- o Summary and explanation of the test, including a short history containing methodology and the special merits and limitations of the test;

- o The chemical, physical, physiological, or biological principles of the procedure.

- o For **Reagents**:

  - The common name, if any, and quantity, proportion, or concentration or each reactive ingredient; and for biological material, the source and measure of its activity;

  - Appropriate cautions or warnings listed in 16 CFR Part 1500; the statement: "For In Vitro Diagnostic Use;" and any other limiting statements appropriate to the intended use of the product;

  - Adequate directions for reconstitution, mixing, dilution, etc.;

  - Appropriate storage instructions;

  - A statement of purification or treatment required for use; and

  - Physical, biological, or chemical indications of instability or deterioration.

* o For **Instruments**:

  - Use or function;
  - Installation procedures and requirements;
  - Principles of operation;
  - Performance characteristics and specifications;
  - Operating instructions;
  - Calibration procedures, including equipment and/or materials;
  - Operational precautions and limitations;
  - Hazards; and
  - Service and maintenance information.

- o Specimen collection and preparation for analysis, describing:

  - Special precautions/preparations;
  - Additives necessary to maintain specimen integrity;
  - Known interfering substances; and
  - Recommended specimen storage, handling, and shipping instructions.

- o A step by step outline of recommended procedures from the reception of the specimen to the obtaining of results. In addition to the following, this should include a list of any points that might improve precision or accuracy:

  - A list of materials provided and instruction for use, e.g., reagents, equipment, etc.;

  - A list of necessary materials that are not provided (include details such as sizes, numbers, types, and quality);

  - A description of the amounts of reagents necessary, and parameters such as time, temperature, etc.;

- A statement related to final reaction stability and any time restrictions on accurate measurements;

- Details of calibration, identifying and listing any necessary preparation of the reference materials, samples, and blanks. Describe the calibration range including the highest and lowest values measured; and

- Details of necessary quality control procedures and materials, e.g., positive and negative controls, acceptable performance limits.

o Explanation of the procedure for calculating the unknown, including the definition of each component of the formula, a sample calculation, and the number of significant figures appropriate for the answer;

o Limitations of the procedure, e.g., identify situations which will have an adverse impact on test results;

o Expected values including the range and how it was established;

o Specific performance characteristics as appropriate including accuracy, specificity, precision, and sensitivity;

* o Bibliography;

* o Name and place of business of the manufacturer, packer, or distributor; and

* o Date of issuance of the last labeling revision by the firm.

EXEMPTIONS FROM LABELING REQUIREMENTS

Shipments or other deliveries of IVD devices are exempt from label and labeling requirements in the above headings and from standards listed under Part 861 provided the following conditions are met:

o A shipment or delivery for an investigation subject to Part 812, Investigational Device Exemption (IDE), if the device is in compliance with the subject IDE; **or**

o A shipment or delivery for an investigation that is **not** in compliance with Part 812 (most IVD's are exempt from the IDE because of the following labeling) if the following conditions are met:

- A product in the laboratory research phase, not represented as an IVD, that is prominently labeled: "For Research Use Only. Not for use in diagnostic procedures;" and

- A product that is being shipped or delivered for product testing prior to full commercial marketing that is prominently labeled: "For Investigational Use Only. The performance characteristics of this product have not been established."

LABELING OF GENERAL PURPOSE LABORATORY REAGENTS AND EQUIPMENT

General purpose items include routine laboratory reagents such as hydrochloric acid and equipment such as glassware whose uses are generally known by persons trained in their use. They do not need to bear the directions for use listed under **Label Requirements for the Immediate Container** and **Labeling Requirements for Inserts and Outer Packaging**, if their labeling meets the requirements listed below. If the product packaging is too small to accommodate a label with sufficient space for the labeling, and if the product is packaged in an outer container which has all of the following on its **labeling,** then only those portions annotated with an asterisk (*) must be on the product **label.**

o **Reagents:**

* - The proprietary and established name;

- A declaration of the established name, if any, and quantity, proportion, or concentration of the reagent ingredient stated in a system generally recognized by the user;

- A statement of the purity and quality including a qualitative statement of any impurities. This can be satisfied by using a statement of conformity with a generally recognized and available standard;

- A statement of warnings or precautions for users as contained in the regulations in 16 CFR Part 1500 and any other appropriate warnings, and the statement: "For Laboratory Use;"

- Net quantity of contents in terms of weight or volume, or numerical count, or any combination thereof;

- Appropriate storage instructions;

* - Name and place of business of the manufacturer, packer, or distributor; and

* - A lot or control number traceable to the manufacturing history of the product.

o **Equipment**

- Product labeling need include only a statement adequately describing the product, its composition, and physical characteristics if necessary for its proper use.

LABELING FOR INVESTIGATIONAL AND 510(K) DEVICES

INTRODUCTION

An "investigational device" is a device that is the object of a clinical investigation or research involving one or more human subjects to determine its safety and effectiveness. This definition also includes "transitional devices" which are devices that had been previously regulated by the FDA as drugs prior to the passage of the Medical Device Amendments, for example, pregnancy test kits.

All newly registered medical device establishments and existing medical device firms introducing new or significantly modified devices must notify FDA of their intent to market the device at least 90 days before introducing the devices into commercial distribution. This is done via a 510(k) Premarket Notification submission which is required by that corresponding section of the FD&C Act. The purpose of this submission, which includes copies of proposed device labeling, is so that FDA can determine whether or not the device as labeled is substantially equivalent to one that was in commercial distribution prior to May 28, 1976. This includes Class I, II, and III devices, or a device that was placed onto the market after that date that was classified by FDA as Class I or Class II. The 510(k) process does not require manufacturers to demonstrate that their devices are identical to marketed devices; only that the devices and their labeled uses be substantially equivalent in terms of safety and effectiveness. Clinical data may be required before FDA can determine whether a device is substantially equivalent under a 510(k).

