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AdvaMed
Advanced Medical Technology Association

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Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

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C5-
7529 01 JUN 29 P3:40

Re: Docket # 01-12226 Medical Devices; Global Harmonization Task Force; Study Group 1; Working Draft "Medical Devices Classification;"

Dear Sir or Madame:

The Advanced Medical Technology Association (AdvaMed) is pleased to provide comments on the draft document entitled "Medical Devices Classification" proposed by Study Group 1 of the Global Harmonization Task Force (GHTF). AdvaMed (formerly the Health Industry Manufacturers Association) represents more than 800 innovators and manufacturers of medical devices, diagnostic products and medical information systems. Our members produce nearly 90 percent of the $68 billion health care technology products consumed annually in the United States, and nearly 50 percent of $159 billion purchased around the world annually. We appreciate and support the efforts of the Food and Drug Administration (FDA) to solicit input from its stakeholders as it engages in the activities of the GHTF.

General Comments:

AdvaMed commends the efforts of the GHTF to develop a single medical devices classification system. We believe that a standardized nomenclature, if structured correctly, has great potential for making the registration of products easier in international markets. If the US industry is to continue its growth in the international marketplace, a common system in which to work will be critical for success. Therefore, we support any efforts to develop a proposal that is acceptable to as many countries as possible.

The four-tiered classification system comprising the approach of the GHTF appears to be more complicated than the current US method. Because the GHTF classification system

is based solely on risk, AdvaMed believes that the impact of shifting from FDA's risk/knowledge-based classification system will be both significant and unwise until the risks presented by a device and its use history are taken into account. A substantial body of device knowledge and post-market experience already exists. The failure to recognize such experience in determining device classification essentially eliminates knowledge derived from decades of medical device use and benefit. Such an approach can prove detrimental to timely patient access to medical technology by creating a backlog in the regulatory product review system, as proven devices will be assessed as if they were new. Furthermore, in going from a risk/knowledge-based classifications system to a risk-based system it seems that historical understanding of classification will be lost. The loss of emphasis on knowledge could impact the design process. Valuable historical information, currently considered during the design phase will no longer be applied under the proposed system.

Although the GHTF document recognizes subsequent reclassification of devices based on post-market experience or technological improvements (Section 6.3), the document does not address classification of existing devices based on post-market experience or technological improvements. Before adopting any new classification system, the status of currently marketed devices must be carefully considered.

Moreover, in discussing subsequent device reclassification the GHTF states, "regulatory authorities are encouraged to include a process for changing the assigned classification of a device, when necessary and to consult with their international counterparts when considering reclassification of a device." Without a defined process, it is difficult to imagine how such reclassification on an international level will occur. The potential for disjointed device reclassification is great and could lead to the defeat of global harmonization. AdvaMed, therefore, proposes that the GHTF proposal include a process for reclassification.

If FDA were to adapt these recommendations to its own regulatory requirements, then some type of grandfather clause for existing devices would be needed. However, if existing devices are grandfathered, the classification of existing and new devices in the US may be inconsistent. Otherwise, US device manufacturers will have to reclassify each of their devices under this system. Adaptation of this classification scheme will involve time and resources on the part of both the FDA and the industry.

Submission requirements may change if universal classification changes for devices already on the market. This would either result in a grandfathering of currently marketed devices or require new submissions for these devices. Adoption of the proposed system could require a legislative change, revision to the current regulations for consistency, and a redefining of submission requirements. Any movement toward acceptance of a new

classification scheme should not be done without careful evaluation of the impact on currently marketed devices.

A universal classification system for medical devices would be useful only if most major countries agree to use the system without significant modifications. The usefulness will diminish proportionally with each major country that refuses to participate. In addition, modification of the classification system by a country to individualize the system will diminish the system's usefulness. For example, if the US would modify the classification with multiple exceptions for specific devices, the usefulness across countries will become diluted. Variance in rule interpretation among countries will also limit the intent and usefulness of adopting a universal classification system. When various countries use this tool to determine device classification, we question the likelihood that they will all consistently arrive at the same classification. Accordingly, we recommend the inclusion in the document of a mechanism by which countries could interpret the requirements in the same way.

One beneficial aspect of using medical device features as part of the classification system would be the additional level of objectivity and predictability in the classification process. This particular component of the proposed GHTF system, along with a knowledge-based system, would incorporate key aspects of medical device use and the development process.

Specific Comments:

2.0 Scope

We suggest incorporating the GHTF definition of "medical device" under this section or under section "4.0 Definitions" in order to clarify the scope. In vitro diagnostic devices (IVDs) were specifically excluded from the scope of the document. AdvaMed recommends that the GHTF describe its intent regarding the classification of IVDs. For combination products, products composed of a device and a drug or a device and a biologic, we recommend that the classification of such combination products be exempt from the specific details of this document and be evaluated according to the final intended use/risks instead of each individual component.

