Contains Nonbinding Recommendations

Safety Considerations to Mitigate the Risks of Misconnections with Small-bore Connectors Intended for Enteral Applications

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Guidance for Industry and Food and Drug Administration Staff

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Preface

Public Comment

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. Introduction

This guidance provides recommendations to manufacturers, FDA reviewers, and other entities involved in manufacturing devices that contain small-bore connectors designed for enteral feeding, as well as those submitting or reviewing premarket notification submissions [510(k)s] for these devices. Small-bore connectors provide a mechanism for the connection between a variety of medical devices including those with enteral and non-enteral (e.g., intravenous) 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.[1,2,3]

This guidance recommends that manufacturers design and test enteral connectors based upon Association for the Advancement of Medical Instrumentation (AAMI)/CN3:2014 (PS), "*Small-bore connectors for liquids and gases in healthcare applications — Part 3: Connectors for enteral applications*" and AAMI/CN20:2014 (PS), "*Small-bore connectors for liquids and gases in healthcare applications — Part 20: Common test methods*" to ensure that each proposed enteral connector is physically incompatible with non-enteral devices. For enteral connectors that do not meet AAMI/CN3:2014 (PS), also known as proprietary connectors or transition connectors, this guidance continues to recommend that manufacturers design and test the devices based upon the AAMI/American National Standards Institute (ANSI)/International Organization for Standardization (ISO) 80369-1 standard "*Small-bore connectors for liquids and gases in healthcare applications — Part 1: General requirements.*"

Furthermore, this guidance document serves to notify manufacturers submitting 510(k)s or modifying a device already cleared for enteral connectors that color-coding, labeling, and tagging attached to the device, by themselves, 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 when submitting a 510(k) or modifying an existing product already cleared via 510(k), a manufacturer should perform a risk assessment to assess the risks 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

Adapter: A device, or a component of a device, whose purpose is to form intermediary connections between two incompatible medical devices.

Enteral connectors: Connectors that attach to devices involved in administration of fluid (liquid) to the gastrointestinal tract or removal of gas or fluids from the gastrointestinal tract. These include nasogastric, nasoduodenal, gastrostomy, and gastrojejunal feeding tubes, including enteral feeding sets, gravity and pump feeding sets, Y-ports and T-set medication ports, enteral pouches, and syringes for feeding and/or administering enteral medication.

Luer: The 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.

Luer Lock Luer Slip

Picture Courtesy of Beaumont Hospitals

Misconnection: Inappropriate connections occurring between two connectors that attach devices with different intended uses or applications, such as enteral feeding systems and non-enteral systems.

Non-enteral connectors: Small-bore connectors on devices that are not involved in enteral (through the gastrointestinal system) feeding systems.

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

Proprietary connector: For purposes of this guidance, small-bore connector designed to conform to the AAMI/ANSI/ISO 80369-1 standard, but does not meet the design requirements of AAMI/CN3:2014 (PS).

Representative market sampling: For purposes of misconnection testing (refer to Section V.B), a sampling of small-bore connectors that are commonly marketed in the United States, and which are representative of connectors that may be present with an enteral connector. These select connectors should include connectors from the medical application types that are identified in AAMI/ANSI/ISO 80369-1.

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

Transition connector: For purposes of this guidance, facilitates enteral-specific connections between the AAMI/CN3:2014 (PS), Part 3 compliant connectors and non-AAMI/ANSI/ISO 80369-1 compliant enteral connectors.

III. Background

Numerous publications regarding patient injury and death from tubing and catheter misconnections indicate that reports of misconnections have increased in frequency over the past several years.[1,2,4-9] Misconnections occur when a connector on a medical device performing a specific function is unintentionally or intentionally attached to a connector from another medical device that performs a completely different function. Small-bore Luer connectors can freely connect to many different medical devices.[2-9] Human factor errors coupled with widespread use of Luer connectors may promote misconnections of enteral to non-enteral devices.[4] To reduce the frequency of connector hazards, the FDA is collaborating with the International Organization for Standardization to develop the AAMI/ANSI/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 premarket 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 intravenous PICC (percutaneously inserted central catheter) lines with Luer connectors.[8,9]