If a device is found by the FDA to be not substantially equivalent and placed into Class III, the firm must demonstrate proof of safety and efficacy to FDA prior to marketing. This demonstration is done via a Premarket Approval application (PMA). The PMA must contain data which show the device to be safe and effective. An approved Investigational Device Exemption (IDE) enables a device to be shipped to researchers in order to collect data before the device is cleared by FDA for commercial distribution.

FDA must approve IDE applications for significant risk devices. Non significant risk devices are subject only to Institutional Review Board (IRB) approval. The IDE exempts device sponsors and investigators from certain regulatory requirements, i.e., those related to: performance standards, misbranding, premarket approval, registration, and listing, for the duration of the study. The IDE application will contain an investigational protocol which details the nature of the study, and the nature of the data to be obtained and furnished to FDA as proof of safety and efficacy. The sponsor provides detailed information on device labeling in the investigational plan. This information may vary depending on the device and the nature of the study, and can extend to such items as any advertisements placed in order to recruit human subjects for the investigation.

PREMARKET NOTIFICATION [510(K)] LABELING

There is no application form, but there is a format for the 510(k) submission contained in 21 CFR 807.81 to 807.97. Information required in the submission includes: a description of the device and its specifications, the class into which the device has been placed by FDA, the firm's registration number, a statement comparing the device to others of comparable type, and copies of labeling and promotional literature. The proposed device labeling submitted in the 510(k) plays an important role.

Labeling information to be included in a 510(k) submission may include:

- o device labels;
- o packaging labeling;
- o special handling or storage conditions;
- o instructions and/or instruction manuals;
- o service manuals;
- o promotional literature such as advertisements, publications, etc.; and
- o other labeling requirements such as UL, F.C.C., etc.

If the device labeling makes new, previously unsubstantiated claims or promotes use of the device for purposes or conditions other than currently marketed similar devices, the FDA would most likely place the device into Class III and it would need premarket approval prior to marketing. In those instances where a device is substantially equivalent to an existing device, or technology currently in use, a firm should attempt to obtain 510(k) clearance rather than go for premarket approval. The savings in time and cost could be considerable.

IDE DEVICE LABELING REQUIREMENTS (21 CFR PART 812.5)

If a device is found by the FDA to be not substantially equivalent and placed into Class III, the firm must submit a PMA to FDA prior to marketing to demonstrate proof of safety and efficacy. The firm must first apply for an Investigational Device Exemption (IDE) to exempt them from certain regulatory requirements for the duration of the study. The IDE application will contain an investigational protocol which details the nature of the study, and the nature of the data to be obtained and furnished to FDA as proof of safety and efficacy. The firm provides detailed information on device labeling in the investigational protocol. This information may vary depending on the device and the nature of the study, and can extend to such items as any advertisements placed in order to recruit human subjects for the investigation. For example, product labeling should be sufficient to insure stability of the test article for the duration of the study (storage requirements, recalibration procedures), bear sufficient directions for proper administration, alert the user of the investigational status of the article, and detail procedures to follow in the event of patient injury.

In addition to any labeling requirements specified in the IDE study protocol, the following general labeling is required:

- Information required in 801.1, i.e., name and place of business of the firm, quantity, and in 801.109, the following statement: "CAUTION: Investigational Device. Limited by Federal (or United States) law to investigational use."
- A description of all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings and precautions.
- Absence of any statements that are false or misleading, or that represent the device as safe and effective for its investigational purpose.
- Any device shipped solely for use on laboratory animals must be labeled: "CAUTION - Device for investigational use in laboratory animals or other tests that do not involve human subjects."

GOOD MANUFACTURING PRACTICE LABELING REQUIREMENTS

INTRODUCTION

Medical device manufacturers must incorporate in their quality assurance (QA) program several elements that relate to labeling in order to meet the requirements of the GMP regulation. The QA program must be adequate to assure that labeling meets the GMP device master record requirements with respect to legibility, adhesion, etc., and assure that labeling operations are controlled so that correct labeling is always issued and used.

Because many activities must be performed and controlled during the development and use of labeling, Table 5.1 is presented as a checklist. It contains a typical sequence of events required to develop and control labeling.

Labeling includes equipment labels, control labels, package labels, directions for use, maintenance manuals, etc. The displays on CRT's and other electronic message panels are considered labeling if instructions, prompts, cautions, and parameter identification information are given.

Various sections of the GMP regulation have an impact on labeling: Section 820.20(a)(2) requires approval or rejection of packaging materials and labeling; and Section 820.40 requires buildings to be of suitable design and have sufficient space for packaging and labeling operations. Section 820.120 deals with specific requirements for the design and control of labeling. It applies to the design application of labeling to assure legibility under normal conditions of use over the expected life of the device; and also to inspection, handling, storage, and distribution of labeling. FDA considers a device to be adulterated if these requirements are not met. These requirements do not apply to the adequacy of labeling content, except to make sure the content meets the labeling specifications contained in the device master record. However, failure to comply with GMP requirements such as proofreading and change control could result in labeling content errors. In such cases, the device is misbranded and adulterated. Labeling content is covered in the section on "Development of Labeling."

Specifications are required in the device master record (820.181, 182) for the content and physical design parameters of labels. Labeling specifications are: engineering drawing and/or artwork for each label, appropriate inspection or control procedures, and appropriate procedures for attaching the labels. All procedures, drawings, and artwork must have the name of the preparer, an approval signature, and a date. The approval signature, date, etc., may be on the backside of artwork or on a label approval form. Further, artwork may contain only an identification code or title if the "content" of the artwork is duplicated on approved engineering drawings or adequately identified (cross-referenced) with respect to the label approval form.

Hardcopy labels, package inserts, and similar labeling are specified and purchased as components. For correct purchase and use of labeling, specifications are usually stated on engineering drawings and/or purchase specifications. Thus, artwork or "copy" alone will not fulfill the device master record requirements for labeling except for the most simplistic labeling such as brief errata sheets.

