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General Requirements & Importance for Labeling of Medical Devices: A Review

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Abstract: Medical device manufacturers see labeling as a important element for maintaining compliance and high safety and character standards, enhancing operational potency, ensuring brand consistency, and supporting company growth. The FDA does not review promotional materials for medical device labeling. Marketing and advertising material for medical devices are not surveyed and cleared by the FDA, However, the regulatory body does make sure that the label and instructions of the product are accurate. They assure that the information on the labels allow for secure use and does not include unsupported claims. The label should be light and easily traceable. Labeling is different for a commercial device versus an investigational device.
Keywords: FDA, Medical device, label.

Introduction:

The term “medical devices” includes everything from highly sophisticated computerized medical equipment down to simple wooden tongue depressors.

A medical device is "an instrument, apparatus, implement, machine, contrivance,

implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."[1]

Labelling is crucial in identifying the medical device and specifying instructions for its proper use. As for drugs, mislabelling of medical devices can result in serious consequences for the user. Hazard warnings or cautions and clear instructions for use are very important.[2]

Background:

Labeling of medical devices is often necessary, both to enable the manufacturers of the devices to meet the requirements for device tracking (i.e. via serial numbering) and to enable customers in the clinical setting to identify and properly employ the devices (i.e. via a model number and/or functional identification of parts). A label for an interventional medical device may be formed as a separate component, for example, being printed on relatively thin biocompatible film (i.e. polyester, polyolefin or fluoropolymer), that is assembled into the device; alternately, a label can be formed on another device component, the primary function of which is independent of that of labeling, for example, by printing, etching or molding marks of the label directly thereon. In either case it is desirable for the label to be readily visible and legible without increasing an overall bulk of the interventional medical device or adversely impacting the function or handling of the device. Although a variety of labeling methods are known in the art, there is still a need for new types of labeling in the medical device industry.[3]

Regulatory Basics for Labeling of Medical Devices:[2]

The United States Food and Drug Administration develops and administers regulations under authority granted by laws passed by Congress that apply to food, drugs, cosmetics, biologics, radiation-emitting electronic products, and medical devices. Of the fourteen laws currently administered by FDA, three directly address the labeling of medical devices

- **The Food, Drug, and Cosmetic (FD&C) Act** - The FD&C Act applies to food, drugs, cosmetics, biologics, and medical devices. Section 201 defines the terms "label" and "labeling" as they apply to medical devices and draws a distinction between these terms. Section 502(f)(I) and (2) requires that device labeling bear adequate directions for use, operating and servicing instructions, and either adequate warnings against dangerous uses to health, or information necessary for the protection of users.
- **The Fair Packaging and Labeling Act (FPLA)** - Because medical devices had previously been defined and regulated by the FD&C Act, Section 5 of the subsequently implemented FPLA Act refers to and makes use of the terms "label" and "labeling." Requirements of the FPLA apply to over-the-counter medical devices distributed by retail outlets.
- **The Radiation Control for Health and Safety Act (RCHSA)** - Section 358(h) of the RCHSA requires manufacturers or distributors of radiation-emitting electronic products, including medical devices, to place certification labeling on their devices.

Labeling regulations promulgated under the above Acts which pertain to medical devices are currently found in the following Part of Title 21 of the Code of Federal Regulations (CFR)

In-Vitro Diagnostics		21 CFR Part 809
Investigational Device Exemptions		21 CFR Part 812
Good manufacturing Practices		21 CFR Part 820
General Electronic Products		21 CFR Part 1010

Why labeling of medical device important?

It is important because of the dangers of misbranding and the associated recalls of such devices, it is important for manufacturers to have the appropriate labeling. Because the Food and Drug Administration (FDA) has some specific regulations regarding what can and cannot be included, it is important for manufacturers to know what to include and how to include it. Similarly, they should also know what cannot be included.

Labels Vs Labeling:[2]

- "Label" defined as a: "Display of written, printed, or graphic matter upon the immediate container of any article"
- "Labeling" as: "All labels and other written, printed, or graphic matter

1. Upon any article or any of its containers or wrappers, or
2. Accompanying such article" at any time while a device is held for sale after shipment or delivery for shipment in interstate commerce.

