Supplementary Guidance on Premarket Notifications for Medical Devices with Sharps Injury Prevention Features; Guidance for Industry and FDA

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

General Hospital Devices Branch
Division of Anesthesiology, General Hospital, Infection Control, and Dental Devices
Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance, contact Patricia Cricenti at (301) 594-1287 or by email at pxc@cdrh.fda.gov.

Additional Copies

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Table of Contents

Supplementary Guidance on Premarket Notifications for Medical Devices with Sharps Injury Prevention Features; Guidance for Industry and FDA

This document is intended to provide guidance. It represents the Agency'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 the Food and Drug Administration (FDA) or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

I. Introductory Information

A. Scope

This document provides supplementary guidance for the submission of a premarket notification [510(k)] for medical devices that incorporate a sharps injury prevention feature (e.g., anti-needlestick feature). Examples of medical devices now available with a sharps injury prevention feature include: IV administration sets and accessories, piston syringes, hypodermic single lumen needles, IV catheters, blood collection devices, needleless access devices/systems, and vial adapters.

This guidance pertains only to the sharps injury prevention features on medical devices. It does not address all 510(k) submission criteria for any particular device. Other relevant guidance documents that contain additional information on 510(k) submission criteria are referenced in (Section I. F).

Some of the criteria relevant to specific devices are repeated in other guidance documents, (e.g., Guidance on Premarket Notifications for Intravascular Administration Sets). Not all the criteria are applicable for every safety feature. Therefore, please read this guidance carefully to determine which parts are applicable.

While sharps injury prevention features are incorporated as components of many finished devices, such as a safety shield that is an integral part of a piston syringe, some sharps injury prevention products are marketed separately as accessories that are attached to devices by the user at the point of use. An example of a sharps injury prevention accessory is a needle shield that is sold as a separate device and is attached to a specified piston syringe before use. This guidance applies to both integrated and separate accessories.

Desirable Characteristics of Devices with Sharps Injury Prevention Features

A number of sources have identified the desirable characteristics of medical devices with sharps injury prevention features.[4-9] These characteristics include the following:

- The device is needleless.
- The safety feature is an integral part of the device.
- The device preferably works passively (i.e., it requires no activation by the user). If user activation is necessary, the sharps injury prevention feature should be engaged with a single-handed technique, allowing the worker's hands to remain behind the exposed sharp.
- The user can easily tell whether the sharps injury prevention feature is activated.
- The sharps injury prevention feature cannot be deactivated and remains protective through disposal.
- The device performs reliably.
- The device is easy to use and practical.
- The device is safe and effective for patient care.

Although each of these characteristics is desirable, some are not feasible, applicable or available for certain health care institutions. For example, needles will always be necessary where alternatives for skin penetration are not available. In addition, a safety feature that requires activation by the user might be preferable to one that is passive in some cases. Each device will be considered on its own merit and ultimately on its ability to reduce injuries. The desirable characteristics listed here should thus serve only as a guideline for device design and selection.

Exclusions

This document does not address sharps containers and needle recapping devices. There is a separate FDA guidance document for sharps containers and needle destruction devices entitled "Guidance on the Content and Format of Premarket Notification [510(k)] Submissions for Sharps Containers" http://www.fda.gov/cdrh/ode/895.pdf.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We

also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

B. Purpose

This guidance is intended to:

1. assist persons (i.e., manufacturers, distributors, or importers) intending to submit a premarket notification [510(k)] submission for devices incorporating a sharps injury prevention feature, and for sharps injury prevention accessories;

2. promote consistency in content of 510(k)s in order to facilitate review by FDA; and

3. guide FDA review staff in conducting and documenting the review of 510(k)'s for devices with sharps injury prevention features, and for sharps injury prevention accessories.

C. Definitions

1. Accessory: a device not essential in and of itself, but adding to the effectiveness of another device.

2. Active Safety Feature: a sharps safety feature that requires a physical action by the user in order to activate the sharps safety feature that is in addition to any actions needed to perform the primary function of the device.

3. Contaminated: the presence or the reasonably anticipated presence of blood or other potentially infectious materials.

4. Hypodermic Single Lumen Needle: a device intended to inject fluids into, or withdraw fluids from, parts of the body below the surface of the skin. The device consists of a metal tube that is sharpened at one end and at the other end joined to a female connector (hub) designed to mate with a male connector (nozzle) of a piston syringe or an intravascular administration set (21 CFR §880.5570).

5. Intravascular Administration Set: a device used to administer fluids from a container to a patient's vascular system through a needle or catheter inserted into a vein. The device may include: the needle or catheter, tubing, a flow regulator, a drip chamber, an in-line filter, an I.V. set stopcock, fluid delivery tubing, connectors between parts of the set, a side tube with a cap to serve as an injection site, and a hollow spike to penetrate and connect the tubing of an I.V. bag or other infusion fluid container (21 CFR §880.5540). This definition includes the use of IV administration sets for subcutaneous infusions.

6. Intravascular Catheter: a device that consists of a slender tube and any necessary connecting fittings and that is inserted into the patient's vascular system for short-term use (less than 30 days) to sample blood, monitor blood pressure, or administer fluid intravenously. The device may be constructed of metal, rubber, plastic, or a combination of these materials (21 CFR §880.5200).

7. Passive Safety Feature: a sharps safety feature that automatically activates, i.e., it does not require any additional action by the user to activate the sharps safety feature.

8. Piston Syringe: a device intended for medical purposes that consist of a calibrated hollow barrel and a movable plunger. At one end of the barrel there is a male connector (nozzle) for fitting the female connector (hub) of a hypodermic single lumen needle. The device is used to inject fluids into, or withdraw fluids from, the body (21 CFR §880.5860).

9. Sharps: an object that can penetrate the skin, including, for example, needles and scalpels.

10. Needleless Systems: device components that provide repeated access to a patient's vascular system without the use of sharps. Fluid flow through the system may be uni/bi-directional, with the latter allowing the user to administer or withdraw fluids or medication.

