Draft Guidance for Industry and Food and Drug Administration Staff - Safety Considerations for 510(k) Submissions to Mitigate the Risks of Misconnections with Small-bore Connectors Intended for Enteral Applications

U.S. Food & Drug Administration

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Preface

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Draft Guidance for Industry and Food and Drug Administration Staff

Considerations for 510(k) Submissions to Mitigate the Risks of Misconnections with Small-bore Connectors Intended for

Enteral Applications

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I. Introduction

This guidance provides recommendations to manufacturers, FDA reviewers, and other entities involved in submitting or reviewing premarket notification submission [510(k)] for devices that contain small-bore connectors designed for enteral feeding. Small-bore connectors provide a mechanism for the connection between a variety of medical devices including those with enteral and parenteral applications. The use of common connector designs, such as luer connectors, has led to unintended connections between devices that have different intended uses and has resulted in serious and sometimes fatal consequences to patients.[1] [4], [2] [5], [10] [6]

This guidance recommends that 510(k) submitters design and test enteral connectors based upon the Association for the Advancement of Medical Instrumentation (AAMI)/American National Standards Institute (ANSI)/International Organization for Standardization (ISO) 80369-1 standard to demonstrate that each proposed enteral connector is physically incompatible with non-enteral devices. Furthermore, this guidance document serves to notify manufacturers submitting 510(k)s for enteral connectors that color-coding and tagging alone are no longer sufficient to satisfy safety concerns regarding misconnection hazards associated with connectors such as 6% tapered luer connectors. Lastly, this guidance recommends that applicants submitting a 510(k) application perform a risk assessment to assess the risk of the proposed enteral connector misconnecting to non-enteral devices.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Definitions

A. Adapter: A device whose purpose is to form intermediary connections between two medical devices.

B. Enteral connectors: Connectors that attach to devices involved in providing access to the gastrointestinal tract (esophagus, stomach and intestines) to deliver nutrients to the patient. These include nasogastric, nasoduodenal, gastrostomy, and gastrojejunal feeding tubes, including enteral feeding sets, gravity and pumped feeding connecting sets, Y-ports and T-set medication ports, enteral pouches and syringes for feeding and/or enteral medication.

C. Luer: AAMI/ANSI/ ISO 80369-1 standard describes the Luer connector as a small-bore “conical fitting with a 6% taper for syringes, needles, and certain other medical equipment.” Luer connectors have a male and a female component that are joined to form a secure, yet detachable leak-proof connection. The connection is achieved by use of a push fitting (a Luer slip) or a screw-in threaded fitting (a Luer lock) that joins the male and the female tapered fittings.

D. Market-share analysis: An evaluation of the marketing of a specific medical device type to determine the most commonly used connectors in the marketplace.

E. Misconnection: Inappropriate connections occurring between two different device entities, such as enteral feeding systems and non-enteral systems.

F. Non-enteral connectors: Connectors on devices not involved in enteral feeding systems.

H. Non-interconnectable connectors: Connectors that have geometries and other design characteristics that prevent stable connections.

G. Side port: Connecting attachment to feeding tube which allows (1) for medication administration and/or flushing and (2) for fluid or air inflation of balloons.

III. Background

Multiple publications regarding patient injury and death from tubing and catheter misconnections indicate that reports of misconnections have gradually increased in frequency.[1-9] [4] Tubing misconnection occurs when tubing to or from a medical device performing a specific function is unintentionally attached to another medical device that performs a completely different function. Small-bore luer connectors

can freely connect to many different medical devices.[2-9] [5] Human factor errors coupled with widespread use of luer connectors may promote misconnections of enteral to non-enteral devices.[3] [7] To reduce the frequency of connector hazards, the FDA is collaborating with the International Standard Organization to develop the ISO 80369 standards.