The engineering drawings or purchase specifications and mounting procedure must specify, as appropriate, the label substrate, dimensions, ink, finish, mounting method, etc., so that the purchased label will remain attached and legible during the customary conditions of processing, storage, handling, distribution, and use.

Front panels, other instrument panels, meters, fuses, pushbuttons, and the like often are labels or contain labels and must, as appropriate, meet GMP master record and control requirements. Component specifications, assembly drawings, and test/inspection procedures are appropriate GMP controls to prevent mixup of meters, pushbuttons, and other labeled instrument controls. Controls to prevent mixups are generally not needed for front and other instrument panels.

Whether a firm considers a software driven display to be labeling or data makes little difference under the GMP regulation, because either way, the finished device labeling or data must meet the device master record specifications. When firms develop and validate

TYPICAL SEQUENCE OF THE GMP CONTROL OF LABELS (TABLE 5.1)

PHASE	DEVICE TYPE		GMP SECTION (PART 820.)	CONTROL ACTIVITY
1. Development	NC*	C*	.120 & .100	Text review. Quality of mounting (rivets, adhesives, etc.). Quality of ink, anodize, etc. Content per 21 CFR 801, 807, 809, company claims and standards.
2. Evaluation	NC	C	.120	Simulated or actual processing (e.g., Sterilization), shipping tests, etc.
3. Documentation	NC	C	.181	Approve, date and change control label drawings.
		C	.121a	A key label must contain control number of finished device.
4. File Sample		C	.182b	Copy of actual label or artwork in the master record. See .181.
5. Procurement	NC	C	.120a	Proofread before release to inventory stock.
		C	.121b	Record signature of proofreader and date.
6. Storage	NC	C	.120d	Store labels so as to prevent mixups.
		C	.121c	Restrict access to labels to authorized persons.
7. Separate Operations	NC	C	.120b	Separate multiple operations to prevent mixups.
8. Area Inspection	NC	C	.120c	Before beginning labeling operations, designee to inspect area & remove extraneous devices & labels.
9. Issuance	NC	C	.120e	Examine for identity and, where appropriate, expiration date and control number. Record date and person examining labels.
10. Inspection	NC	C	.160	Inspect finished device per written procedure.
		C	.161	Designee must check all acceptance records & test results & see that records are present and complete.

* NC = Noncritical; C = Critical

software, they should also review these electronic displays to see that the "labeling" meets all applicable requirements, such as adherence to specifications in the master record, correct parameter identification, agreement with the instruction manual, and, of course, correct display of performance data.

When reviewing or auditing labeling operations, it is wise to keep in mind that the GMP regulation contains flexible requirements and thus allows flexibility in a quality assurance program. The degree of labeling control needed to satisfy the GMP regulation varies considerably for different devices and operations. In order to avoid wasting money and increasing the cost of health care, manufacturers need to give considerable and prudent thought to the appropriate level of control needed for their operations as allowed by 820.5. Information and guidelines presented in this chapter should aid manufacturers in making these decisions. The level of control needed should be reconsidered when products are added or changed. Likewise, the controls needed and success of the existing control program **must** be reviewed during QA system audits.

GENERAL DEVICE LABELING REQUIREMENTS

Label Integrity

All labels must be designed and applied to devices and containers so that the labels will remain in place and legible during the customary conditions of distribution, storage, and use. Likewise, other labeling such as user instructions should remain legible during customary storage and use. Note that 820.120(a) which states "Labels shall be designed, printed, and applied so as to remain legible..." refers to the actual design of the label and mounting method--not just testing or inspection of these to show that design requirements have been met. [Inspection is covered by the second sentence of 820.120(a), and by 820.120(e), 820.20(a), 820.80 and 820.160.] For example, labeling printed by machines onto plastic in vitro diagnostic media plates is sometimes smeared and thus is inadequate [FD&C 502(f)]. The manufacturers of such devices must assure that the print is legible and will remain legible until used.

Some magazines use "wet" ink which smears when touched by sweaty or oily fingers. Obviously, this type ink will not meet the GMP design requirements for package inserts, instruction manuals, etc.

Labels may be mounted by adhesives, screws, rivets, drive screws, etc., or printed or etched onto panels and/or onto controls. The labels should be located so that they will be seen but not be abraded during use. (Some of us have seen the unbelievable cases where safety labels on ladders and riding lawnmowers were placed in the foot rest areas. Of course, they were scrubbed off after a few uses!)

Receipt and Inspection

Upon receipt, all packaging and labeling materials, including preprinted containers, inserts, and preprinted packaging materials must be examined and, if deemed necessary by the company, tested to assure conformance with specifications. Also, samples of labels must be proofread by a designated individual(s). After being accepted by a responsible individual, these components may be placed into inventory or into production. These inspections must be recorded in the device history record as required by 820.80(a) and 820.120 to show that inspection and proofreading were performed. The inspection record for device labeling should be kept simple.

Area Separation and Inspection

All labeling and packaging operations should be separated to the degree necessary (820.5 and 820.40) to **make certain** there are no mixups between similar products or labels. Separation may be either a physical or spatial separation or by performing the labeling and packaging at different times for different devices. Separation is not required when mixups are impossible such as the case of labeled front panels that only fit the intended family of instruments (devices).

The likelihood of a labeling mixup determines how stringent production area controls should be. For example, label control need not be stringent if only dissimilar products and labeling are processed. Before beginning any packaging and labeling operation in which mixup could occur, the production area and equipment for the operation **must** be thoroughly examined to make certain that any devices and labeling materials remaining from previous operations have been removed. It is important to make certain that the surrounding area, tables, packaging lines, printing machines, and other equipment are cleared of labels and other materials used in the previous operation.

Unused labeling that contains pre-coded serial numbers, manufacturing date, expiration date, control number, etc., should be destroyed and not returned to the label storage area. The GMP regulation does not require reconciliation of the number of labels used versus the number issued, although this control is recommended for some devices, such as when different sizes of the same product are being packaged or otherwise labeled.