AAMI/ANSI/ISO 80369-1 was published on December 15, 2010, and recognized by the FDA on March 14, 2011, as noted on the FDA's Recognized Consensus Standards webpage (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/results.cfm). 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, and also establishes specific misconnection testing methods. AAMI/CN3:2014 (PS) Part 3 was published on December 2, 2014 and recognized by the FDA on February 11, 2015. AAMI/CN3:2014 (PS) Part 3 specifies the dimensions and recommendations for the design and functional performance of small-bore connectors intended to be used on medical devices and accessories that have an enteral application. In addition, AAMI/CN20:2014 (PS) Part 20 was published on December 2, 2014 and recognized by the FDA on February 11, 2015. AAMI/CN20:2014 (PS) Part 20 specifies test methods to support the functional requirements for the small-bore connectors identified in AAMI/ANSI/ISO 80369-1. The FDA's recognition of AAMI/ANSI/ISO 80369-1, AAMI/CN3:2014 (PS) Part 3, and AAMI/CN20:2014 (PS) Part 20, and the Agency's concern regarding enteral to non-enteral misconnections prompted the FDA to publish the current guidance. Through the combined efforts of industry, medical device purchasers, healthcare professionals, and the appropriate regulatory authorities, the risk of misconnection can be optimally mitigated.

IV. Scope

The recommendations made in this guidance are applicable to connectors that are part of, or form connections to, enteral devices intended for administration of fluids (e.g., enteral formulas and medications) and other nutritional substances. These products are all regulated under 21 CFR 876.5980, and include the following devices:

- Enteral feeding tubes (product code KNT);
- Enteral specific transition connectors (PIO);
- Gastrostomy tubes (KNT, KGC, FPD and FHT);
- Gastrointestinal tubes with enteral specific connectors (PIF);
- Gastrojejunal tubes (KNT);
- Nasogastric tubes (KNT, BSS, FEF, FFW and FPD); and
- Nasoduodenal tubes (KNT).

The recommendations also apply to connections located directly on feeding tubes:

- Extension/administration sets (KNT); and
- Feeding reservoirs/spikes, and syringes (KNT, FMF).

This guidance also addresses side ports and adapter connections. Ports for balloon inflation are not addressed in this guidance.

V. Recommendations

The FDA recommends that devices with connectors that are part of, or form connections to, enteral feeding tubes conform to AAMI/CN3:2014 (PS) Part 3. If such devices with an existing 510(k) clearance have been modified in order to conform to this standard, and the modifications would trigger the need for a new 510(k), FDA does not intend to object if firms submit a declaration of conformity to AAMI/CN3:2014 (PS) Part 3 in an "add-to-file" to their existing 510(k) rather than submitting a new 510(k).[10] Please note the devices with such connectors remain subject to requirements such as GMP requirements (21 CFR 820), including design controls (21 CFR 820.30), and registration and listing (21 CFR 807).[11] In the event a manufacturer creates or modifies device connectors such that they do not fully conform to the AAMI/CN3:2014 (PS) Part 3 standard, e.g., proprietary and transition connectors, FDA expects the manufacturer to submit a 510(k) for FDA review when a 510(k) submission is required. For more information on when to submit a 510(k), please see FDA's guidance, "Deciding When to Submit a 510(k) for a Change to an Existing Device" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm).

Given that AAMI/ANSI/ISO 80369-1 establishes a framework for testing different connectors, but does not identify the specific connectors to be evaluated, even if devices with proprietary or transition connectors conform to AAMI/ANSI/ISO 80369-1, the FDA recommends that full test reports, containing the test protocol, results, any deviations, and conclusions, be submitted as part of the 510(k) submission when a 510(k) submission is required.

A. Connector materials

The FDA recommends that enteral connectors be made of rigid or semi-rigid materials, as described in the currently FDA-recognized version of AAMI/ANSI/ISO 80369-1, Clause 4 or in AAMI/CN3:2014 (PS) Part 3 as appropriate. In addition, it is recommended that the connectors be made of materials with a modulus of elasticity either in flexure or in tension greater than 700 MPa, in accordance with AAMI/CN3:2014 (PS) Part 3. Testing verifying the materials chosen should be conducted according to ASTM D747 "*Standard Test Method for Apparent Bending Modulus of Plastics by Means of a Cantilever Beam,*" ASTM D790 "*Standard Test Methods for Flexural Properties of Unreinforced and Reinforced Plastics and Electrical Insulating Materials*," or equivalent method. 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.

[10] Any device that is represented to conform to an FDA-recognized standard and does not conform to such standard in all respects is adulterated under section 501(e)(2) of the FD&C Act, 21 U.S.C. § 351(e)(2).

[11] Manufacturers' continuing obligations under the quality system regulations in 21 CFR part 820 require control of supply and outgoing product for compliance with design specifications. Compliance with these obligations may be evaluated during routine inspections.

B. Mechanical testing of enteral connectors to assess incompatibility

For connectors that do not conform to AAMI/CN3:2014 (PS) Part 3, 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. The following components should be tested:

- connectors for the following device types:
  - intravascular devices;
  - hypodermic applications;
  - breathing systems and driving gas devices;
  - urethral/urinary devices;
  - limb cuff inflation devices; and
  - neuraxial devices.

