United States. Thus, the FDA plays a major role in test system development, from its inception to its retirement.

CATEGORIZATION CRITERIA

According to the CLIA standards, waived test systems “are simple laboratory examinations and procedures which are cleared by FDA for home use; employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible, or pose no reasonable risk of harm to the patient if the test is performed incorrectly.”

Nonwaived test systems are categorized as moderate or high complexity. Each laboratory test system is graded for its level of complexity by assigning scores of 1, 2, or 3 for each of the seven criteria listed in Table 1. A score of 1 indicates the lowest level of complexity, while a score of 3 indicates the highest level. (A score of 2 will be assigned to a criteria when the characteristics for a particular test are intermediate between the descriptions listed for scores of 1 and 3.) After the scores are totaled, test systems receiving scores of 12 or less are categorized as moderate complexity, while those receiving scores above 12 are categorized as high complexity.

On its website, the FDA maintains a searchable database, which it updates monthly. This database lists records of the test systems categorized by the FDA since 2000 as well as those categorized by the Centers for Disease Control and Prevention (CDC) prior to that date. The database can be accessed at this site: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm and is searchable by: test system name, analyte name, complexity, specialty and/or date of categorization.

Additional articles in this issue of Insights discuss other ways that the FDA affects laboratory medicine.

>> CONTINUED ON PAGE 4
TABLE 1 Criteria to Categorize Nonwaived Test Systems

<table>
<thead>
<tr>
<th>Criteria Score of 1</th>
<th>Criteria Score of 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Knowledge</strong></td>
<td></td>
</tr>
<tr>
<td>• Minimal scientific and technical knowledge is required to perform the test, and Knowledge required to perform the test may be obtained through on-the-job instruction.</td>
<td>• Specialized scientific and technical knowledge is essential to perform preanalytic, analytic, or postanalytic phases of the testing.</td>
</tr>
<tr>
<td><strong>2. Training and experience</strong></td>
<td></td>
</tr>
<tr>
<td>• Minimal training is required for preanalytic, analytic, and postanalytic phases of the testing process, and Limited experience is required to perform the test.</td>
<td>• Specialized training is essential to perform the preanalytic, analytic, or postanalytic testing process, or Substantial experience may be necessary for analytic test performance.</td>
</tr>
<tr>
<td><strong>3. Reagents and materials preparation</strong></td>
<td></td>
</tr>
<tr>
<td>• Reagents and materials are generally stable and reliable, and Reagents and materials are prepackaged or premeasured, or require no special handling, precautions, or storage conditions.</td>
<td>• Reagents and materials may be labile and may require special handling to assure reliability, or Reagents and materials preparation may include manual steps such as gravimetric or volumetric measurements.</td>
</tr>
<tr>
<td><strong>4. Characteristics of operational steps</strong></td>
<td></td>
</tr>
<tr>
<td>• Operational steps are either automatically executed (such as pipetting, temperature monitoring, or timing of steps) or are easily controlled.</td>
<td>• Operational steps in the testing process require close monitoring or control, and may require special specimen preparation, precise temperature control, or timing of procedural steps, accurate pipetting, or extensive calculations.</td>
</tr>
<tr>
<td><strong>5. Calibration, Quality Control and Proficiency Testing materials</strong></td>
<td></td>
</tr>
<tr>
<td>• Calibration materials are stable and readily available, Quality Control materials are stable and readily available, and External Proficiency Testing materials, when available, are stable.</td>
<td>• Calibration materials, if available, may be labile, Quality Control materials may be labile, or not available, or External Proficiency Testing materials, if available, may be labile.</td>
</tr>
<tr>
<td><strong>6. Test system troubleshooting and equipment maintenance</strong></td>
<td></td>
</tr>
<tr>
<td>• Test system troubleshooting is automatic or self-correcting, or clearly described, or requires minimal judgment, and Equipment maintenance is provided by the manufacturer, is seldom needed, or can easily be performed.</td>
<td>• Troubleshooting is not automatic and requires decision-making and direct intervention to resolve most problems, or Maintenance requires special knowledge, skills, and abilities.</td>
</tr>
<tr>
<td><strong>7. Interpretation and judgment</strong></td>
<td></td>
</tr>
<tr>
<td>• Minimal interpretation and judgment are required to perform preanalytic, analytic, and postanalytic processes, and Resolution of problems requires limited independent interpretation and judgment.</td>
<td>• Extensive independent interpretation and judgment are required to perform the preanalytic, analytic, or postanalytic processes, and Resolution of problems requires extensive interpretation and judgment.</td>
</tr>
</tbody>
</table>
Manufacturers and the FDA