    Needleless mechanisms include:

    - Pre-pierced septum and blunt cannula: On this type of system, a blunt cannula, which is placed on the syringe or secondary set, can be aseptically inserted into a pre-pierced septum on a Y-site, injection adapter, or extension set.

    - Valved connector (also called reflux valve): On this type of system, a valved connector prevents the flow through the connector until a mating Luer connector is aseptically inserted; the valve then opens.

- Capped Luer connector with a manual clamp: Capped Luer connectors are the same as those commonly used at the catheter end of IV sets. The mating Luer fitting of a syringe or secondary set can be aseptically connected directly to the Luer port. A manual clamp is included on the tubing above the Y-site to prevent fluid flow while attaching or detaching a connection; when the port is not in use, it is capped to maintain a closed system. Alternately, a pre-pierced septum injection adapter, recessed needle injection adapter, or valved connector can be aseptically placed on the Luer connector of the capped Luer Y-site to provide a self-sealing site. (See ECRI Aug./Sept. 1994, Vol. 23, No. 8-9.)

D. Abbreviations

ANSI	American National Standards Institute
ASTM	American Society for Testing and Material
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
DDIGD	Division of Dental, Infection Control, and General Hospital Devices
DSMICA	Division of Small Manufacturers International and Consumer Assistance
FDA	Food and Drug Administration
FR	Federal Register
IRB	Institutional Review Board
ISO	International Organization for Standardization
IV	Intravascular
NIOSH	National Institute of Occupational Safety and Health
NSE	Not Substantially Equivalent
OCS	Office of Compliance and Surveillance
ODE	Office of Device Evaluation
OSHA	Occupational Safety and Health Administration
SE	Substantially Equivalent
SMDA	Safe Medical Devices Act of 1990

E. Device Modifications

21 CFR §807.81, specifies that a premarket notification submission is required when significant modifications are made to a cleared 510(k). Persons intending to market a modified medical device should refer to the FDA guidance document entitled, "Deciding When to Submit a 510(k) for a Change to an Existing Device," http://www.fda.gov/cdrh/ode/510kmod.html.

A special 510(k) is for manufacturers who intend to modify their own currently 510(k) cleared legally marketed device. The manufacturer has determined that a new 510(k) is needed for the modification(s) and the modification does not affect the intended use of the device or the basic fundamental scientific technology of the device. The risk analysis section of the special 510(k) should contain documentation that performance tests, including simulated clinical and/or clinical studies and bench tests, were performed (Section II. F.). The guidance document, "The New 510(k) Paradigm Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications; Final Guidance," http://www.fda.gov/cdrh/ode/parad510.html contains additional detail on eligibility criteria. 21 CFR §820.30 contains design controls information.

F. Supplementary Guidance Documents, Standards, and Other Documents

Other guidance documents may be useful when accumulating data/information to submit in a premarket notification [510(k)] submission. The guidance documents listed are available on the Internet or from DSMICA at (800) 638-2041 or (301) 443-6597.

1. Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing, http://www.fda.gov/cdrh/g951.html

2. Guidance on the Content of Premarket Notification [510(k)] Submissions for Piston Syringes, http://www.fda.gov/cdrh/ode/odegr821.html

3. Guidance on Premarket Notification [510(K)] Submissions for Short-Term and Long-Term Intravascular Catheters, http://www.fda.gov/cdrh/ode/824.pdf

4. Guidance on the Content of Premarket Notification [510(k)] Submissions for Hypodermic Single Lumen Needles, http://www.fda.gov/cdrh/ode/odegr450.html

5. Human Factors Principles for Medical Device Labeling, http://www.fda.gov/cdrh/dsma/227.html

6. ODE Blue Book Memorandum #91-1, Device Labeling Guidance, http://www.fda.gov/cdrh/g91-1.html

7. Guidance for Industry and for FDA Staff; Use of Standards in Substantial Equivalence Determinations, http://www.fda.gov/cdrh/ode/guidance/1131.html

8. Guidance on Premarket Notifications for Intravascular Administration Sets, http://www.fda.gov/cdrh/ode/guidance/1189.html

You should also refer to the regulation, Federal Register notice, and standard listed below.

1. 21 CFR Part §801, Device Labeling

2. Intravascular Device-Related Infections Prevention: Centers for Disease Control and Prevention, (60 FR 49978, September 27, 1995)

3. ANSI/AAMI HE48-1993: Human Factors engineering guidelines and preferred practices for the design of medical devices (available from the Association for the Advancement of Medical Instrumentation (703) 525-4890 or (800) 332-2264).

II. Use of Standards

Submitters may choose to use recognized voluntary consensus standards and other standards when designing and testing their devices. See "Guidance for Industry and for FDA Staff, Use of Standards in Substantial Equivalence Determinations" http://www.fda.gov/cdrh/ode/guidance/1131.pdf.

III. Information that a 510(k) for Devices with Sharps Injury Prevention Features Should Contain

A. Cover Letter

The 510(k) regulation, 21 CFR §807, Subpart E, specifies the required information for inclusion in the 510(k) submission. The general 510(k) guidance, "510(k) Manual - Premarket Notification: 510(k) - Regulatory Requirements for Medical Devices" http://www.fda.gov/cdrh/manual/510kprt1.html explains the basic requirements in detail. As noted in Section I.A., you should also refer to applicable FDA guidance on the specific device for submission recommendations.

For regulatory purposes, accessories are classified in the same class as the device to which they are assembled (e.g., a piston syringe needle shield is the same class as the piston syringe).