For each of the device types listed above, manufacturers should identify in their premarket submissions the most commonly sold or used non-enteral connectors found in U.S. markets, as determined from a representative sample analysis, against which the subject device should be tested.

Regarding testing, to demonstrate non-interconnectable characteristics, the proposed connector should not provide a secure connection with a non-enteral connector when assembled with moderate force, and should easily disengage. As described in AAMI/ANSI/ISO 80369-1, Annex B, and AAMI/CN3:2014 (PS) Part 3, Clause 6, 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 submitting a new 510(k) or modifying an existing 510(k)-cleared device, a manufacturer should conduct a risk assessment to demonstrate that the risk of misconnection has been effectively mitigated with the enteral product. There should be objective evidence to demonstrate that the risks have been reduced to acceptable levels according to the currently FDA recognized version of ISO 14971 or equivalent. For example, the manufacturer may document selection of appropriate material (Section V.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 V.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 secure attachment to connectors of non-enteral devices. As supported by AAMI/CN3:2014 (PS) Part 3, Annex A, color-coding, labeling, and tagging or imprinting (e.g., "feeding only," "medication only") on the device, by themselves, are not sufficient to mitigate health concerns from enteral misconnection.[8,9] However, for connectors for which non-interconnectability has been demonstrated (Sections V.A, B, and C, above), color-coding, labeling, and tagging or imprinting on the connector could also be incorporated into the product design.

E. Side ports, transition connectors, adapters, and syringes

To reduce the likelihood of misconnections, the FDA recommends that side port connectors that are used for flushing and/or drug administration be tested similarly to the enteral connectors described in Sections V.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 outlined in AAMI/ANSI/ISO 80369-1, Clause 5.8 and Annex B, or an equivalent alternative, to demonstrate that enteral flushing/drug administration side ports are non-interconnectable with connectors of non-enteral devices. The use of enteral only syringes may also be used as part of the mitigation of this issue.

Side port 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.

If the risk of use is acceptable, transition connectors may temporarily be necessary within GI applications (e.g., for tubes with both suctioning and feeding functions or for connection between proprietary and AAMI/CN3:2014 (PS) Part 3 compliant connectors). In certain limited circumstances, use of an adapter can provide for medication delivery until connectors meeting the standard are in wide-spread use, in order to avoid deprivation of care.

Syringes are also often used in enteral applications. Syringes used for enteral feeding should only attach to enteral connectors. Therefore, the FDA recommends that mechanical testing should be performed according to recommendations described in Section V.A, B, and C of 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. Instructions for use might include statements such as:

- "The ____ (device) connection is intended to connect to _____ (compatible devices)."

The FDA recommends that enteral labeling, including the instructions for use, 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. "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 information in the instructions for use regarding the design features of their device that may mitigate the risk of misconnections, the 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 device applications: …"

Information regarding the potential to misconnect with other device applications should be included as a warning in the instructions for use. Specific connector types that have the potential to misconnect, and those that were demonstrated to misconnect, should be specified in the instructions for use.

In addition, for the connectors for which non-interconnectability is demonstrated, labeling and tagging or imprinting (e.g., "feeding only," "medication only") on the connector could be incorporated into the product design.

G. Usability and human factors testing

Proprietary connectors with claims of non-interconnectability to all other medical application types should include usability and/or human factors testing to confirm there is no unacceptable risk, as described in the currently FDA recognized version of AAMI/ANSI HE75, *Human Factors Engineering – Design of medical devices.* For additional information on this topic see FDA's draft guidance "Applying Human Factors and Usability Engineering to Optimize Medical Device Design" (http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm259748.htm), which represents FDA's proposed approach on this topic. When final, this document will supersede FDA's guidance entitled "Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management" (http://www.fda.gov/downloads/MedicalDevices/.../ucm094461.pdf) (Issued July 18, 2000). Usability testing in relation to enteral connectors is also described in AAMI/CN3:2014 (PS) Part 3 Annex E.

VI. Future Considerations

AAMI/ANSI/ISO 80369-1 provides general requirements for demonstrating non-interconnectability of small-bore connectors, while AAMI/CN3:2014 (PS) Part 3 specifies the

dimensions and requirements for the design and functional performance of small-bore connectors intended to be used on enteral medical devices and accessories. This guidance provides advice to manufacturers of enteral connectors on mitigation of the risk of enteral small-bore connector misconnection hazards. As future standards are developed and recognized for this clinical application, FDA will update this guidance as appropriate to communicate our recommendations to stakeholders.

VII. References

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