FDA regulations are recorded in Title 21 of the Code of Federal Regulations, commonly abbreviated as “21 CFR.” This is the reference for not only food and drugs, but also for biologics (including blood and blood components) and medical devices. Establishments that manufacture in vitro diagnostic (IVD) devices must follow these regulations in order to obtain clearance to market their products in the United States.

The FDA outlines a three-step process for manufacturers to obtain market clearance for a new medical device:

1. **Ensure that the product is indeed a medical device.**
   Other provisions of the FD&C Act apply if it is actually a drug or a biologic.

2. **Determine how the FDA may classify the device.**
   The classification identifies the level of regulatory control that is necessary to assure the safety and effectiveness of the medical device. It also determines the next steps to be completed to obtain market clearance – general controls, special controls, premarket notification [510(k)], or premarket approval (PMA).

3. **Develop data and/or information necessary to submit a marketing application.**
   For some 510(k) submissions and most PMA applications, clinical performance data is required. If this is the case, the clinical trials must be conducted in accordance with the Investigational Device Exemption (IDE) regulations in addition to the market clearance rules.

**PREMARKET REQUIREMENTS: LABELING, REGISTRATION, LISTING**

Manufacturers must also ensure that devices are properly labeled in accordance with the FDA’s labeling regulations. Once market clearance is obtained, manufacturers must register their establishments and list the type of devices they plan to market. Registration and listing, which must be done annually, provides the FDA with the location of medical device establishments and the devices manufactured at those establishments. Knowing where devices are made increases the nation’s ability to prepare for and respond to public health emergencies.

Labeling regulations, establishment registration, and medical device listing are part of the general controls to which all IVDs are subject, regardless of their classification. Class I devices may be exempt from the other general controls of the Good Manufacturing Practice (GMP) regulation and premarket notification [510(k)].

The GMP regulation is a Quality Systems (QS) requirement that covers the design, packaging, labeling and manufacturing of a medical device. Premarket notification allows manufacturers to present evidence that their device is at least as safe and effective as a device that is already on the market.

**CLASSIFICATION OF IVDs**

The FDA classifies IVD devices as Class I, II, or III according to the level of regulatory control that is necessary to assure their safety and effectiveness. This classification determines the appropriate premarket process to use: general controls, special controls, premarket notification [510(k)], or premarket approval (PMA).

**CLASS I:** Class I devices are subject to the least regulatory control, usually “general controls” will suffice. They present minimal potential for harm to the user and are often simpler in design than Class II or Class III devices. Most Class I devices are exempt from premarket notification and/or the GMP regulation. Examples of Class I devices include elastic bandages, examination gloves, and hand-held surgical instruments.

**CLASS II:** Class II devices are those for which general controls alone are insufficient to assure safety and effectiveness. In addition to complying with general controls, Class II devices are also subject to special controls, which may include special labeling requirements, mandatory performance standards, and postmarket surveillance. Examples of Class II devices include powered wheelchairs, infusion pumps, and surgical drapes.

>> CONTINUED ON PAGE 6
CLASS III: Class III, the most stringent regulatory category for devices, includes devices for which insufficient information exists to assure safety and effectiveness solely through general or special controls. Class III devices are usually those that support or sustain human life, are of substantial importance in preventing impairment of human health; or present a potential, unreasonable risk of illness or injury. Premarket approval is the required process of scientific review to ensure the safety and effectiveness of Class III devices. Examples of Class III devices include replacement heart valves, silicone gel breast implants, and implanted cerebella stimulators.

POSTMARKET REQUIREMENTS: QUALITY SYSTEMS, MEDICAL DEVICE REPORTING

Once on the market, manufacturers must comply with postmarket surveillance (PS) controls. These controls include the QS GMP regulation and the Medical Device Reporting (MDR) regulation. The MDR regulation is an adverse event reporting program (and is discussed in another article in this issue of Insights); and the GMP regulation was described earlier. An example of PS Controls is shown below.