Storage

All printed packaging and labeling materials, including preprinted containers, inserts and preprinted packaging materials, **must** be stored in an area and manner suitable to prevent mixups (820.40, 820.120). Labeling should be identified and segregated to the degree necessary to prevent mixing of similar labeling. Access to labeling should be limited to authorized personnel.

Storage control should be appropriate for the number and kind of devices. For example, a firm that manufactures only one product with one label does not need an elaborately controlled storage area. Similarly, a firm with only a few types of devices having dissimilar labeling would not normally require stringent control.

One case that requires dedicated attention to storage and control is prelabeled "sterile" but "not-yet-sterilized" devices. Firms must make **absolutely certain** that mixups cannot occur. Also **make certain** that all such samples, if used for market promotion, are sterile or stamped with a manifest caution statement because a packaged and labeled market-promotion sample might be used by the recipient. Quality awareness training is required by Section 820.25 and marketing personnel must be informed of labeling control requirements and the consequences of a violation.

Label Check and Record

When issued for use, labeling **must** be carefully examined to make certain the contents of the labeling comply with the labeling specifications in the device master record for the specific device being produced. This examination **must** include any control numbers or expiration dates used on the labels. A record of this issuance check, including the date and name of the person performing the examination, **must** be made in the device history record.

If used, expiration dates **must** reflect the time after final packaging during which the device is fit for its intended use when stored and used per its labeling. The manufacturer should have stability test data which establishes the interval that the device remains fit for use.

If label mixups **cannot** occur--for example, a firm makes only one device or uses only one label--and there are no control numbers or expiration dates, the original inspection when the labeling was placed into inventory is an adequate check for compliance with the master record specifications. A second check need not be performed because it serves no purpose (820.5). If, however, there is any possibility that incorrect labeling can be used, a second check **must** be made when the labeling is issued for application, packaging, or shipping.

Changes

Labeling is part of the device master record; therefore, all changes to labeling **must** be made under a formal change control system similar to that required for specifications [820.100(a)(2)]. Any changes to labeling **must** be formally reviewed and authorized before implementation.

When making changes to primary aspects of a device and to primary documentation, the review group must determine if any secondary items such as labels or instructions are affected and also need changing. There should be a check-off block on change-order forms for recording that the effect of the primary change on labeling was considered and appropriate action was taken.

Relabeling and Over-labeling

Over-labeling by placing a new label over an old label is discouraged by FDA but is acceptable as long as the new label and its use meet GMP requirements (820.120, 820.115) for attachment, legibility, reprocessing, and change control. (Over-labeling is also discouraged in some foreign countries.)

ADDITIONAL LABELING REQUIREMENTS FOR CRITICAL DEVICES

Labeling for critical devices **must** meet the noncritical device labeling requirements and meet the three additional requirements in 820.121 as covered below.

Control Number

Critical device labeling **must** contain a control number, serial number, letters, etc., for traceability. This means a control number for the finished device, and not the label itself. Most labeling, however, also contains another number, such as a drawing number, for control of labeling configuration and procurement.

The control number for traceability need not be on every label on the device; however, the control number **must** appear on the unit label that goes to the ultimate user. The label on a shipping carton for bulk items does not meet this requirement because bulk items may go to a central distribution point in the user-facility and the shipping carton would most likely be discarded. In order to meet this traceability requirement, a label that would most likely reach the nurse or other user station **must** have the control number.

Proofreader's Signature

Before releasing labeling for critical devices to inventory, samples of labeling **must** be proofread as required for noncritical devices. In addition, the signature of the proofreader and the date of the proofreading **must** be recorded in the device history record.

Access Restriction

Access to labeling **must** be restricted to authorized personnel. Labeling also should be stored in an adequately segregated area to minimize the chance of mixups. Although the access requirement applies to labeling for critical devices, it is also recommended for labeling for noncritical devices because it increases the control over the label storage area with no significant increase in cost.

STERILE DEVICE LABELING

Special attention should be given to the labeling of sterile devices. Devices that are not sterile in their entirety (for example, sterility may be needed only for the lumen of certain devices) **must** be labeled to properly inform users what is actually intended to be "sterile" in the package. For example, a possible limiting statement might be:

> "**Caution:** Only the fluid path of the set is sterile and nonpyrogenic. Do not use in a sterile or aseptic area without proper precautions."

Some devices are intended to be sterilized by the user before use. In this situation, the labeling should provide adequate information as to at least one suitable method of sterilization and any precautions or safeguards to be followed. For example, the labeling should describe any:

- special cleaning methods required;
- changes in the physical characteristics of the device that may result from reprocessing which affect its safety, effectiveness, or performance; and
- limit on the number of times resterilization and reuse can be done without affecting the safety or effectiveness of the device.

In the case of single-use sterile devices, some manufacturers include labeling to advise against resterilization and reuse. Some devices are simply not designed or constructed to be recleaned, and may not be capable of withstanding the necessary recleaning and resterilization procedures. Where reuse is common practice, manufacturers are encouraged to provide the information described in the above list.

The label of multi-device kits or packages containing a combination of sterile and nonsterile products **must** not state or imply that all contents are sterile.

The need for users to have instructions on how to open a sterile device package to avoid contamination of the device also needs to be evaluated, and when necessary, such instructions should be included in the labeling.

When a manufacturer modifies a device, the manufacturer must also review the labeling to make certain that it reflects current revisions and specifications. Some manufacturers identify labeling with a drawing number plus a revision code or date as an aid in identifying current labeling. The package insert or other labeling for in vitro diagnostic products is **required** to contain the revision date [21 CFR 809.10(b)(15)].

Shelf-life dating solely for package integrity and sterility is not usually required by FDA for general medical devices. There may be a need for expiration dating when a particular component of a device, such as a battery or diagnostic reagent, has a finite useful life. Labeling for in vitro diagnostic devices [809.10(a) and (b)] requires an expiration date or some other means by which users may be assured of quality at the time of use. This requirement applies to both sterile and nonsterile in vitro diagnostic devices.

