Guidance for Industry and FDA Review Staff

Guidance on Premarket Notifications for Intravascular Administration Sets

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

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Patricia Cricenti, HFZ-480, 9200 Corporate Boulevard, Rockville, Maryland 20850. 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 Irene Naveau at (301) 594-1287 or email IMN@cdrh.fda.gov.

Additional Copies

Additional copies are available from the World Wide Web CDRH home page: http://www.fda.gov/cdrh/ode/gudance/1189.pdf or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system and enter the document number 1189 followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

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I. Introductory Information

A. Scope

This document provides guidance for the submission of a premarket notification [510(k)] for intravascular (IV) administration sets and accessories. IV administration sets and accessories include extension sets, IV stopcocks/manifolds, in-line filters, flow regulators, fluid delivery tubing, vial adapters, IV transfer sets and needleless access devices/systems. This document also pertains to subcutaneous and blood administration sets and to transfusion filters.

This document does not address all 510(k) application criteria for IV administration sets and accessories. Other guidance documents that contain additional information are referenced under "Supplementary Guidance Documents and Standards," (Section I.I., page 8). Some criteria in this guidance are also repeated within other guidance documents, (e.g. Supplementary Guidance on the Content of Premarket Notification 510(k) Submissions for Medical Devices with Sharps Injury Prevention Features). All the criteria are not applicable to each device or feature. Therefore, please read the guidance documents carefully to determine which parts are applicable.

While needleless system features are incorporated as integral components of many finished devices, (e.g., a Y-site connector), some needleless systems are marketed separately as "accessories" and are attached to other devices by the user at the point of use. This guidance applies to both the integrated and separate accessories.

B. Purpose

This guidance is intended to:

1. assist persons intending to submit a premarket notification [510(k)] submission for an IV administration set, with or without a needleless system feature, and for accessories to IV administration sets; and

2. guide FDA review staff in conducting and documenting the evaluation of 510(k)s for IV administration sets and their accessories.

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[1] This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

C. Definitions

a. Devices

1. Accessory: a device not essential in and of itself, but adding to the effectiveness of another device (definition adapted from Webster's Dictionary).

2. Anti-Siphon Valve: an accessory to an IV administration set that protects against unregulated gravity fluid infusion or blood reflux (definition developed for the purpose of this guidance document).

3. Backcheck Valve: an accessory to an IV administration set which allows for uni-directional fluid flow and serves as a multiple access site for the injection of fluids (definition developed for the purpose of this guidance document).

4. Blood Administration Set: a device used as part of a system to administer and filter blood and/or blood components to a patient (definition developed for the purpose of this guidance document).

5. Filter: an accessory to or component of an IV administration set; a device that is designed to eliminate entrapped air and/or inadvertent particulates and microbial contaminants from solutions prior to patient administration (definition developed for the purpose of this guidance document).

6. 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 a needle or catheter, tubing, flow regulator, drip chamber, in-line filter, I.V. set stopcock, fluid delivery tubing, connectors between parts of the set, side tube with a cap to serve as an injection site, a hollow spike to penetrate and connect the tubing to an I.V. bag or other infusion fluid container (ref. §880.5440, FDA Classification). This definition does not preclude the intended use of IV administration sets for use with subcutaneous infusions.

7. IV Flow Regulator: an accessory to an IV administration set that is a device used to control the flow of intravenous solutions (definition developed for the purpose of this guidance document).

8. IV Manifold: an accessory to an IV administration set which provides multiple access ports and regulates the directional flow of fluids for simultaneous/alternate intravenous therapy (definition developed for the purpose of this guidance document).

9. IV Stopcock: an accessory to an IV administration set which regulates the directional flow to a patient's vascular system, and provides an access port(s) for the administration of solutions (definition developed for the purpose of this guidance document).

10. Needleless System: device components that provides 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 (definition developed for the purpose of this guidance document).