Examples of Classification Names of Medical Devices with Sharps Injury Prevention Features

Class	Panel	Product code	Common Name
II	80	MEG	Piston Syringe with Safety Feature
II	80	FMI	Hypodermic Single Lumen Needle/Vial Adapter
II	80	FPA	Intravascular Administration Set
II	80	FOZ	Intravascular Catheter
II	80	LHI	Vial Adapter
II	80	FMI	Vacuum Tube Holder

B. Information Required

A 510(k) must include either: 1) a summary of the safety and effectiveness information in the 510(k) upon which an equivalence determination could be based (510(k) Summary, 21 CFR 807.92); or 2) a statement that safety and effectiveness information will be made available to interested persons upon request (510(k) Statement, 21 CFR 807.93).

In addition, persons who submit a 510(k) must certify, to the best of their knowledge, all information is truthful and accurate and that no material fact has been omitted (Truthful and Accurate Statement, 21 CFR §807.87(k)).

In addition, each 510(k) submission should include an Indication for Use Statement for the device. See http://www.fda.gov/cdrh/ode/indicate.html for the recommended format.

In sum, provide the following 3 documents:

1. Truthful and Accuracy Statement (see Appendix A)

2. 510(k) Summary or Statement (see Appendix B)

3. Indications for Use Statement (see Appendix C)

C. Labels and Labeling

1. General Information

Provide copies of the labels and labeling for the device (labels and labeling may be submitted in draft form) in sufficient detail to describe the device, its intended use, and the directions for its use. The format and content of labeling is described under 21 CFR Part 801.

- Labels include information affixed directly to the device or its container or packaging.

- Labeling includes professional or patient package inserts, promotional literature, videos, and other information that accompanies the device, or is presented with it.

Safe and effective use of sharps safety features depends upon labeling that is legible and designed for readability and comprehension. Guidance for writing clear labeling and considerations on human factors are contained in human factors and labeling guidance documents noted earlier in this document.

2. Labeling Considerations for Sharps Injury Prevention Features

FDA will assess the device based upon (1) the indications for use or intended use statements in the submitted labeling, or (2) if the use is not explicit in the labeling, the intended use that is commonly understood by health care professionals for the specific device. Furthermore, FDA believes some safety feature designs cannot be labeled for intravascular injection because of insufficient needle length or visual obstruction of the injection site.

You should consider the following directions for use:

a. Device compatibility and safety are critical concerns for a sharps injury prevention accessory that is sold separately and connected to a device at the point of use, such as a sheath for a piston syringe. It is important that the labeling for an accessory include the following:

   - the specific devices which are compatible with the accessory (e.g., trade names and/or models of syringes, device specifications); and

   - how to safely and properly connect or attach the sharps injury prevention accessory to the specified devices and how to discard after use.

b. Explain in sufficient detail how to prepare and properly use the sharps injury prevention feature. Potential factors include, for example:

   - limitations on hand size or dexterity (note that these types of limits may raise concerns);

   - position of the hands on the device at all times during use for safe operation;

   - appropriate aseptic technique, particularly when there are differences compared to commonly used devices that do not have the safety feature;

- how to safely activate the features after use;
- how to determine with certainty, that the safety feature is activated (e.g., visually, an audible click, a stop mechanism), whether the safety feature is an active or passive system;
- pre or post-use decontamination procedures that are necessary and which are safe, such as pre-swabbing a septum;
- instructions on how to safely transport a prepared device with an exposed sharp to the point of use; and
- how to properly dispose of a used device in accordance with applicable regulations (e.g., OSHA, CDC) and institutional policy.

c. If a device is intended for use with a specific drug or biologic, this should be stated in the labeling. The intended use of a drug/biologic with a subject device should be consistent with the approved drug/biologic labeling.

d. Labeling should prominently note if the device with the sharps injury prevention feature is part of a "system" marketed by the submitter that requires the use of other "system" devices or accessories to ensure safe and effective use. Warnings and precautions on mixing incompatible devices and accessories with the system may be warranted. Device and/or component compatibility should be specified in labeling and in the 510(k).

e. Manufacturers are encouraged to develop user education and training materials on safety devices such as illustrations, pictures, posters, cards, or other visuals to help clarify and reinforce the directions for use.

f. Labeling should include any and all applicable precautions on the safe and effective use of a device with a safety feature. This may include one or more of the following:

- Keep hands behind the needle at all times during use and disposal.
- Do not attempt to override or defeat the locking safety mechanism.
- Visualization of blood flashback is impeded.
- Leakage of fluid may occur when disconnecting components.

- Single Use Only
- Sterile
- Use aseptic technique.
- Use a one-handed technique.
- Properly Dispose in Sharps Container.
- Any other contraindications, precautions, or warnings that pertain to the specific sharps injury prevention feature.

D. Device Description

You should include a complete description of the sharps injury prevention feature and describe how it is incorporated as an integral component of the overall device. You should include descriptions of all sizes and variations of the safety feature for all models and types of devices of which it is a component. For accessories, describe all variations of the accessory device.

1. General Description

   You should provide a summary description of the device with the safety feature. You should describe its general features and mechanism of operation.

2. Drawings/Pictures/Illustrations

   You should provide visual representations of the device with the safety feature, or the accessory (e.g., photographs, detailed drawings, or engineering drawings), labeled and in sufficient detail to facilitate the evaluation of the nature and operation of the safety feature.

3. Intended Use and Indications for Use

   You should provide a statement of the intended use of the device and indications for use including any pertaining to the sharps injury prevention feature. The intended use and indications for use statement should be consistent with the labeling. The information in the 510(k) should support the intended use statement.

   The intended use and indications for use statement is critical in defining the type and amount of data that are needed in the submission. FDA believes that claims related to prevention of diseases, reduction of needlestick injuries, and other benefits need to be supported by data.

You should provide a statement of all indications for use and any proposed claims pertaining to those indications. Submit an Indication for Use form (refer to Appendix C-Indications for Use).