Because this document focuses on initial classification and does not consider existing classification systems, we recommend adding the following statements at the end of the third paragraph:

"The process for both initial classification and for any subsequent reclassification should include consideration of all existing classifications in other jurisdictions. Performance

data, available from the device manufacturer, should be included in any consideration for reclassification."

4.0 Definitions

Central Circulatory System

AdvaMed suggests that the term "Central Circulatory System" be changed to "Principal Circulatory System." Although the definition includes the coronary arteries, the term central describes the larger arteries and veins and not a branch such as the coronary arteries. By using the word "Principal" it moves the group of vessels defined in the draft as a more functional role rather than an anatomical role. The word principal would also describe a life sustaining function. Central is more connected to anatomy and relative size as compared to different parts of the system.

Duration of Use

Clarification of the term "continuous" is recommended as it is unclear whether this refers to one single use of the device that is uninterrupted. For example, hemodialyzers presumably would fall into "short term" because each use of the device is approximately 4 hours long (even though dialysis sessions can occur three times per week). Would guide wires and catheters be transient since they are frequently exchanged for others? Would catheter introducers be short term because they remain in the body greater than 60 minutes?

Intended Use

AdvaMed recommends adding a definition for "intended use." The definition in 21 CFR 801.4 would provide a logical starting point for defining intended use.

Invasive Device

This definition, unlike FDA's definition, of non-invasive does not include simple venipuncture used for blood sampling (21 CFR 812.3 (k)). Based on device history and experience, inclusion of simple venipuncture as non-invasive is appropriate, and we recommend that GHTF adopt this interpretation of non-invasive.

In Vitro Diagnostic

If the Study Group adds a discussion on the application of this proposal to IVDs, then we suggest adding a definition for IVDs.

Medical Device

As we stated under the "Scope" section of the document, we suggest adding the GHTF definition of "medical device."

6.0 Recommendations

Section 6.1 Primary Recommendations

Because these recommendations appear to apply to regulatory authorities, we propose modifying the title to "Primary Recommendations for Regulatory Authorities."

This section indicates that the rules should be capable of accommodating future technological developments that may be difficult to predict now. Therefore, we suggest that this guidance make provisions for the possibility that new devices may not fit into the categories and rules as currently defined. Since the future for new devices can't be completely known, these provisions should be flexible and consider product knowledge, together with risk, to ensure reasonable classification. Perhaps, the Study Group could take some examples of technologies currently under development and run them through the rules to determine if the resulting classifications make sense. From the results of this exercise, the rules could be adjusted accordingly.

The fourth bullet point states, "the determination of class should be based on a set of rules derived from those features of devices that create risk." The level of risk (patient and/or user) needs to be specified. We also recommend that determination of class should consider the intended use of the device.

Section 6.2 Factors Influencing Device Classification

This section indicates that regulatory authorities may assign names/number of the individual risk classes based on local preference. It is recommended that the four classes be identified in a common manner that is recognized by all countries instead of allowing local preference to identify the classes. If the goal is to harmonize the classification of devices, the identification of classes should be harmonized as well.

Strict application of a rules-based approach could miss product knowledge that may result in an inappropriate risk class designation for a device. Therefore, we propose adding the following paragraph to this section:

> "Information about a device could lead to a classification different from application of the classification rules alone. If such information is available and

helpful for a proper and reasonable classification, the manufacturer should consult with the appropriate regulatory authority for confirmation of the classification."

Section 6.3 Subsequent Reclassification of a Device

This section indicates that reclassification may occur based on future experience and knowledge. We have observed the reclassification process to be cumbersome and time-consuming in the US and expect that international coordination would present even greater challenges. AdvaMed suggests that GHTF establish mechanisms by which reclassification can be accomplished. We further recommend strengthening this paragraph indicating individual country authorities should not reclassify devices without obtaining agreement from other countries.

Section 6.4 Proposed General Classification System for Medical Devices

Figure 1

We recommend revising Figure 1, General Classification System, by providing a more detailed definition of each risk level based on the information contained in the classification rules and flow diagram. Device examples are provided in the table, but information on device characteristics for each risk level is not provided. This information is more important than listing devices that will obviously fall in the risk level. We suggest either adding a column to the table for device characteristics, or adding a note under the table stating that details regarding the characteristics of various devices in each class are provided in Section 8.0. Once the characteristics have been defined, it would be appropriate to reassess the levels of risk defined in the document.

For the Class C Risk Level, we recommend reversing the words from "High-moderate risk" to "Moderate-High" risk.

7.0 The Determination of Device Class

#2: We suggest changing 'intended purpose' to 'intended use'.

#4 Notes

We recommend adding a statement under the NOTE in item 4 that the information in item 4 may specifically apply to a device that contains animal or human tissue, cells, etc, and/or medicinal products.

8.0 Classification Rules

To clarify each classification rule, AdvaMed recommends providing specific examples of devices for each rule.