On July 9, 2010, the FDA issued a letter to healthcare professionals, hospital purchasing departments and manufacturers of enteral feeding tubes regarding luer lock misconnections. The FDA advised manufacturers to assess the risks of misconnections for their devices and provide proposed solutions with validation for pre-market review. At that time, some manufacturers were using color coding and labeling to reduce the risk of misconnections; others were creating proprietary connectors designed to be incompatible with non-enteral devices. However, recent reports of adverse events have demonstrated that reliance on color-coding of enteral devices alone cannot adequately mitigate the risk of misconnections, especially with similarly color-coded PICC (percutaneously inserted central catheter) lines on the market.[8] [8] [9] [9],

AAMI/ANSI/ISO 80369-1 was published on December 15, 2010 and recognized by the FDA on March 14, 2011. AAMI/ANSI/ISO 80369-1 provides general requirements for small-bore connectors for liquids and gases in healthcare applications. It provides a framework for testing connectors of different medical applications against each other to ensure non-interconnectability. AAMI/ANSI/ISO 80369-1 establishes specific testing methods that can be used to demonstrate non-interconnectability. The FDA’s recognition of AAMI/ANSI/ISO 80369-1 and the agency’s concern over enteral to non-enteral misconnections prompted the FDA to release the current guidance.

IV. Objective

The FDA is issuing this guidance to recommend methods for reducing the likelihood of unintended connections between enteral connectors and non-enteral medical devices. These methods include use of rigid or semi-rigid materials (as described in AAMI/ANSI/ISO 80369-1, Clause 4), performance of mechanical force testing (as described in AAMI/ANSI/ISO 80369-1, Clause 5.8 and Annex B, or equivalent), and conduct of a risk assessment which confirms that the risk of misconnection of the enteral connector with non-enteral medical devices will be mitigated. This guidance also informs manufacturers that the FDA no longer considers color and/or labeling of connectors as adequate measures to mitigate risks of misconnection associated with enteral devices.

V. Scope

The recommendations made in this guidance are applicable to connectors which are part of or form connections to enteral feeding tubes (Product Code KNT, 21 CFR 876.5980), including gastrostomy tubes (KNT, KGC, FPD and FHT), gastrojejunal tubes (KNT), nasogastric tubes (KNT, BSS, FEF, FFW and FPD) and nasoduodenal tubes (KNT). This includes connections located directly on feeding tubes, extension

sets, feeding bag/spikes and syringes. This guidance also addresses side ports and adapter connections.

VI. Recommendations

- FDA recommends that 510(k) submissions for devices with connectors which are part of or form connections to enteral feeding tubes include a declaration of conformity to AAMI/ANSI/ISO 80369-1 in addition to the following specific recommendations. Given that ISO 80369-1 establishes a framework for testing different connectors, but does not identify the specific connectors to be evaluated, even if a declaration of conformity is made, FDA recommends that a full test report, containing the test protocol, results, any deviations, and conclusions, be submitted as part of the 510(k).

A. Connector materials

The FDA recommends that enteral connectors be made of rigid or semi-rigid materials, as described in AAMI/ANSI/ ISO 80369-1, Clause 4, with testing according to ASTM D747 or ASTM D790, or equivalent. Use of rigid or semi-rigid materials will reduce the likelihood of forced fits between flexible connectors that are not intended to connect with each other.

B. Mechanical testing of enteral connectors to assess incompatibility

The FDA recommends mechanical force testing of enteral connectors following AAMI/ANSI/ ISO 80369-1, Clause 5.8, Annex B methods, or an equivalent alternative, to demonstrate that enteral connectors are non-interconnectable with connectors from other health care applications, as listed below.

- connectors for the following device types:
    - intravascular devices;
    - hypodermic applications;
    - breathing systems and driving gas devices;
    - urethral/urinary devices;
    - limb cuff inflation devices;
    - neuraxial devices
- the cones and sockets described in ISO 5356-1:2004 and ISO 5356-2:2006;
- the nipples described in EN 13544-2:2002; and
- the temperature sensor connectors and mating ports specified in Annex DD of ISO 8185;2007.

For each of the device types listed above, manufacturers should identify in their premarket submission the most commonly sold or used non-enteral connectors found in U.S. markets, or within a subset or specific sector of the U.S. market, as determined from a market-share analysis.

To demonstrate non-interconnectable characteristics, the proposed connector

should not provide a secure connection when forcefully assembled to any surface of the connectors described above, and should easily disengage. As described in AAMI/ANSI/ ISO 80369-1, Annex B, the test connectors should be appropriately conditioned and assembled by applying a specified axial force and torque for a specified amount of time. Then, without activating any latch or disengagement mechanism, an axial force of separation should be applied to the assembled connectors to verify that the connectors disengage. Threaded connectors should be tested with both clockwise and counterclockwise rotation.