Although not required by regulation, most manufacturers of complex devices and sterile devices voluntarily use lot or serial numbers for production control and, if the need arises, to expedite failure investigations, repairs, modifications, or recalls. Lot, batch, or other control numbers are required for:

- o critical devices (820.121);
- o some products subject to radiological health standards; and
- o in vitro diagnostic devices [809.10(a)(9)].

Adequate labeling for a medical device requires proper design and procurement of the labels and labeling. Design includes labeling content that meets the requirement of the GMP regulation as well as the needs of the customer. To achieve these goals a number of concepts must be kept in mind such as: writing to the reader, referring to the actual device in labeling, obvious identification of the controls used, etc.

CONTRACT STERILIZATION

Finished devices that are terminally sterilized by a firm other than the manufacturer pose a unique labeling problem. A common industry practice is to send the finished device in its final packaging to a contractor for sterilization. The final packaging is labeled as sterile even though the goods are unsterile during shipment from the manufacturer to the contractor. Specific restrictions apply in this instance, and a written agreement between the parties must be in effect [820.150(e)]. The requirements for the labeling of in process sterile goods in transit to the contract sterilizer are addressed in detail by Section 801.150, and covered previously under **Other Exemptions** in this booklet. Extreme care must be taken in this situation to eliminate the possibility of an unsterilized product being mistaken for a sterilized product. A firm should seriously consider the use of "visual indicator" labeling to distinguish between product before and after sterilization, e.g., the use of indicator tape with bands that develop color upon exposure to steam or ethylene oxide, or stick-on "dots" which change color upon exposure to radiation. Bear in mind that visual indicators will provide confidence that the product has been exposed to a sterilant and not that the product **is** sterile. A firm should also consider the use of dosimeters, i.e., a product that undergoes an irreversible change in physical or chemical properties that is proportional to the amount of exposure to a sterilant. Some contract sterilizers affix labeling to a contractor's product in the form of a sterilization number stamped upon the device container, or outer shipping containers. Firms who use the contract sterilizer's lot number as assurance that their devices have undergone sterilization should determine, via an audit of the facility if possible, that sterilization lot numbers are applied after, not before, being subject to sterilization.

Regulations on distribution are contained in 21 CFR 801, Subparts A and E; and GMP Sections 820.150, 820.160 and 820.161. Devices that have been sterilized, held, or shipped to the manufacturer's warehouse or other **controlled** distribution point before final release must be properly labeled. The pallets, or designated unit, must be marked to indicate the status of the device such as "sterilized: awaiting test results," or an equivalent statement. The company must be able to show that it has control of the devices until final release and, if necessary, could have them destroyed or returned for reprocessing. For this reason, a distributor's warehouse or facility is not considered a controlled distribution point.

RADIATION-EMITTING DEVICE LABELING

INTRODUCTION

Labeling of radiation-emitting products applies to medical devices; all products which emit ionizing, or nonionizing electromagnetic or particulate radiation; and products which emit sonic, infrasonic, or ultrasonic radiation as the result of operation of an electronic circuit. Radiation-emitting devices include products that emit radiation either by design (e.g., X-ray equipment) or as a consequence of operation (e.g., television set), but exclude products that emit radiation as a result of the decay of a radioactive element or isotope (e.g., an ionization type smoke detector). Section 358 of the Radiation Control for Health and Safety Act (RCHSA) of 1968 authorizes the development of Federal standards for these types of radiation producing products. These standards are contained within the regulations listed under 21 CFR Part 1000. The corresponding regulations are listed by product type in subsequent headings of this section. This booklet will cover only those portions of these standards related to product labeling and will not attempt to address technical specifications contained in the standards. Thus, the nature and placement of labeling may vary from those previously discussed under **General Device Labeling;** however, the concepts of "label" and "labeling" remain the same, e.g., the "label" of a device might consist of a warning label on the console of an X-ray system, as well as a red indicator light on the panel; the "label" of a television receiver might consist not only of the name of the manufacturer, date of manufacture, and user caution statements, but also of labels **inside** the receiver related to high voltages and X-ray shielding.

At the present time, as a matter of choice and practicality, FDA does not choose to actively regulate some common household products such as radios and incandescent light bulbs; however, if such products were found to pose a consumer hazard, the FDA could choose to regulate them. A good example of a hazard to consumers is the cordless telephone. As a result of consumer complaints, and confirmed injuries due to the placement, volume, and frequencies of ringers in certain brands of telephones, FDA set and enforced guidelines to prevent hearing injuries.

This section will cover labeling of radiation-emitting medical and other electronic devices. Due to the amount of technical data contained in the corresponding sections of the CFR, reprints of the CFR sections pertaining to laser labeling will be used where appropriate to demonstrate format requirements. Numbers appearing in parentheses next to subject headings are the corresponding sections of 21 CFR.

GENERAL LABELING REQUIREMENTS FOR ELECTRONIC PRODUCTS (1010.3)

Manufacturers of electronic products covered under a performance standard shall provide the following information on a tag or label permanently affixed or inscribed on the product. The following information should be readily viewable when the product is fully assembled:

- o The full name and address of the manufacturer of the product.
  - Alternately, the product can contain the full name and address of a company or individual other than the manufacturer, provided that the full name and address of the actual manufacturer has been previously identified to the Director of the Center for Devices and Radiological Health (CDRH). (This alternative is necessary so that CDRH can identify manufacturers of particular models of devices in those instances where the listed distributor uses different manufacturers for each model.)
  - Abbreviations such as Co., Inc., or their foreign equivalents, and the initials of the first and middle names of individuals may be used.
- o The place and month and year of manufacture.
  - The place of manufacture may be expressed in a code if the code has been previously supplied to the Director of CDRH.
  - The month and year of manufacture cannot be coded or abbreviated. The month and a four digit number for the year must appear as follows:
    "**MANUFACTURED: (Insert Month and Year of Manufacture)**"

In a case where it is not feasible to affix identification labeling in accordance with the above, the Director of CDRH may approve an application for an alternate means of identification.