The classification rules do not seem to address intended use and indications for use as FDA considers when classifying a device. Special controls and the risk the device poses to the patient and/or user are not addressed. These points, along with the knowledge base for device types, seem to be appropriate in terms of assessing risk and reducing the burden for manufacturers. For example, approximately 8 years ago, all gelatin sealed grafts were Class III devices. Today, all synthetic grafts (with the exception of endovascular grafts) are Class II. If this knowledge-based system evaporates, so would the progress that has been made in the direction of least burdensome requirements.

Rule #1

The comment indicates "return" or "reinfusion" into the body comes under Rule #2 but these terms do not appear in Rule #2. For clarification, we recommend adding these under Rule #2.

Rule #2:

We recommend adding further definition by inserting the following:

> "-if they may be connected to an active medical device in Class B or a higher class, or, (or and/or)
> -if they are intended for use...."

Rule #3

We recommend changing the comment section to read "...treat or modify substances that will eventually be delivered into the body."

Rule #6

We recommend clarifying the last bullet point of Rule #6 which states "intended for transient use are in Class B unless they are intended to administer medicines by means of delivery system, if this is done in a manner that is potentially hazardous taking account of the mode of application, in which they are in Class C" to better understand the types of devices for which this rule applies.

Rule #6 mentions that reusable instruments are Class A and single use instruments are Class B. This classification seems to be reversed, especially in today's world regarding the concerns with transmissible agents. Possibly the need for higher regulatory controls increases with sterile, single use devices as compared to non-sterile devices that must be cleaned and sterilized before use and each subsequent use. AdvaMed recommends that the GHTF add a rationale for distinguishing between single use and multiple use. Reusable devices delivered sterile are still in a lower class than the single use surgical invasive device

Rules #6 and #7

The phrase "defect of the heart" is used to describe Class D devices. Unfortunately, this term is not defined and should be defined in Section 4.0 noting a reference to anatomical defects, valvular disease, pacing problems, or coronary artery disease. The fact that coronary arteries are buried in the definition of "central circulatory system" (propose change to "principal circulatory system") leads to confusion as to what is meant by the term "defect of the heart".

Rules #6, #7, and #8

We recommend defining the term "biological effect" in order to distinguish this type of device from a device with a medicinal product that is described in Rule #13. The classes for devices that have a "biological effect or to be wholly or mainly absorbed" includes Class C (Rule #6) and Class D (Rules #7 and #8). This seems to be inconsistent since a device that has a "biological effect or to be wholly or mainly absorbed" would be difficult to remove from the body regardless if the use is transient, short-term, or long-term. The class for devices with these characteristics needs to be standardized regardless of use and be tied into Rule #13 for devices with medicinal products. Therefore, we suggest adding a reference to Rules #6 through #8 regarding Rule #13 (medicinal product). These characteristics are used extensively in these types of devices and a direct reference to the rule will be helpful to the user of the document.

Rule #9

Shifting from FDA's system of classification to Rule #9 would move devices like vascular grafts from FDA's moderate risk (Class II) designation to GHTF's high risk (Class D). This would tend to negate the recent publication of special controls for vascular grafts and the reclassification of vascular grafts with diameters less than 6 mm to Class II. This trend would move the progress in classification back approximately 10 to 15 years. Furthermore, this approach does not represent the spirit and intent of the least burdensome concept.

Rule #10:

We recommend adding further definition by inserting "or" as follows:

> "-if they are intended to supply energy....., or
> -if they are intended to image in vivo distribution of radiopharmaceuticals, or
> -if they are intended to allow direct...."

Rule #14

We recommend the deletion of classification Rule #14. This rule states, "all devices manufactured from or incorporating animal or human cells/tissues/derivatives thereof, whether viable or non-viable, are Class D." As explained in the document, various jurisdictions subject such devices to different controls and it is expected that subsequent harmonization efforts will address such devices. For these reasons, it is inappropriate to include a classification category for such devices, let alone subject such devices to the highest risk device classification category.

Decision Trees

In the flow chart for Rule #6, we suggest adding a bullet point to the top oval for Rule #6 that states, "Single Use surgical instrument" since it is also a Class B device. We also recommend adding bullet points "Medicinal product incorporated" to the last box under Rule #6. These are also Class D devices.

For further clarification, we recommend incorporating boxes and diamonds for (1) Single Use Surgical Instruments - Class B; and (2) Reusable Surgical Instruments - Class A into the flow charts for Rules #7 and #8.

AdvaMed appreciates the opportunity to provide comments for consideration by the Global Harmonization Task Force as it develops documents to harmonize regulatory approaches among nations. Further, we endorse the comments provided to you by the National Electronic Manufacturers Association.

Sincerely,

Janet Trunzo

Janet Trunzo
Vice President
Technology and Regulatory Affairs

cc: Maurice Freeman