Postmarket Surveillance (PS) Controls

522 Postmarket Surveillance Studies Program

The 522 Postmarket Surveillance Studies Program encompasses design, tracking, oversight, and review responsibilities for studies mandated under section 522 of the FD&C Act. The program helps ensure that well-designed studies are conducted effectively and efficiently in the least burdensome manner possible.

To achieve this, the FDA has established an automated internal tracking system that identifies and monitors active 522 PS studies to help ensure that all study commitments are fulfilled in a timely manner.

In addition to this, the agency has launched a publicly available webpage to keep all stakeholders informed of each study’s progress.

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pss.cfm

RESOURCES:

1. IVDs are medical devices that analyze human body fluids to provide information for the diagnosis, prevention, or treatment of a disease.
2. The Federal Food, Drug and Cosmetic (FD&C) Act defines “labeling” as: “all labels and other written, printed, or graphic matter upon any article or any of its containers or wrappers, or ‘accompanying’ such article at any time while a device is held for sale after shipment or delivery for shipment in interstate commerce. The term ‘accompanying’ is interpreted liberally to mean more than physical association with the product. It extends to posters, tags, pamphlets, circulars, booklets, brochures, instruction books, direction sheets, fillers, etc. ‘Accompanying’ also includes labeling that is brought together with the device after shipment or delivery for shipment in interstate commerce.”
3. For more information, see the FDA website: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/default.htm

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FDA Solicits Comments on Guidance Document

On July 12, 2011, the FDA distributed a guidance document for comment purposes only: Draft Guidance for Industry and Food and Drug Administration Staff – Enforcement Policy for Premarket Notification Requirements for Certain In Vitro Diagnostic and Radiology Devices (docket #1752).

The FDA has identified certain Class I and Class II in vitro diagnostic (IVD) and radiology devices that have established safety and effectiveness profiles and for which it believes 510(k) review is not necessary to assure device safety and effectiveness.

The guidance document lists several class II devices that the FDA intends to “downclassify” and exempt from 510(k) – premarket notification – requirements, since the agency believes

- the safety and effectiveness of these devices is sufficiently well established,
- they have sufficiently controlled risks,
- general controls are sufficient, and
- a 501(k) review is not needed to assure the safety and effectiveness of these devices.

For the Class I devices that are the subject of the document, the FDA intends to propose an amendment to the classification regulations to exempt these devices from 510(k) requirements. In the interim period, while the FDA proposes and finalizes such downclassification and exemption, the agency intends to exercise “enforcement discretion” with regard to 510(k) submission requirements for the devices (Class I, Class II and radiology) listed in this guidance.

Other requirements of the FD&C Act will still be enforced. These include, but are not limited to:

- Registration and listing,
- Labeling,
- Good Manufacturing Practice (GMP) requirements,
- Medical Device Reporting (MDR) requirements.

This guidance document, and subsequently the downclassification and exemptions, applies only to the specific Class I, Class II and radiology devices listed in the document.

The guidance document, including the list of applicable devices, and the instructions for making comments can be found on the FDA website: http://www.fda.gov/MedicalDevices/DeviceRegulation andGuidance/GuidanceDocuments/ucm262071.htm

Comments and suggestions should be submitted within 90 days of publication of the notice announcing the availability of the draft guidance. (published July 12, 2011; comment period ends October 11, 2011)
Medical Device Reporting

REPORTING ADVERSE EVENTS

According to the Food and Drug Administration (FDA), an adverse event is “any undesirable experience associated with the use of a medical product in a patient.”

The event is serious and should be reported to the FDA when the patient outcome is death, life-threatening, hospitalization, disability or permanent damage, and/or birth defect. You should also report to the FDA if you believe medical or surgical intervention was necessary to prevent a serious event.

Since 1984, the FDA Medical Device Reporting (MDR) regulations have required firms who have received complaints of device malfunctions, serious injuries, or deaths associated with medical devices to notify the FDA of the incident. However, numerous reports – including a 1986 General Accounting Office (GAO) study – showed that there was widespread underreporting. The GAO study showed that less than one percent of device problems occurring in hospitals were reported to the FDA, and the more serious the problem with a device, the less likely it was to be reported. A GAO follow-up study in 1989 concluded that despite full implementation of the Medical Device Reporting (MDR) regulations, serious shortcomings still existed. Partly to address these shortcomings, the Safe Medical Devices Act (SMDA) became law in 1990.