Labeling and Advertising:

The distinction between labeling and advertising, both of which draw attention to the article to be sold, is often superficial nebulous. Both are used for a similar purpose, i.e. to provide information about the product.

Misbranding:

A device is misbranded if:

- Its labeling is false or misleading in any particular;
- It is in package form and its label fails to contain the name and place of business of the manufacture, packer, or distributor; and an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count;
- Any required wording is not prominently displayed as compared with other wording on the device, or is not clearly stated;
- Its label does not bear adequate directions for use including warnings against use in certain pathological conditions; or by children where its use may be dangerous to health; or against unsafe dosage, or methods, or duration of a ministration or application
- It is dangerous to health when used in the dosage or manner or with the frequency or duration prescribed, recommended or suggested in the labeling; or
- It does not comply with the color additives provisions listed under Section 706 of the Act.
- If the device's established name (if it has one), its name in an official compendium, or any common or usual name is not prominently printed in type at least half as large as that used for any proprietary name;
- If the device is subject to a performance standard and it does not bear the labeling prescribed in that standard;
- If there is a failure or refusal to comply with any requirement prescribed under the FD&C Act, Section 5 18 on notification and other remedies, or failure to furnish any materials or information requested by or under Section 519 on reports and records; or
- If it has any representation that creates an impression of official approval because of the possession by the firm of an FDA registration or premarket notification number.

FALSE OR MISLEADING LABELING:

- A drug or device is misbranded if its labeling proves false or misleading in any particular. A “false impression” may result not only from a false or deceptive statement, but may also be instilled in the mind of the purchaser by ambiguity or misdirection. It may also be caused by failure to inform the consumer or facts that are relevant to those statements actually made.
- A device can be misbranded by making reference to a medical device registration, or premarket notification number assigned by FDA in response to a firm’s filing requirements under the FD&C Act.

Examples of false representations are:

- Incorrect, inadequate or incomplete identification;
- Unsubstantiated claims of therapeutic value;
- Inaccuracies concerning condition, state, treatment, size, shape or style;
- Substitution of parts or material; and
- Use of the prefix “U.S.” or other similar indication suggesting Government or Agency approval or endorsement of the product.

Examples of misleading labeling include:

- Ambiguity, half-truths, and trade puffery;
- Expressions of opinion or subjective statements; and

- Failure to reveal material facts, consequences that may result from use, or the existence of difference of opinion.

General Device Labeling:

The general labeling requirements for medical devices are contained in 21 CFR Part B 801. These regulations specify the minimum requirements for all devices. Later sections in this chapter discuss any additional requirements needed for specific categories of devices

General labeling provisions

Name and Place of Business:

- The label of a device shall contain the name and place of business of manufacturer, packer, or distributor including the street address, city, state, and zip code.
- If the firm's street address is in the local telephone directory, the street address can be omitted.
- If the firm listed on the label is not the manufacturer, the firm information must be qualified by an appropriate statement such as, "Manufactured for ..." or "Distributed by... "

Intended Use

- If a packer, distributor, or seller intends a device for uses other than those intended by the person from whom he received the device, these parties must furnish adequate labeling in accordance with the new intended use.
- If a manufacturer knows or has information indicating that his device is to be used for conditions or purposes other than which it was intended, he is required to provide adequate labeling in accordance with such other uses. (An example of this might be a manufacturer of dental X-ray equipment who is routinely selling his product to podiatrists.)

Adequate Directions

- "Adequate directions for use" means directions under which the layman can use a device safely and for the purposes intended. This includes:

➢ Statements of all purposes for which and conditions under which the device can be used;
➢ Quantity of dose for each use and usual quantities for persons of different ages and physical conditions;
➢ Frequency of administration;
➢ Duration of application;
➢ Time of administration in relation to other factors;
➢ Route or method of application; and
➢ Any preparation necessary for use.

False or Misleading Statements:

- A device is misbranded if it makes a false or misleading statement with respect to another device, drug, food, or cosmetic.