4. Device Specifications

You should provide the specifications for the device. Explain the basis for the specifications and state the tolerances.

a. Physical Specifications

(1) You should state the dimensions and volumes, length, width, height, thickness, inner diameter (ID), outer diameter (OD), diameter of housing, gauge, cannula/needle tip configuration, priming volume, residual volume in injection access port or in syringe, and dimensions of other features.

For fixed recessed needle safety devices, you should describe how you determined that the housing dimensions for the recessed needle prevent finger access, and that the needle dimensions meet the requirements of the intended use (e.g., venipuncture, septum access).

For needle shields, you should provide dimensions and show that the shield completely encloses the needle and prevents finger access when activated.

For hypodermic needles, you should explain how the dimensions compare to unprotected hypodermic needles.

For a retractable device, you should provide dimensions and show that the sharps feature is fully retracted within the housing of the device.

(2) Connector type: luer lock, slip fit, etc.

You should describe the compatibility of the connectors to other legally marketed devices.

(3) Color: color of components.

You should state any specific purpose of a color, e.g., to allow visualization or differentiation of device models or sizes.

(4) Opacity: opaque, transparent, etc.

You should provide an evaluation of how the opacity of the materials affects operation of the device. For example, if a safety shield is opaque or distorts the underlying field, then describe how safe and effective use is possible (e.g., visualization of flashback or entry of needle into skin).

(5) Markings and scales: color, type of scales, etc.

You should explain how the markings and scales can be read under all potential conditions of use (e.g., when a needle shield is retracted before use when filling a syringe, inverted, etc.).

(6) Special features:

You should describe any unique physical features and specifications of the device not mentioned above.

b. Mechanical Specifications

(1) Strength of materials: tensile, flexural, elongation, etc.

You should state the specification and tolerances, pass/fail test criteria, and the basis for the specification and criteria.

(2) Rigidity of safety shield or sheath: rigid, elastic

You should demonstrate the safety of non-rigid shields or sheaths.

(3) Strength of joints, bonds, connections, hinges, valves, locking mechanisms, etc.

You should demonstrate the strength of joints, bonds, connections, hinges, valves, locking mechanisms, etc.

c. Biocompatibility Specifications

You should provide the biocompatibility category of the device, described in the guidance, "Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing," http://www.fda.gov/cdrh/g951.html which includes a matrix that categorizes devices based on risk of exposure, and designates the type of testing needed for various medical devices.

d. Sterilization (see Appendix E)

6. Materials

Provide a complete listing of all materials (specific trade and scientific nomenclature) used in fabricating the sharps injury prevention feature. This information is particularly essential for the fluid pathway. It is helpful to present the information in the form of a listing, noting the component name followed by specific material identifier (e.g., part number and material). Please note that the generic class alone (e.g., polyvinylchloride (PVC)) is not adequate since there are many formulations of material compositions. Identify any lubricants and their amounts, PVC plasticizers, bonding agents, other additives, and all colors (e.g., ink, dyes, markings, radiopaque materials) used in manufacturing the device.

E. Descriptive Comparison to a Legally Marketed Device

FDA recommends that you identify a legally marketed device that is similar in intended use and technology (i.e., "products of comparable type" as required by 21 CFR §807.87(f)). For example, a new syringe with a safety shield should be compared to a legally marketed syringe with a safety shield. If known, you should state the 510(k) number for the legally marketed device. You may claim equivalence to more than one device. You should compare and contrast the following aspects of your device and the comparison device.

Design features and specifications of the devices

You should describe how differences may affect safety and effectiveness. Side by side comparisons, whenever possible, are desirable (see Appendix D Sample Comparison Table).

Intended use

You should state the intended use as well as all claims of the new device and the legally marketed predicate device(s).

Other aspects of labeling

To facilitate comparison, you should include clear representations of the legally marketed device(s), unless the labeling for the legally marketed device has ample information. Labeling includes labels, instructions for use, and promotional material.

All materials used to fabricate the devices

You should identify the materials used to fabricate your device and, if possible, the comparison device.

The technological aspects

You should describe the technological aspects of the sharps injury prevention components and how they integrate into the device.

F. Verification/Validation Tests

1. Introduction

You should provide a list of the tests used to demonstrate that the device conforms to its specifications.

A tabular listing of the feature or specification with the corresponding test may facilitate review.

If the tests for the primary device are based on recognized standards, then information or data derived from tests using these standards need not be submitted, provided a statement of intended conformity or declaration of conformity is submitted. Further information about standards is available in the guidance document, "Guidance for Industry and for FDA Staff, Use of Standards in Substantial Equivalence Determinations" http://www.fda.gov/cdrh/ode/guidance/1131.html and "The New 510(k) Paradigm," http://www.fda.gov/cdrh/ode/parad510.html.

Submission of performance data is necessary when no recognized consensus standards are available and when a comparison of descriptive information alone, such as labeling and specifications, is insufficient to establish substantial equivalence. Generally, performance data are necessary for devices with sharps injury prevention features.

When submitting test reports, provide the test protocol (sample size, justification for the sample size, pass/fail criteria, basis for criteria, test methodology, controls/legally marketed predicate devices), a summary of the data, and analysis of the data including statistics, results and conclusions. Include a representative sampling of completed report forms/questionnaires.

Data demonstrating drug/biologic compatibility are necessary if the device is dedicated to a specific drug or biologic product.

FDA does not prescribe specific test protocols for analyzing sharps injury prevention devices. This guidance provides an overview of information that FDA believes you should consider. Where there is no applicable standard or

recognized method to assess an aspect of performance, you may devise a test method that meets the stated test objective or other ways to demonstrate equivalency with a predicate device.

2. Types of Tests

FDA recommends that you submit bench, biocompatibility, and simulated clinical use test data. Pre-clinical and actual clinical use data should be submitted when requested, or as noted in the discussion that follows.