    Needleless mechanisms include:

    - Prepierced 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. (ref. ECRI Aug./Sept. 1994, Vol. 23, No. 8-9).

11. Vial Adapter: a device designed to facilitate the withdrawal of drugs/solutions from a vial and may/may not have a needleless device component as part of its design (definition developed for the purpose of this guidance document).

    b. Non-devices

12. Contaminated: the presence or the reasonably anticipated presence of blood or other potentially infectious materials (ref. 29 CFR §1910.1030(b), OSHA Bloodborne Pathogens).

13. Indications For Use: a general description of the disease or condition that the device will diagnose, treat, cure, or mitigate, including a description of the patient population for which the device is intended (FDA definition).

14. Intended Use: the objective intent of the person(s) legally responsible for the labeling of the device. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the device. The objective intent may, for example, be shown by labeling claims, advertising matter, or by oral or written statements by such persons or their representatives. It may be shown by the circumstances that the device is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised (ref. §801.4, FDA Labeling).

15. Predicate Device: a device that was legally marketed in the U.S. prior to May 28, 1976 (preamendment), or a device which has been reclassified from Class III to Class II or I, or a device which has been found to be substantially equivalent through the premarket notification 510(k) process (FDA definition).

D. Abbreviations

AAMI	Association for the Advancement of Medical Instrumentation
ANSI	American National Standards Institute
ASTM	American Society for Testing and Materials
CDC	Centers for Disease Control and Prevention
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
DDIGD	Division of Dental, Infection Control, and General Hospital Devices
DEHP	Diethylhexylphthalate
DSMA	Division of Small Manufacturers' Assistance
ECRI	Emergency Care Research Institute
FDA	Food and Drug Administration
FR	Federal Register
ID	Inner Diameter
IRB	Institutional Review Board
ISO	International Organization for Standardization
IV	Intravascular
NIOSH	National Institute of Occupational Safety and Health
NSE	Not Substantially Equivalent
OD	Outer Diameter
ODE	Office of Device Evaluation
OSHA	Occupational Safety and Health Administration
SE	Substantially Equivalent
SMDA	Safe Medical Devices Act of 1990

E. Regulatory Authority and Classification of Medical Devices

The FDA regulates medical devices under authority of the Federal Food, Drug, and Cosmetic Act (FD&C Act). The FDA classified medical devices that were in commercial distribution prior to the 1976 amendments to the FD&C Act, or so-called pre-amendments devices, into one of three regulatory classes: Class I, II, or III. The class establishes the regulatory controls that are necessary to provide reasonable assurance of the device safety and effectiveness. Class I devices are subject to general controls. Class II devices are subject to general controls and special controls (as amended by the Safe Medical Devices Act of 1990). Class III devices are subject to premarket approval procedures. Call FDA's Division of Small Manufacturers

Assistance (DSMA) at 1-800-638-2041 for guidance on general controls.

F. Device Modifications

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

G. The 510(k) Paradigm: Alternate Approaches to Demonstrating Substantial Equivalence

Section 510(k) of the FD&C Act requires a person who intends to introduce a device into commercial distribution to submit a premarket notification, or 510(k), to the FDA at least 90 days before commercial distribution is to begin. Section §513(i) of the Act stipulates that the FDA may issue an order of substantial equivalence, only upon making a determination that the device to be introduced into commercial distribution is as safe and effective as a legally marketed device.

In "A New 510(k) Paradigm," (http://www.fda.gov/cdrh/ode/parad510.html) the FDA describes alternate approaches to the traditional method of demonstrating substantial equivalence. The first alternative, the "Special 510(k): Device Modification," utilizes design controls of the Quality System Regulation, while the second alternative, the "Abbreviated 510(k)," relies on the use of special controls and consensus standards to facilitate 510(k) review. These alternative approaches minimize or eliminate the need to review the data for those aspects of the device addressed by recognized standards. It is anticipated that use of the alternatives will conserve the Agency's review resources while facilitating the introduction of safe and effective devices into interstate commerce.