The SMDA provided the FDA with two additional postmarketing activities:

• Postmarket Surveillance – for the monitoring of products after their clearance to market; and
• Device Tracking – for maintaining traceability of certain devices to the user level.

Additionally, it requires user facilities (i.e. hospitals, nursing homes, clinical laboratories, etc.) to report:

• device-related deaths to the FDA and the device manufacturer;
• device-related serious injuries to the manufacturer (or to the FDA if the manufacturer is not known); and
• to the FDA, on an annual basis, a summary of all reports submitted during that period.

See Table 1 for a summary of user facility reporting requirements. Table 2 offers a summary of manufacturers’ reporting responsibilities.

Table 1  Summary of Reporting Requirements for User Facilities

<table>
<thead>
<tr>
<th>REPORTER</th>
<th>WHAT TO REPORT</th>
<th>REPORT FORM #</th>
<th>TO WHOM</th>
<th>WHEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>User Facility</td>
<td>Death</td>
<td>Form FDA 3500A</td>
<td>FDA &amp; Manufacturer</td>
<td>Within 10 work days</td>
</tr>
<tr>
<td>User Facility</td>
<td>Serious injury</td>
<td>Form FDA 3500A</td>
<td>Manufacturer; FDA only if manufacturer is unknown</td>
<td>Within 10 work days</td>
</tr>
<tr>
<td>User Facility</td>
<td>Annual reports of death &amp; serious injury</td>
<td>Form FDA 3419</td>
<td>FDA</td>
<td>January 1</td>
</tr>
</tbody>
</table>

CONTINUED ON PAGE 9
CONTINUED FROM PAGE 8

MEDICAL DEVICE REPORTING

Table 2 Summary of FDA Reporting Requirements for Manufacturers

<table>
<thead>
<tr>
<th>REPORTER</th>
<th>WHAT TO REPORT</th>
<th>WHEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Deaths, serious injuries, and malfunctions</td>
<td>Within 30 calendar days from becoming aware of an event</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Events that require remedial action to prevent an unreasonable risk of substantial harm to the public health and other types of events designated by FDA</td>
<td>Within 5 work days from becoming aware of an event</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Baseline reports to identify and provide basic data on each device that is the subject of an MDR report</td>
<td>With above reports, when device or device family is reported for the first time. Interim and annual updates are also required if any baseline information changes after initial submission</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Annual Certification</td>
<td>Coincide with firm’s annual registration dates</td>
</tr>
</tbody>
</table>

Additional modifications were incorporated in the MDR regulations to help the FDA and manufacturers detect and correct problems in a timely manner, by providing a mechanism to identify and monitor significant medical device adverse events. The MedWatch program was established as part of this mechanism. It is an effective means for user facilities to report significant adverse events or problems with medical products. Reports can be submitted online: https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm or, if preferred, the report form can be downloaded. Once completed, it can be faxed or mailed to the MedWatch offices.

Regardless of how it is submitted, user facilities must keep a record of the report; the MDR regulations require user facilities to “establish and maintain MDR files.” Requirements include written procedures that provide:

- for timely and effective identification, communication, and evaluation of adverse events;
- a review process for determining whether the event is reportable;
- assurance of timely transmission of complete reports, and
- compliance with documentation and record-keeping requirements.

In addition, user facilities must establish and maintain MDR event files. These files may be written or electronic, must be “prominently identified as such and filed to facilitate timely access;” and must be kept for two years from the date of the event. They must include “information in the possession of the user facility or references to information related to the event. This includes all documentation of the reporting decisions and decision-making process, and copies of all completed MDR forms and other information submitted to the FDA, distributors, and manufacturers.”

Although the FDA has legal sanctions available to enforce the requirements of the MDR regulations, the agency relies on the goodwill and cooperation of all affected groups to accomplish the regulation’s objectives. Manufacturers take full advantage of this by issuing voluntary recalls of products. The recalls are sometimes due to issues that the manufacturers discover, but many times, are due to the adverse events reported by user facilities. This in itself underlines the importance of the reporting process.