The manufacturer must furnish the Director of CDRH with a complete listing of all brand names and the names and addresses of the individuals or companies for which electronic products are manufactured under a standard.

Electronic products intended for United States Government use may be exempted from the above upon application to the Director of CDRH by the manufacturer, assembler, or a U.S. department or agency.

All products intended solely for export shall be labeled or tagged to show that they are intended for export.

The manufacturer of any electronic product covered by an exemption from performance standards (i.e., standards, other than labeling, which are not covered in this chapter) must permanently attach a tag or label stating:

"This electronic product has been exempted from the Food and Drug Administration radiation safety performance standards prescribed in the Code of Federal Regulations, Title 21, Chapter I, Subchapter J, pursuant to Exemption No.__, Granted on _____."

IONIZING RADIATION-EMITTING PRODUCTS

Television Receivers (1020.1)

A television receiver is an electronic product designed to receive and display a television picture through broadcast, cable, or closed circuit television. Digital monitors which display a fixed (non-moving) image, e.g., computer screens, are excluded from the standard.

- o Any receiver capable of producing radiation in excess of the standard through component failure or improper adjustment shall have a permanently affixed or inscribed warning label listing the high voltage specification and instructions for adjusting the high voltage to the specified value.

Cold-cathode Gas Discharge Tubes (1020.20)

Cold-cathode discharge tubes are devices designed to demonstrate the effects of a flow of electrons or the production of X-rays.

- o Manufacturers shall provide applicable safety instructions, instructions for use, and power source specifications for each tube.
  - Each enclosure or tube shall have permanently affixed polarity identification of the terminals.
  - Tubes designed for heat, fluorescence, or magnetic effect must have a warning indicating that excess power application may result in x-radiation.
  - Tubes designed for x-radiation must bear a warning that the device produces X-rays when energized.
- o The required tags or labels must be visible when the device is fully assembled for use.

Diagnostic X-ray Systems (1020.30)

Diagnostic X-ray systems incorporate one or more certified components.Certified components are X-ray system components manufactured after certain dates listed in 21 CFR 1020.30(a)(i). Both diagnostic X-ray systems and computed tomography X-ray systems manufactured before November 29, 1984, are subject to the following requirements:

- o The control panel containing the main power switch shall have a statement reading: **"WARNING: This X-ray unit may be dangerous to patient and operator unless safe exposure factors and operating instructions are observed."**
- o Temporarily installed compatible components must bear the following labeling: **"Temporarily Installed Compatible Component.** This certified component has been assembled, installed, adjusted, and tested by me according to the instructions provided by the manufacturer. Signature; Company Name; Street Address, City, State, Zip Code, and Date of Installation."

- Temporarily installed noncompatible components must bear the following labeling: "**Temporarily Installed Noncompatible Component.** This certified component has been assembled or installed by me, but could not be assembled, installed, adjusted, and tested by me according to the instructions provided by the manufacturer because other already existing components of the system do not meet the compatibility specifications of the certified component being installed, and there are no commercially available certified components of a similar type that are compatible with the system. Signature, Company Name, Street Address, City, State, Zip Code, and Date of Installation."

Radiographic Equipment (1020.31)

- If the device has the capability of overriding the positive beam limitation (PBL) in case of system failure, the override key or switch shall be labeled: "FOR X-RAY FIELD LIMITATION SYSTEM FAILURE."

- If the device has the capability of overriding the automatic X-ray field size adjustment in case of system failure, the override switch shall be labeled: "FOR X-RAY FIELD LIMITATION SYSTEM FAILURE."

Fluoroscopic Equipment (1020.32)

- If the device has the capability of overriding the automatic X-ray field size adjustment in case of system failure, the override switch shall be labeled: "FOR X-RAY FIELD LIMITATION SYSTEM FAILURE."

Cabinet X-ray Systems (1020.40)

- At least one indicator shall be visible from each door, access panel and port, and labeled: "X-RAY ON."

- If a cabinet X-ray system is designed to admit humans, it must bear the following additional labeling:

  - Any controls which can be used to initiate X-ray generation must be labeled:

    "CAUTION: X-RAYS PRODUCED WHEN ENERGIZED"

  - Each port shall have a clearly visible label stating:

    "CAUTION: DO NOT INSERT ANY PART OF THE BODY WHEN SYSTEM IS ENERGIZED - X-RAY HAZARD."