C. Enteral connector risk assessment

When an applicant submits a new 510(k) application, they should provide a risk assessment to demonstrate they have effectively mitigated the risk of misconnection with their new product. There should be objective evidence that risks have been reduced to acceptable levels according to ISO 14971:2007 or equivalent. For example, the applicant may provide evidence of selection of appropriate material (Section VI . A , above) and quantitative mechanical testing data to demonstrate that the proposed enteral connector has a reduced risk of forming stable attachments to connectors routing into non-enteral devices (Section VI . B , above).

D. Inadequacy of color-coded and labeled connectors

AAMI/ANSI/ ISO 80369-1, Clause 5.8, provides an approach and testing method (Annex B) for reducing misconnection hazards by designing enteral connectors physically incapable of stable attachment to connectors of non-enteral devices. Color-coding and labeling alone are not sufficient to mitigate health concerns from enteral misconnection. 8,9 However, for connectors for which non-interconnectability has been demonstrated (Sections VI . A , B , and C , above), color-coding and tagging of the connector could also be incorporated into the product design.

E. Side ports, adapters, and syringes

To reduce the likelihood of misconnections, the FDA recommends that sideport connectors that are used for flushing and/or drug administration be tested similarly to the enteral connectors described in Sections VI . A , B , and C of this guidance. This means that the connectors should be made of rigid or semi-rigid materials, and mechanical testing should be performed according to recommendations given in AAMI/ANSI/ ISO 80369-1, Clause 5.8 and Annex B, or an equivalent alternative, to demonstrate that enteral flushing/drug administration sideports are non-interconnectable with connectors of non-enteral devices.

Sideport connectors that are used with inflation devices have different risk profiles, and do not necessarily need the same testing as other enteral connectors. However, the FDA recommends that manufacturers identify risks and design mitigations to reduce risks of misconnection.

Adapters are used to connect enteral devices and provide additional connection points where misconnection events can occur. 3 To mitigate misconnection via adapters, the FDA recommends that adapters be treated similarly to enteral connectors, as described in Section VI.A, B, and C within this guidance. This means that they should be made of rigid or semi-rigid materials, and mechanical testing should be performed according to recommendations described in AAMI/ANSI/ ISO 80369-1, or an equivalent alternative, to demonstrate that adapters are specific and compatible for enteral applications only and are non-interconnectable with the connectors of non-enteral devices.

Therefore, the FDA recommends that mechanical testing should be performed according to recommendations described in Section VI . A , B , and C within this guidance.

F. Labeling

In considering approaches to labeling of a specific enteral device, the interpretation of the device name and/or claims are of high importance. The FDA recommends a simplified labeling strategy designed for easy interpretation of connectors to avoid potential confusion. Labeling might include statements such as:

- “The ____ (device) connection is intended connect to _____ (compatible devices)”

The FDA recommends that enteral labeling not include the terms “enteral-only” and “Non-IV.” “Enteral-only” may be misleading in that it may be interpreted to mean compatibility with all other enteral connectors, but incompatibility with non-enteral connectors. Although this guidance describes testing to demonstrate incompatibility with non-enteral connectors, additional testing would be needed to demonstrate compatibility with all other enteral connectors. “Non-IV” is not appropriate because the term “non-IV” does not encompass all the testing that is needed to demonstrate non-connectability with connectors used in other medical applications. When a device manufacturer wants to provide labeling information regarding the design features of their device that may mitigate the risk of misconnections, FDA recommends statements such as the following:

- “The ____ (device) connection is intended to reduce the risk of misconnection between the following connectors/applications: …”
- “The (device/connector) was tested to demonstrate a reduced likelihood of a misconnection in the following areas: …”

G. Usability and human factors testing

Although usability and/or human factors testing is not usually required, applicants can submit evidence that these tests were performed within their 510(k). Future proprietary connectors may need usability and/or human factor testing to confirm there is no unacceptable risk, as described in AAMI/ANSI HE75:2009.[11] [10]

VII. Future Considerations

AAMI/ANSI/ISO 80369-1 provides general requirements for demonstrating non-interconnectability of small-bore connectors. This guidance provides advice to manufacturers of enteral connectors on mitigation of the risk of enteral small-bore connector misconnection hazards. Once final, this guidance will represent the current FDA recommendations for all 510(k) enteral connector applications. As future standards are developed for this clinical application, FDA will update this guidance as appropriate to communicate our recommendations to stakeholders.

VIII. References

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