RESOURCES:

Focus: COLA criteria ORG 9 and ORG 10

ORG 9: Does the laboratory have a procedure for the FDA voluntary reporting of device-related adverse events?

ORG 10: Does the laboratory have documented education of its personnel in the FDA procedure for voluntary reporting of device-related injuries and/or malfunctions?

According to the Food and Drug Administration (FDA), an adverse event is “any undesirable experience associated with the use of a medical product in a patient.” The event is serious and should be reported to FDA when the patient outcome is: death, life-threatening, hospitalization, disability or permanent damage, and/or birth defect. You should also report to the FDA if you believe medical or surgical intervention was necessary to prevent a serious event.

Inaccurate test results that are reported to the health care professional may lead to medical situations that fall under this definition, and thus are reportable events. Reportable device malfunctions or problems may relate to any aspect of a test, (including hardware, labeling, reagents or calibration, or to user error – since the latter may be related to faulty instrument instructions or design).

To monitor post-market activities, the FDA and manufacturers compile the data obtained from voluntary reports. This helps to expedite any necessary corrective actions and/or recall of the medical devices.

Example scenario: Your patients send their glucose results – obtained from their personal glucose meters – to your office via an electronic download. Upon review, you notice several patients have elevated values, so the patients are asked to come in for testing. Glucose specimens sent to the laboratory are significantly lower than the results being reported on the patients’ meters. Upon further review, you notice that this problem occurs only on a particular device. You call the FDA to see if any problems have been reported for this device. You discover that there were none, and you are given the opportunity to report the problem you’ve identified. As a result, the FDA contacts the manufacturer, who launches an investigation, which reveals that the test strips associated with the device were causing elevated glucose results.

You can see how having a procedure for voluntarily reporting device-related adverse events can and will benefit you and your patients. Be sure to train your staff (and document this training) so that they are aware of how to report device failures or malfunctions.

Refer to the COLA Accreditation manual or any of COLA’s education resources (both are available at www.COLAcentral.com) for support. You can also use the compliance modules on the COLAcentral website to store documents, monitor daily operations, and much more!

For more information, visit the FDA website:  
http://www.fda.gov/Safety/MedWatch/default.htm

To submit a report or view FAQ, visit:  
https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
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Join us in Dallas for Two Great New Hematology Sessions!
On Friday, October 21 these new hematology sessions will be presented by Albert Rabinovitch, MD, PhD.

Dr. Albert Rabinovitch has emphasized the perspective of solid science and excellent patient care throughout his storied career.

Dr. Rabinovitch is Pathologist - Director with NovoMetrics, a laboratory consulting organization. In addition to pathology practice and device manufacturer medical direction, he has decades of active voluntary involvement in clinical hematology laboratory instrumentation. He has served as a past Chair of the College of American Pathologist’s Hematology Resource Committee, as a member of the CLSI Consensus Committee on Hematology, and as Vice-Chair of its Consensus Committee on Quality Systems and Laboratory Practices.

10:30am – 12noon
Hematology Interlaboratory Patient Comparisons

This topic explores the various sources of variation and error associated with hematology test results from the perspectives of biological variation, total error, medical goal setting, enhanced use of proficiency testing surveys, intersystem bias, and alternative forms of assessment. It presents the various factors involved in meeting two types of goals with respect to CBC test results:

General Goals:
- Define a system to assess if a fresh blood sample yields comparable results across multiple hematology analyzers within a given system of laboratories – not usually a manufacturer’s claim
- Define “comparable” in analytic, statistical, and medical senses

Medical Goals:
- Ensure that test results accurately reflect patient condition
- Determine if changes in serial samples reflect patient change rather than instrument variation (bias and imprecision)
- Assess if bias shifts patients from one diagnostic group to another
- Decide if serial changes in one patient are significantly different from normal biological variability

Learning Objectives:
- Review and apply criteria for assessing interlaboratory agreement of patient results
- Evaluate data sources to assess state-of-the-art against expert performance goals
- Use provided tools to perform interlaboratory comparisons

1:00pm – 2:30pm
Validation, Verification and Quality Assurance of Automated Hematology Analyzers

An automated hematology complete blood count (CBC) analyzer must provide physicians with reliable medical data for patient management. Truthful data depend upon robust system design, initially validated by the manufacturer and then verified by the end-user laboratory. Because CBC analyses are performed on a heterogeneous suspension of blood cells, particular attention to various preexamination aspects are critical to success in generating accurate patient results. While automated hematology analyzers share the same quality control (QC) principles as automated chemistry analyzers, they also have unique characteristics that require some specialized approaches to QC.