You should submit valid scientific evidence to demonstrate that its device is as safe and effective as the claimed legally marketed device. Anecdotal reports are unacceptable as primary evidence of comparable safe and effective performance.

a. Bench/Engineering Tests

Bench/engineering tests should evaluate the safety feature using worst case simulated static and dynamic forces. Tests should include a dry and wet environment caused by body fluids or fluids being administered. You should include the following:

- force to attach and detach connections;
- force to (de)activate the safety feature;
- reaction force generated by the activation mechanism, if any (e.g., with a passive spring loaded feature, or an elastic component);
- number of activations to failure;
- number of injection port accesses to failure for needleless ports with valves and diaphragms; and
- pressure and leak tolerance for pre-slit septa under extreme conditions of use when used with specific blunt cannulae or other types of needleless access devices.

Additional bench/engineering tests should include the following:

- FDA believes that data demonstrating drug/biologic and device container compatibility for each specific drug/biologic are necessary if the device is intended for use with a specific drug or biologic product. FDA believes that biocompatibility data according to ISO 10993-1 are necessary for the device when intended for general use (Section II, D, 5,c). A comparison of

materials between the new device and a legally marketed predicate device may suffice when the new device and the predicate device have a broad, fluid administration intended use. If the device labeling indicates that a specific drug or biologic product is to be stored in the device, FDA believes stability data supporting the recommended storage conditions are needed. You should follow the CDER drug stability testing protocol described in "Guidance for Industry on Container Closure Systems for Packaging Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Documentation," CDER/CBER, May 1999 http://www.fda.gov/cder/guidance/1714fnl.pdf.

- Puncture resistance of shield or sheath: the force to failure (puncture). Tests should include all forms of sharps used with the device. You should apply the sharps at various angles to simulate worst case conditions and compare the puncture force to other similar devices.

- Flow: rate of fluid flow through the device. You should apply pressure simulating extremes of potential conditions of use (e.g., force applied to piston, or flow through an access port) with comparisons to a similar device without the safety feature.

- Accuracy testing: When your device has atypical or unusual markings, e.g., inverted syringe markings, you should demonstrate that accurate doses can be administered.

b. Microbiological Tests

The use of a needleless device may decrease the risk of needlestick injuries and the potential for bloodborne infections to the healthcare worker. However, due to the potential for microbial contamination of the fluid pathway with the use of pre-slit septa and bi-directional valves, there could be an increased risk of infection to the patient.

A device with a safety feature, such as a needleless device with a reflux valve or pre-slit septum that facilitates bi-directional fluid flow, may affect the microbiological integrity of the device. Tests that evaluate this factor should be provided. For example, a needleless septum should be evaluated to determine if extreme use conditions such as repeated insertions into the female luer or pre-slit septum, and static insertion over a period of hours allow greater/lesser entry of microorganisms into the sterile fluid path. You should compare the device to legally marketed devices with this safety feature.

You should provide results from a simulated use test that includes parallel comparison testing with a similar device. You should design the comparison testing to mimic the device's use in a clinical setting. Testing should consist of repeated challenges to the subject and control devices by external contamination with a known amount of microorganisms ($\geq 10^3$ cfu/site). You should conduct simulated use testing with a known microbial challenge that represents a "worst case" in terms of organism number and type to demonstrate that the recommended procedures are effective for removing microorganisms from the device. The time frame for testing should exceed 24 hours and the number of microbial challenges in the study should approximate the number of user interactions with the access site that would be expected clinically.

You should provide a detailed protocol for the study that includes the procedure for the study, and appropriate test organism(s) that are commonly found as skin or IV line contaminants such as *Staphylococcus aureus* or *Staphylococcus epidermis*. You should describe the methods used to prepare the challenge organism(s), method of device contamination, access procedure with a specific blunt cannula or other type of needleless access device included in the labeling, and time and culture procedures. The protocol should explain the rationale for selecting the challenge microorganism(s) used as inoculum, the type of environment in which the study was conducted, the positive and negative controls used in the study, and the sample size used in the study. The recommended cleaning and disinfecting procedures for insertion and reinsertion into the needleless access site should be validated using microbiological techniques.

You should provide an analysis of the study results and conclusions, as well as the actual test data.

c. Risk Analysis and Pre-clinical Animal Tests

Devices with a safety feature may unexpectedly increase risks to patients or users. You should conduct a careful risk analysis to determine whether pre-clinical tests of the safety and effectiveness of the device in an appropriate animal model, in addition to bench tests, are warranted prior to beginning either simulated use or clinical use tests. A risk analysis is particularly prudent for invasive devices, devices with unique designs, or in cases where simulations alone may not adequately mimic clinical use and there is a significant risk to patients. For example, needles that automatically retract while in a vessel or body cavity, or sharps with unique designs may inordinately traumatize tissue or cause other unpredictable clinical effects.

The 510(k) should include a risk analysis, including whether or not pre-clinical animal tests were conducted.

d. Simulated Clinical Use and Actual Clinical Use Tests

The 510(k) should include data from tests in which the device is evaluated by health care professionals who typically use the type of device (nurses, doctors, phlebotomists, etc.). In most cases, data from only a simulated use test will suffice. The following sections provide more detail on these tests, including important factors to consider, and when clinical data may be needed.

The factors discussed below influence the conduct and content of a simulated or clinical test.

Intended Use and Indications for Use Statements

Similarity of devices

Device type

User and patient population

Statistical considerations

Intended Use and Indications for Use Statements: The intended use of the device is the functional purpose of the device. It may be stated in labeling or may be commonly understood, such as with a hypodermic syringe. Labeling may also prescribe indications for use which are the diseases or conditions that the device is intended to treat, prevent, or diagnose. The performance tests for a 510(k) demonstrate that the device achieves its intended use as safely and effectively as the claimed equivalent legally marketed device.

All devices with a sharps injury prevention feature have a primary and secondary intended use. The primary use is the therapeutic, preventative, or diagnostic intent of the device. For example, a hypodermic needle and syringe are intended to inject fluid into, or withdraw fluid from the body. The secondary intended use associated with all sharps safety features is that the feature will help prevent sharps injuries when using the device for its primary intended use. Devices with sharps injury prevention features cleared by the FDA have contained a statement that the device aids in the prevention of needlestick injuries.