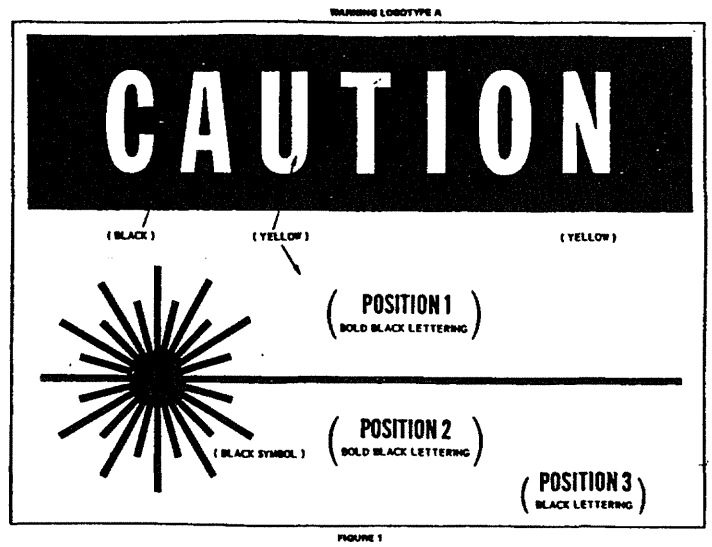
LIGHT-EMITTING PRODUCTS

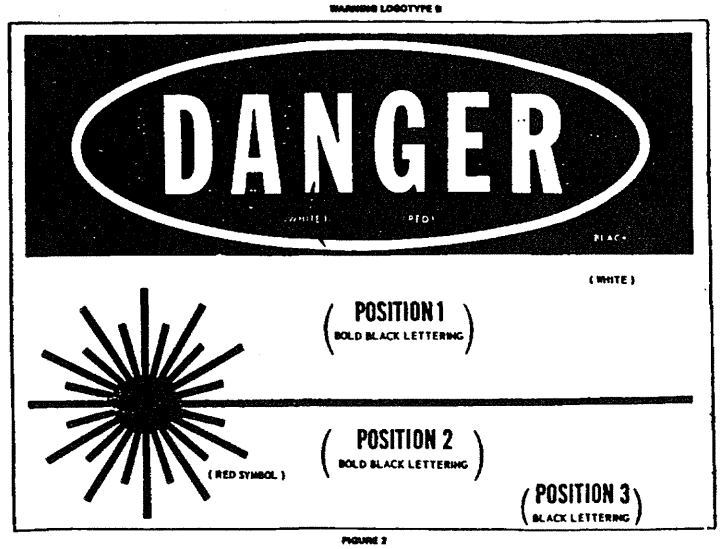
Lasers (1040.10)

Lasers are devices capable of producing intense radiation at a specific wavelength both for medical and industrial purposes. In addition to the general labeling requirements for firm name, street address, state, and zip code, lasers require labeling specific to their type, class, wavelength, and power output. Due to the numerous combinations of

labeling types dictated by class, wavelength, and power output, it would not be practical to cover each in specific detail in this booklet. Instead, use the following sample label types in conjunction with the following reprints of CFR sections to demonstrate specific labeling requirements.

SAMPLE LASER LABELS





(g) *Labeling requirements.* In addition to the requirements of §§ 1010.2 and 1010.3, each laser product shall be subject to the applicable labeling requirements of this paragraph.

(1) *Class IIa and II designations and warnings.* (i) Each Class IIa laser product shall have affixed a label bearing the following wording: "Class IIa Laser Product—Avoid Long-Term Viewing of Direct Laser Radiation."

(ii) Each Class II laser product shall have affixed a label bearing the warning logotype A (Figure 1 in this paragraph) and including the following wording:

[Position I on the logotype]

"LASER RADIATION—DO NOT STARE INTO BEAM"; and

[Position 3 on the logotype]

"CLASS II LASER PRODUCT".

(2) *Class IIIa and IIIb designations and warnings.* (i) Each Class IIIa laser product with an irradiance less than or equal to 2.5×10^{-3} W cm^{-2} shall have affixed a label bearing the warning logotype A (Figure 1 of paragraph (g)(1)(ii) of this section) and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—DO NOT STARE INTO BEAM OR VIEW DIRECTLY WITH OPTICAL INSTRUMENTS"; and,

[Position 3 on the logotype]

"CLASS IIIa LASER PRODUCT".

(ii) Each Class IIIa laser product with an irradiance greater than 2.5×10^{-3} W cm^{-2} shall have affixed a label bearing the warning logotype B (Figure 2 in this paragraph) and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—AVOID DIRECT EYE EXPOSURE"; and,

[Position 3 on the logotype]

"CLASS IIIa LASER PRODUCT".

(iii) Each Class IIIb laser product shall have affixed a label bearing the warning logotype B (Figure 2 of paragraph (g)(2)(ii) of this section) and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—AVOID DIRECT EXPOSURE TO BEAM"; and,

[Position 3 on the logotype]

"CLASS IIIb LASER PRODUCT".

(3) *Class IV designation and warning.* Each Class IV laser product shall have affixed a label bearing the warning logotype B (Figure 2 of paragraph (g)(2)(ii) of this section), and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION"; and,

[Position 3 on the logotype]

"CLASS IV LASER PRODUCT".

(4) *Radiation output information on warning logotype.* Each Class II, III, and IV laser product shall state in appropriate units, at position 2 on the required warning logotype, the maximum output of laser radiation, the pulse duration when appropriate, and the laser medium or emitted wavelength(s).

(5) *Aperture label.* Each laser product, except medical laser products and Class IIa laser products, shall have affixed, in close proximity to each aperture through which is emitted accessible laser or collateral radiation in excess of the accessible emission limits of Class I and Table VI of paragraph (d) of this section, a label(s) bearing the following wording as applicable.

(i) "AVOID EXPOSURE—Laser radiation is emitted from this aperture," if the radiation emitted through such aperture is laser radiation.

(ii) "AVOID EXPOSURE—Hazardous electromagnetic radiation is emitted from this aperture," if the radiation emitted through such aperture is collateral radiation described in Table VI, item 1.

(iii) "AVOID EXPOSURE—Hazardous x-rays are emitted from this aperture," if the radiation emitted through such aperture is collateral radiation described in Table VI, item 2.

(6) *Labels for noninterlocked protective housings.* For each laser product, labels shall be provided for each portion of the protective housing which has no safety interlock and which is designed to be displaced or removed during operation, maintenance, or service, and thereby could permit human access to laser or collateral radiation in excess of the limits of Class I and Table VI. Such labels shall be visible on the protective housing prior to displacement or removal of such portion of the protective housing and visible on the product in close proximity to the opening created by removal or displacement of such portion of the protective housing, and shall include the wording:

(i) "CAUTION—Laser radiation when open. DO NOT STARE INTO BEAM." for Class II accessible laser radiation.

(ii) "CAUTION—Laser radiation when open. DO NOT STARE INTO BEAM OR VIEW DIRECTLY WITH OPTICAL INSTRUMENTS." for Class IIIa accessible laser radiation with an irradiance less than or equal to 2.5×10^{-3} W cm^{-2}.

(iii) "DANGER—Laser radiation when open. AVOID DIRECT EYE EXPOSURE." for Class IIIa accessible laser radiation with an irradiance greater than 2.5×10^{-3} W cm^{-2}.