Learning Objectives:
- Summarize the elements of an effective manufacturer’s validation program for CBC analyzers
- Perform a satisfactory end-user clinical laboratory verification of CBC analyzer performance
- Assess the unique aspects of the heterogeneous hematology specimen that require special attention to ensure that CBC analyzers are not “fooled” into yielding wrong results
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Resources & References

**FDA CLIA homepage:**
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm

**Categorization criteria:**
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124208.htm

**In vitro diagnostics homepage:**
http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/default.htm

**Medical device homepage:**
http://www.fda.gov/MedicalDevices/default.htm

**Medical device database listing:**
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm

**Medical device reporting homepage:**
http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm

**Medical Device Reporting for User Facilities (pdf):**

**Recall list:**
http://www.fda.gov/MedicalDevices/Safety/RecallsCorrectionsRemovals/ListofRecalls/default.htm

**Safety communications:**
http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm181502.htm

**Medical devices – latest news:**
http://www.fda.gov/MedicalDevices/NewsEvents/News/default.htm

**Code of Federal Regulations (CFR), 21 CFR, subchapter H Medical Devices:**

**Quality Systems / Current Good Manufacturing Practices:**
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/default.htm

**July 12, 2011 Guidance on “downclassification”:**
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm262071.htm

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Glossary of FDA Terms


**Agency / FDA** – U.S. Food and Drug Administration

**CFR** – Code of Federal Regulations

**Federal Register (FR)** – Publication of the federal government to establish new regulations or to change existing regulations.

**General Controls** – All ivD products are subject to general controls. They provide the FDA with the means of regulating devices to ensure their safety and effectiveness and include provisions that relate to adulteration, misbranding, banned devices, notification (including repair, replacement or refund), records and reports, restricted devices, and the following:

1. **Establishment Registration** of companies which are required to register with the FDA, under 21 CFR Part 807.20, such as manufacturers, distributors, repackagers and relabelers.

   [Owners or operators of places of business (also called establishments or facilities) that are involved in the production and distribution of medical devices intended for use in the United States are required to register annually with the FDA. This process is known as establishment registration. Registration and listing provides FDA with the location of medical device establishments and the devices manufactured at those establishments. Knowing where devices are made increases the nation’s ability to prepare for and respond to public health emergencies.]

2. **Medical Device Listing** (with the FDA) of devices to be marketed.

   [Most establishments that are required to register with the FDA are also required to list the devices that are made there and the activities that are performed on those devices. Registration and listing provides FDA with the location of medical device establishments and the devices manufactured at those establishments. Knowing where devices are made increases the nation’s ability to prepare for and respond to public health emergencies.]


   [Manufacturers must establish and follow Quality Systems to help ensure that their products consistently meet applicable requirements and specifications. The Quality Systems for FDA-regulated products (food, drugs, biologics, and devices) are known as current good manufacturing practices (cGMP’s).]

4. **Labeling** devices in accordance with labeling regulations in 21 CFR part 801 or 809.

   [The Federal Food, Drug and Cosmetic (FD&C) Act defines “labeling” as “all labels and other written, printed, or graphic matter upon any article or any of its containers or wrappers, or ‘accompanying’ such article at any time while a device is held for sale after shipment or delivery for shipment in interstate commerce. The term ‘accompanying’ is interpreted liberally to mean more than physical association with the product. It extends to posters, tags, pamphlets, circulars, booklets, brochures, instruction books, direction sheets, fillers, etc. ‘Accompanying’ also includes labeling that is brought together with the device after shipment or delivery for shipment in interstate commerce.”]

5. **Submission of a premarket notification [510(k)]** before marketing a device. [See below for definition of premarket notification.]

**GMP / Good Manufacturing Practices** – (also referred to as Quality Systems under 21 CFR 820) This regulation provides the framework that all manufacturers must follow by requiring that manufacturers develop and follow procedures and fill in the details that are appropriate to a given device according to the current state-of-the-art manufacturing for that specific device.