Prominence of Statements :

- A word, statement or other required information may lack the required prominence and conspicuousness for the following reasons: -

– If it fails to appear on the part or panel that is displayed under customary conditions of purchase;
– If the package contains sufficient space and the required information fails to appear on two or more panels, each of which is designed to render it to be displayed under customary conditions of purchase;
– Failure to extend required labeling over package space provided;
– Lack of sufficient label space for required labeling due to placement of non- required labeling on the package; or

- Smallness or style of type, insufficient contrast between labeling and package background, designs which obscure labeling, or overcrowding of labeling which renders it unreadable.

- Exemptions may be granted in those instances where device labeling lacks sufficient space for required labeling provided that:

- Existing label space is not taken up by including non-required information or by giving prominence to a portion of the required labeling; and
- Existing label space is not used for any representations in a foreign language.

- All labeling shall be in English with the exception of products distributed solely within Puerto Rico or a U.S. territory where the predominant language is other than

English. In these instances the predominant language may be substituted for English.

- If any representation on the device label or labeling appears in a foreign language, then all required labeling shall also appear in that foreign language.

Examples of the problems faced during labeling:

- Dialysis bag pin not clearly labeled so fluid did not infuse
- New cardiac catheterization kit changed to non-sterile outer package; staff unaware and thought entire package was sterile.

Over The Counter (OTC) Device Labeling: [1]

Principal Display Panel **21 CFR 801.60**

- The principal display panel is that portion of the label which is intended to be displayed, presented, shown, or examined under customary conditions for retail sales.
- Statement of Identity **21 CFR 801.61**
  The statement of identity of the device must be listed on the principal display panel.
- It must list the common name
- Indications for use
- Bold type,
- Reasonably sized generally parallel to the base of the package
- Net Quantity of Contents Statement **21 CFR 801.62**
- The label of an over-the-counter (OTC) device in package form must contain a statement of net quantity of contents in terms of weight, measure, numerical count; or a combination of numerical count and weight, measure.

Prescription Device Labeling:

- A device which, because of any potentiality for harmful effect, or the supervision of the method of its use, or the collateral measures necessary to its use is not safe unless under a practitioner licensed by law to direct use this device, and hence for which "adequate directions for use" cannot be written, is exempt from such provided:
- It is in the possession of either a licensed practitioner or persons lawfully engaged in the manufacture of distribution of the product;
- Its labeling bears an Rx statement, i.e., "Caution: Federal law restricts this device to sale by or on the order of a (Insert name of physician, dentist or other licensed practitioner);"
- Its labeling bears information for use including, indications, effects, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions under which the device can safely be used; and
- All labeling other than labels and carton bears the date of issuance or date of the latest revision.

In-Vitro Diagnostic Medical Device Labeling Requirements:[3]

- **FDA –** In Vitro Diagnostic Products For Human Use- 21 CFR Part 809
- **International:** In-Vitro Diagnostic Directive (IVDD), October 27, 1998

EN 591:2001 – Instructions for Use In-Vitro Diagnostics, Instructions for Professional Use EN 592:2002 – Instructions for Use In-Vitro Diagnostics, Instruments for Self-Testing

Electronic Labeling: [3]

Medical Device User Fee and Modernization Act (MDUFMA)

- Prescription devices used within the confines of a health care facility may provide labeling for those devices solely in electronic form
- Paper form must be provided upon request of the user without additional cost

International Labeling:

- CE Marking: The CE Mark must appear in a visible, legible and indelible form on the device or its sterile pack and on the instructions for use.
- As far as practical and appropriate, information needed to use the device safely must be on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging (MDD).
- Instructions for use must be included in the packaging for every device.
- Where appropriate, the information should take the form of symbols.

Quality System Regulation:[4]

The QA program must be adequate to ensure that labeling meets the GMP device master record requirements with respect to legibility, adhesion, etc.

- Label Integrity
- Receipt and Inspection
- Area Separation and Inspection
- Storage
- Label Check and Record
- Changes
- Relabeling and Over-labeling
- Control Number

Conclusion:

Labeling is very important to medical device firms because there is often a direct relationship between device misuse and the labeling, especially in the direction for use. Two of the most important aspects in labeling devices is to be cognizant of who will be using the device and how it is to be used.

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4. Medical Device Quality Systems Manual: A Small Entity Compliance Guide, December 1996, 1st edition , 2-5.

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