(iv) "DANGER—Laser radiation when open. AVOID DIRECT EXPOSURE TO BEAM." for Class IIIb accessible laser radiation.

(v) "DANGER—Laser radiation when open. AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION." for Class IV accessible laser radiation.

(vi) "CAUTION—Hazardous electromagnetic radiation when open." for collateral radiation in excess of the accessible emission limits in Table VI, item 1 of paragraph (d) of this section.

(vii) "CAUTION—Hazardous x-rays when open." for collateral radiation in excess of the accessible emission limits in Table VI, item 2 of paragraph (d) of this section.

(7) *Labels for defeatably interlocked protective housings.* For each laser product, labels shall be provided for each defeatably interlocked (as described in paragraph (f)(2)(iv) of this section) portion of the protective housing which is designed to be displaced or removed during operation, maintenance, or service, and which upon interlock defeat could permit human access to laser or collateral radiation in excess of the limits of Class I or Table VI. Such labels shall be visible on the product prior to and during interlock defeat and in close proximity to the opening created by the removal or displacement of such portion of the protective housing, and shall include the wording:

(i) "CAUTION—Laser radiation when open and interlock defeated. DO NOT STARE INTO BEAM." for Class II accessible laser radiation.

(ii) "CAUTION—Laser radiation when open and interlock defeated. DO NOT STARE INTO BEAM OR VIEW DIRECTLY WITH OPTICAL INSTRUMENTS." for Class IIIa accessible laser radiation with an irradiance less than or equal to 2.5×10^{-3} W cm^{-2}.

(iii) "DANGER—Laser radiation when open and interlock defeated. AVOID DIRECT EYE EXPOSURE." for Class IIIa accessible laser radiation when an irradiance greater than 2.5×10^{-3} W cm^{-2}.

(iv) "DANGER—Laser radiation when open and interlock defeated. AVOID DIRECT EXPOSURE TO BEAM." for Class IIIb accessible laser radiation.

(v) "DANGER—Laser radiation when open and interlock defeated. AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION." for Class IV accessible laser radiation.

(vi) "CAUTION—Hazardous electromagnetic radiation when open and interlock defeated." for collateral radiation in excess of the accessible emission limits in Table VI, item 1 of paragraph (d) of this section.

(vii) "CAUTION—Hazardous x-rays when open and interlock defeated." for collateral radiation in excess of the accesible emission limits in Table VI, item 2 of paragraph (d) of this section.

(8) *Warning for visible and/or invisible radiation.* On the labels specified in this paragraph, if the laser or collateral radiation referred to is:

(i) Invisible radiation, the word "invisible" shall appropriately precede the word "radiation"; or

(ii) Visible and invisible radiation, the words "visible and invisible" or "visible and/or invisible" shall appropriately precede the word "radiation."

(iii) Visible laser radiation only, the phrase "laser light" may replace the phrase "laser radiation."

(9) *Positioning of labels.* All labels affixed to a laser product shall be positioned so as to make unnecessary, during reading, human exposure to laser radiation in excess of the accessible emission limits of Class I radiation or the limits of collateral radiation established to Table VI of paragraph (d) of this section.

(10) *Label specifications.* Labels required by this section and § 1040.11 shall be permanently affixed to, or inscribed on, the laser product, legible, and clearly visible during operation, maintenance, or service, as appropriate. If the size, configuration, design, or function of the laser product would preclude compliance with the requirements for any required label or would render the required wording of such label inappropriate or ineffective, the Director, Office of Compliance (HFZ-300), Center for Devices and Radiological Health, on the Director's own initiative or upon written application by the manufacturer, may approve alternate means of providing such label(s) or alternate wording for such label(s) as applicable.

(h) *Informational requirements*—(1) *User information.* Manufacturers of laser products shall provide as an integral part of any user instruction or operation manual which is regularly supplied with the product, or, if not so supplied, shall cause to be provided with each laser product:

(i) Adequate instructions for assembly, operation, and maintenance, including clear warnings concerning precautions to avoid possible exposure to laser and collateral radiation in excess of the accessible emission limits in Tables I, II-A, II, III-A, III-B, and VI of paragraph (d) of this section, and a schedule of maintenance necessary to keep the product in compliance with this section and § 1040.11.

(ii) A statement of the magnitude, in appropriate units, of the pulse durations(s), maximum radiant power and, where applicable, the maximum radiant energy per pulse of the accessible laser radiation detectable in each direction in excess of the accessible emission limits in Table I of paragraph (d) of this section determined under paragraph (e) of this section.

(iii) Legible reproductions (color optional) of all labels and hazard warnings required by paragraph (g) of this section and § 1040.11 to be affixed to the laser product or provided with the laser product, including the information required for positions 1, 2, and 3 of the applicable logotype (Figure 1 of paragraph (g)(1)(ii) or Figure 2 or paragraph (g)(2)(ii) of this section). The corresponding position of each label affixed to the product shall be indicated or, if provided with the product, a statement that such labels could not be affixed to the product but were supplied with the product and a statement of the form and manner in which they were supplied shall be provided.

(iv) A listing of all controls, adjustments, and procedures for operation and maintenance, including the warning "Caution—use of controls or adjustments or performance of procedures other than those specified herein may result in hazardous radiation exposure."

(v) In the case of laser products other than laser systems, a statment of the compatibility requirements for a laser energy source that will assure compliance of the laser product with this section and § 1040.11.

(vi) In the case of laser products classified with a 7 millimeter diameter aperture stop as provided in paragraph (e)(3)(i) of this section, if the use of a 50 millimeter diameter aperture stop would result in a higher clsssification of the product, the following warning shall be included in the user information: "CAUTION—The use of optical instruments with this product will increase eye hazard."

(2) *Purchasing and servicing information.* Manufacturers of laser products shall provide or cause to be provided:

(i) In all catalogs, specification sheets, and descriptive brochures pertaining to each laser product, a legible reproduction (color optional) of the