**IDE** – an approved or considered approved Investigational Device Exemption under 21 CFR 812 and section 520(g) of the FD&C Act.

**IVD / In Vitro Diagnostic Products** – those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

FDA classifies IVD products into Class I, II, or III according to the level of regulatory control that is necessary to assure safety and effectiveness. The classification of an IVD (or other medical device) determines the appropriate premarket process: general controls, special controls, premarket notification [510(k)], premarket approval (PMA).

**Class I device:** Class I devices are subject to the least regulatory control. They present minimal potential for harm to the user and are often simpler in design than Class II or Class III devices.

Class I devices are subject to general controls as are Class II and Class III devices. Most Class I devices are exempt from 510(k) and/or good manufacturing practices (GMP) regulation. Examples of Class I devices include elastic bandages, examination gloves, and hand-held surgical instruments.

>> CONTINUED ON PAGE 15
CONTINUED FROM PAGE 14
GLOSSARY OF FDA TERMS

**Class II device:** Class II devices are those for which general controls alone are insufficient to assure safety and effectiveness, and existing methods are available to provide such assurances. In addition to complying with general controls, Class II devices are also subject to special controls. Special controls may include special labeling requirements, mandatory performance standards and postmarket surveillance. Examples of Class II devices include powered wheelchairs, infusion pumps, and surgical drapes.

**Class III device:** Class III is the most stringent regulatory category for devices, and includes devices for which insufficient information exists to assure safety and effectiveness solely through general or special controls. Class III devices are usually those that support or sustain human life; are of substantial importance in preventing impairment of human health; or present a potential, unreasonable risk of illness or injury. Premarket approval (PMA) is the required process of scientific review to ensure the safety and effectiveness of Class III devices. Examples of Class III devices include replacement heart valves, silicone gel-filled breast implants, and implanted cerebella stimulators.

**Medical Device Amendments** – amendments to the Food, Drug, and Cosmetic Act signed into law on May 28, 1976. The amendments gave FDA authority to regulate medical devices.

**Premarket Approval (PMA)** – the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices, the most stringent type of device marketing application required by the FDA, any premarket approval application for a Class III medical device, including all information submitted with or incorporated by reference.

[Due to the level of risk associated with Class III devices, the FDA has determined that general and special controls alone are insufficient to assure the safety and effectiveness of Class III devices. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by the FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s). An approved PMA is, in effect, a private license granting the applicant (or owner) permission to market the device.]

**Premarket Notification [510(k)]** – a premarket submission made to the FDA to demonstrate that the device to be marketed is at least as safe and effective, i.e., substantially equivalent, to a legally marketed device that is not subject to PMA. Submitters must compare their device to one or more similar legally marketed devices and make and support their substantial equivalency claims.

**PMA amendment** – information an applicant submits to the FDA to modify a pending PMA or a pending PMA supplement.

**PMA supplement** – a supplemental application to an approved PMA for approval of a change or modification in a Class III medical device, including all information submitted with or incorporated by reference.

**Postamendment device** – a device that is commercially distributed on or after May 28, 1976, the date the Medical Device Amendments of 1976 were signed into law.

**Preamendment device** – a device that was commercially distributed before May 28, 1976, the date of the Medical Device Amendments of 1976 were signed into law.

**Serious, adverse health consequences** – any significant adverse experience, including those which may be either life-threatening or involve permanent or long term injuries, but excluding injuries that are nonlife-threatening and that are temporary and reasonably reversible.

**Special Controls** – may include special labeling requirements, mandatory performance standards and postmarket surveillance. Class II devices are subject to special controls, in addition to complying with general controls.

**Statement of material fact** – a representation that tends to show that the safety or effectiveness of a device is more probable than it would be in the absence of such a representation. A false affirmation, or silence, or an omission that would lead a reasonable person to draw a particular conclusion as to the safety or effectiveness of a device also may be a false statement of material fact, even if the statement was not intended by the person making it to be misleading or to have any probative effect.

**Transitional Devices** – devices that were regulated as drugs prior to the May 28, 1976, the date the Medical Device Amendments were signed into law. Any device that was approved by the New Drug Application (NDA) process is now governed by the PMA regulations. The original NDA approval number is maintained.