If your device has any indications relating your device's safety feature to disease prevention, such as preventing acquired immune deficiency syndrome (AIDS) or hepatitis, we recommend that you

provide clinical data showing the rate of reduction of the incidence of the disease.

Similarity of Devices: Simulated and clinical use tests are not required for devices that are identical to a legally marketed device. In lieu of simulated and clinical use performance data requirements, you should submit available published literature on the marketed device and a discussion of the literature. The submitted comprehensive comparative analysis of the intended use and technological features of the new device to the claimed legally marketed device as noted in Section II.E. should support the claim that the devices are identical or the new device has a minor variation. FDA may recommend obtaining simulated or clinical use data if there is insufficient literature or new questions of safety and effectiveness on the marketed device.

If you are unable to support the claim that the new device is identical to the legally marketed predicate device or if there are any major technological differences between the new and legally marketed device, FDA recommends that you provide at least simulated use data.

Device Type: There are several types of devices with sharps injury prevention features, and studies should be adapted to the variables associated with the particular devices. For instance, substitute safety devices have been designed without sharps (e.g., needleless systems). While it is self-evident that these devices will not cause sharps injuries, there are other comparative safety and effectiveness factors to consider and evaluate, such as risk of contamination. Studies of intravenous catheters will have much different response variables than those for phlebotomy needles. Different types of devices also pose different degrees of inherent risk.

User and Patient Population: You should consider variables in the patient and health care professional user populations. If the device will be exposed to many conditions of use, testing of the device should take these variables into account to accurately judge the performance of the device. For example, the potential for sharps injury may be different for those treating HIV and hepatitis patients as opposed to other patients. Sharps injury may vary between institutions, within different services in institutions, and within services over time. Training, the learning curve, and the experience of users will vary.

Statistical Considerations: Protocols should be devised, whenever possible, based upon statistical considerations, such as

sample size, response variables, pass/fail criteria, comprehensive report forms/questionnaires, proper controls, and appropriate statistical test methods. This guidance is not intended to provide a detailed discussion of statistical considerations. There is ample literature on the subject. However, to assist you, the next section will expand upon sample sizes for assessing sharps injury prevention for simulated use and clinical tests.

3. Sample Size

An important question for a performance test is how many devices need to be tested. A test may be amenable to statistical methods to determine sample size. Sometimes precedent has established an acceptable sample size. In other cases, sample size is based on a prospective clinical estimation and qualitative endpoints.

An adequate sample size is needed to achieve statistical confidence that a device measurably decreases the incidence of needlestick injuries. In response to public and FDA advisory committee comments, FDA proposes one approach to establishing a scientifically sound basis for sample sizes to assess needlestick injury.

A sample size can be based upon a confidence interval of an observed failure rate in a test run of "N" devices. The failure is a needlestick injury or significant problem with the safety feature that may lead to an injury. The upper limit of the interval serves as the worst case approximation for the "true" failure rate of the new device.

The following tables, generated using STAT EXACT TURBO® statistical software, list the upper 95% and 99% confidence limits based on the binomial distribution for an observed failure of 0, 1, 2, or 3 devices in a test sample of 100, 200, and 500 devices[1].

Upper Bound of 95% Confidence Limit

	Number of devices tested			
	100	**200**	**500**	**1000**
Failures				
0	3.6%	1.8%	0.7%	0.3%
1	5.4%	2.7%	1.1%	0.6%
2	6.9%	3.5%	1.4%	0.7%
3	8.3%	4.3%	1.7%	0.9%

Upper Bound of 99% Confidence Limit

[1] C.R.C Handbook of Tables for Probability and Statistics, 2nd Edition, William H. Beyer, Editor

	Number of devices tested			
Failures	**100**	**200**	**500**	**1000**
0	5.2%	2.6%	1.1%	0.5%
1	7.1%	3.6%	1.5%	0.7%
2	8.8%	4.5%	1.8%	0.9%
3	10.3%	5.3%	2.2%	1.1%

Statistical Note: Because a confidence interval generally involves both the upper and lower limits, when dealing only with one limit the actual confidence levels become 97.5% and 99.5% for 95% and 99%, respectively, because the 5% and 1% differences are split equally between the two tails of the distribution curve.

Thus, for example, if there were no failures observed in a test run of 500 devices, we would be 97.5% confident that the true failure rate were no higher than 0.7% and 99.5% confident that it were no higher than 1.1%.

If, on the other hand, there were two failures among 200 devices tested, the true failure rate could be as high as 3.5% (95% upper bound) or 4.5% (99% upper bound).

From this model, it is apparent that lower sample sizes increase the chance of accepting a device that has a potentially higher injury rate even if no failures in the test are reported. However, the larger sample sizes needed to detect real differences in needlesticks are not feasible.

Recommendation: On balance, FDA believes that a simulated use or clinical test of devices with sharps injury prevention features needs to include a sufficient number of devices to provide confidence in the performance of the device. FDA believes that for many devices with sharps safety features it is feasible to test at least 500 devices, which will enable detection of grossly defective devices at a 1% level (see previous confidence tables). Generally, sample size depends upon the nature of the device, the feasibility of the particular study, and the clinical significance of the test results.

Under the proposed sample size model, a successful test should report zero (0) sharps injuries or failures of the protection feature that could lead to a sharps injury in all test samples. If a test includes a failure, FDA recommends that you include a detailed explanation of the failure and steps taken to ensure that the failure has been corrected (e.g., redesign). FDA believes a complete retest is then necessary. You should report all data, including any failed tests.

No test control device is needed for comparison of a sharps injury endpoint since the endpoint is predetermined as a 0% rate of injury. A test control device, such as the claimed equivalent marketed device, is still recommended to provide a comprehensive performance comparison as discussed in items 5 and 6 below.

FDA will consider alternative approaches to sample size determinations, provided there is sufficient justification to support the alternative approach.

4. Simulated Use Study

a. Introduction

A simulated use study by health care professional volunteers is a test that mimics actual clinical use except that patient substitutes are used (e.g., instructional models or animals) rather than actual patients. The pre-clinical data noted in item F.2.c. may also serve as part of simulated testing if done by health care professional volunteers. The use of fruit instead of an instructional model may mimic a subcutaneous (SC) or intramuscular (IM) route of administration. The simulated use test will help (1) isolate problems with the device and optimize the design, (2) identify deficiencies in labeling, and (3) evaluate the type of training needed before the device is used clinically.

There are no standardized, validated methods to simulate clinical use of sharps injury prevention features. You should devise a protocol specific for your device. (There are an increasing number of studies in the literature concerning methodology of safety feature evaluation that may be helpful.) The protocol should be comprehensive (e.g., should include a clear objective, determination of sample size, how the number of evaluators was determined and selected, definitions of terms and evaluation parameters, and how the data will be analyzed).

If you submit only a simulated use test, you should justify how the simulated use study is a sufficient substitute for a clinical test. You should also identify the clinical factors associated with the device and how those factors were incorporated into the simulation.

b. Study Considerations

The evaluators should include a variety of health care professionals who routinely use the basic type of device being tested. Bias should be minimized by selecting a sufficient number of participants who will each use a large enough sample of devices (such as 1/8 of the total number) to allow them to gain familiarity with the device and to provide objective opinions. The volunteers/participants should have no conflicting financial interest in the device, but they may be compensated for their evaluations. Studies incorporating more than one test institution will decrease test bias.

The simulated tests should include comparison to at least one legally marketed control device. The control device selected should have the same intended use and, ideally, similar safety features.

The device should be tested under conditions that simulate the critical clinical variables (e.g., models to simulate patients, gloved hands, dry and wet fingers, one-handed technique).

You should make every effort to devise and execute the simulation properly. You should include all data points in the analysis. A deficient protocol or incomplete data may not provide sufficient information to support a substantial equivalence determination. This may result in the need for additional simulated data or even a confirmatory clinical study.

c. Test Preparation and Report

Commencement of a study should be preceded by a program to instruct the participants on the study protocol and to ensure (1) uniformity of technique, including adherence to universal precautions, (2) consistent observations, scoring, and evaluations, and (3) complete data collection.

The evaluators should record the results of testing on report forms/questionnaires. Examples of questionnaires are available on the Internet, see www.TDICT.org, www.NIOSH.gov, or www.ECRI.org. You may use the data elements mentioned below or develop an in-house report form/questionnaire with appropriate elements. Separate report forms may be used to report adverse effects and performance. It may be advisable to use an observer who will also comment on the testing.

d. Report Forms/Questionnaires

The questions on report forms may be scored differently (e.g., forced responses, graded responses). There should be ample space for narrative comments. You should include the following data elements (not necessarily an exhaustive list):

- general introductory questions for tracking purposes, such as date, time periods, name of institution, evaluator's name
- numbers and types of devices used by the evaluator
- graded ability of the user to perform the intended function of the device such as injection, administering fluid

- graded ability of the user to visualize important use factors, such as scales, flashback

- any required changes in usual technique, such as modifications of one-handed use

- ability to maintain aseptic technique while extracting the device from packaging, preparing, and using the device

- ease of activation of the safety feature, and resistance to unintended activation

- all adverse effects or problems encountered, whether it's device or user related, such as a sharps injury, multiple venipunctures required, safety feature failed to remain activated, line disconnection

- comparison of perceived or actual time required to use the safety device to the control/legally marketed device and impact upon user acceptance

- ability to detect activation of safety feature, and comments on associated problems with detection that may be encountered during actual clinical use,

- opinion on extent of learning curve with use of device

- whether training is mandatory and what type of training is needed

- necessary changes to the labeling

- a general assessment of the comparative acceptability of the device, including pros and cons of the device

- space for any other comments or noteworthy observations

- the characteristics and experience of the participants (e.g., left or right handed, size of hand according to a defined scale, gender, age, number of similar devices used/day, work environment).

5. Clinical Tests

a. Introduction

Actual use of a device is needed when clinical variables are unpredictable or difficult to simulate, such as with a complex vascular access procedure. A simulation may itself raise questions about the potential clinical performance of a device. As noted in item F.2.d., some claims need to be supported by clinical data.

b. Study Considerations

As with the simulated use study, starting an in-use clinical study should be preceded by an in-service program to instruct the participants on the study protocol. This ensures (1) uniformity of technique, including adherence to universal precautions; (2) consistency of observations, scoring, and evaluations; and (3) complete data collection.

FDA suggests that you carefully plan the protocol with the aid of health care professionals. There is ample published literature on devising protocols.

If a clinical study is needed, it must be conducted in accordance with the investigational device exemption regulations (21 CFR Part 812). Informed consent and institutional review board approval are mandatory. Venipuncture devices and devices that do not contact the patient are considered non-significant risk devices. Only the local Institutional Review Board (IRB) and not FDA must approve a non-significant risk device study. Venipuncture devices are also considered minimal risk devices under the IRB regulations.

Immediate recording of the results for a test device may be difficult, particularly in a busy clinical service. A periodic record keeping process and third party observer may be necessary.

Monitoring of the study is critical. Adequate monitoring helps ensure that data are being collected as needed, that protocol deviations are minimized, and that patients' rights and welfare are protected.

c. Test Protocol

An actual use clinical protocol and its execution are more complex than a simulation. Additional considerations include site selection, IRB review, patient volunteer enrollment, additional clinical observations, on site record keeping, informed consent requirements,

specification of test conditions, etc.

A control device is needed, such as a legally marketed device, for performance comparison of the sharps safety feature and any other relevant clinical endpoints. The health care professional volunteer should use both the new device and the control device.

Published data or institutional historical control data may suffice in lieu of a study control. For example, if evaluating the infection rate with a new device, there may be historical control data for comparative purposes. If historical control data is used, you should provide a rationale for its use.

6. Summary

The salient points of the performance data section are as follows:

- FDA believes that indications for use that relate to reducing the incidence of disease transmission need to be supported with clinical data. Samples sizes to support such indications may be prohibitive.
- Performance data should include bench, biocompatibility, and simulated use data.
- Pre-clinical animal tests are advisable in some instances to minimize undue risk to test volunteers and patients.
- You should establish sample sizes that are consistent with study requirements and sound scientific principles. Guidance is provided in this document.
- All important response variables should be included in studies when devising the protocol.
- When clinical data are not included, you should demonstrate that the simulated use study alone is adequate.

G. Sample Device

Provide a sample of the device to facilitate evaluation.

H. Safe and Effective Medical Devices with Sharps Injury Prevention Features

This guidance is one of several actions initiated by FDA to help prevent sharps injuries and contamination. FDA has recommended the elimination of sharps in IV administration sets. The guidance document "Guidance on the Content and Format of Premarket Notification

[510(k)] Submissions for Sharps Containers," http://www.fda.gov/cdrh/ode/895.pdf is based on OSHA regulations and industry standards. You should also review the guidance document "Guidance on Premarket Notification for Intravascular Administration Sets," http://www.fda.gov/cdrh/ode/guidance/1189.html.

FDA recommends that manufacturers, importers, and/or distributors keep pace with the literature and consider recommendations from health care worker organizations, researchers, standard setting organizations (see ANSI/AAMI human factors information previously cited), and regulatory agencies when designing devices.

I. Future Revisions

This guidance may be revised on a periodic basis based on FDA's research and review of the literature, consideration of public comment, and/or FDA advisory committee recommendations.

IV. References

Maximum Residue Limits for Ethylene Oxide, Ethylene Chlorohydrin, and Ethylene Glycol. FDA Proposed Rule, June 23, 1978, (43 FR 27482).

ANSI/AAMI/ISO 10993-7:1995 Ethylene oxide sterilization residuals.

Guideline on Validation of the Limulus Amebocyte Lysate (LAL) Test as an End-Product Endotoxin Test, December 1, 1987, http://www.fda.gov/cder/guidance/old005fn.pdf.

Occupational Exposure to Bloodborne Pathogens; Needlesticks and Other Sharps Injuries; Occupational Safety and Health Administration, Final Rule Part IX, Dept. of Labor January 18, 2001, (66 FR 5318).

FDA Safety Alert: Needlestick and Other Risks from Hypodermic Needles on Secondary I.V. Administration Sets-Piggyback and Intermittent I.V. April 16, 1992.

Jagger J, Hunt EH, Brand-Elnaggar J, Pearson RD. Rates of Needlestick Injury Caused by Various Devices in a University Hospital. New Engl J Med 1988; 319:284-288.

ECRI Health Devices 29 (2-3) Needlestick-Prevention Devices Evaluation Update Feb-March 2000 75-81

ECRI Health Devices Needlestick-Prevention Devices Oct 1999, Vol 28, Number 10, p.379-408.

National Institute for Occupational Safety and Health (NIOSH)/Centers for Disease Control and Prevention (CDC) Preventing Needlestick Injuries in Health Care Settings Nov. 1999 Publication No. 2000-108.

APPENDIX A - PREMARKET NOTIFICATION TRUTHFUL AND ACCURATE STATEMENT

[Refer to §807.87(k)]

I certify, in my capacity as [Title], that I believe, to the best of my knowledge, that all data and information submitted in this 510(k) Premarket Notification Submission is truthful and accurate and that no material fact has been omitted.

[signature]

_____
[Name]
[Title]

_____
[Date]

APPENDIX B - 510(k) STATEMENT

[Refer to §807.93]

I certify, that in my capacity as (the position held in company by person required to submit the premarket notification, preferably the official correspondent in the firm), I will make available all information included in this premarket notification on safety and effectiveness within 30 days of request by any person if the device described in the premarket notification submission is determined to be substantially equivalent. The information I agree to make available will be a duplicate of the premarket notification submission, including any adverse safety and effectiveness information, but excluding all patient identifiers, and trade secreted and confidential commercial information, as defined in 21 CFR §20.61.

Certified:_____[Signed]_____

[Date]_____

APPENDIX C - INDICATIONS FOR USE STATEMENT

510(k) Number: (if known)

Device Name:

Indications for Use:

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

APPENDIX D - SAMPLE COMPARISON TABLE

Factors	New Device	Legally Marketed Device
Intended use		
Indication for use		
Technological features		
Materials		
Specifications: Physical Mechanical Biological Other		

APPENDIX E - STERILIZATION INFORMATION

For a device sold sterile, you should provide the following information, as detailed in the **Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA**, http://www.fda.gov/cdrh/ode/guidance/361.html.

- The sterilization method that will be used (e.g., dry heat, moist heat, EO, radiation);
- A description of the method that will be used to validate the sterilization cycle, but not the validation data itself;
- A description of the packaging to maintain the device's sterility, not including package integrity testing data;
- If sterilization involves EO, the maximum levels of residuals of EO and ethylene chlorhydrin that remain on the device (note: the ethylene glycol residual level was dropped from this updated guidance because the recognized standard, "ANSI/AAMI/ISO 10993-7:1995 Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide sterilization residuals," does not include measurement of ethylene glycol residuals);
- If the product is labeled "pyrogen free," a description of the method used to make the determination, e.g., limulus amebocyte lysate (LAL);
- The SAL (e.g., 10^{-6} for all devices, except 10^{-3} for devices only contacting intact skin); and
- In the case of radiation sterilization, the radiation dose.