H. General Principles Regarding Presentation of Data

1. Editorial Considerations: The 510(k) should be carefully reviewed for scientific and technical soundness and edited before it is submitted to FDA. It should be proofread to assure that all pages/sections are included and are properly indicated, consecutive, distinctly copied, and legible.

2. Abbreviations: Standard abbreviations acceptable to a significant peer reviewed journal should be used wherever possible. All other abbreviations should be identified at the beginning of each section in which they are used or in footnotes to tables and graphs.

3. Data Availability: This document outlines typical circumstances of data review. It is not possible to anticipate all situations that may require FDA review. Thus, those submitting applications should be aware that they may be asked to submit additional data, to present data in another format or to provide more detailed explanations of the

information submitted, as required to evaluate device equivalence.

Applicants should keep data used for the 510(k) application on file in a controlled and well-organized format. This will allow the applicant to expeditiously supply FDA with additional information or analysis, if required. Errors in data that are identified by the applicant after submission to FDA should be brought to FDA's attention immediately.

4. Tables and Graphs: Well-constructed tables are fundamental to the reporting and evaluation of data. All tables should be clearly identified and captioned with symbols keyed to a footnote or accessible reference page that adequately indicates the nature of the data.

   Graphs should supplement, not replace, data tables. They should be of a high quality.

5. Published Literature: Published methods or data referenced in study reports should be made available to FDA upon request. Reprints of other referenced published reports or data should also be made available to FDA upon request. All referenced reports and data should be summarized including an explanation how it relates to the current submission. Reference citations should be complete (e.g., title, author, volume, pages, and year).

6. Protocols and Data Analysis: Test reports, when submitted, should include the protocol (objectives, precise description of materials, experimental methods, controls), observations, statistical methods and analyses, conclusions and comments. Do not submit raw data unless requested by FDA. Additional specific directions on protocols are included in sections that follow.

7. Reference to Submitted Data: The applicant may reference any information previously submitted to FDA, in support of the 510(k). If the applicant did not submit the referenced data he/she should provide, or have the submitter provide, a letter of authorization to FDA on the letterhead of the original submitter of the data. Often, if the data are not extensive, resubmitting data in the 510(k) will facilitate the review of the document.

I. Supplementary Guidance Documents and Standards

The following guidance documents are relevant to IV set submissions and are available from DSMA [(800)638-2041 or (301)443-6597]:

1. General Program Memorandum (Bluebook) #G94-1: FDA-modified ISO Standard 10993-1: "Biological Evaluation of Medical Devices"

2. ODE Blue Book Memorandum #K90-1: 510(k) Sterility Review Guidance

3. ODE Blue Book Memorandum #91-1, Device Labeling Guidance

4. 21 CFR Part §801, Device Labeling (Code of Federal Regulations)

5. Blue Book 510(k) Memorandum #86-3: Guidance on the Center for Devices and Radiological Health's Premarket Notification Review Program

6. Write It Right: Recommendations for Developing User Instruction Manuals for Medical Devices Used in Home Health Care (HHS Publication FDA 93-4258)

7. Human Factors Principles for Medical Device Labeling (FDA Contract No. 223-89-6022)

8. Guidance on the Content of Premarket Notification 510(k) Submissions for Hypodermic Single Lumen Needles

9. Premarket Notification 510(k) Regulatory Requirements for Medical Devices (HHS Publication FDA 95-4158)

10. Supplementary Guidance on the Content of Premarket Notification 510(k) Submissions for Medical Devices with Sharps Injury Prevention Features

11. ISO 8536-4:1998, Infusion Equipment for Medical Use-Part 4

12. ANSI/AAMI BF7:1989, American National Standard for Blood Transfusion Micro-Filters

13. ISO 1135-4:1987, Transfusion Equipment for Medical Use

14. ISO 594, Conical Fittings with a 6% (Luer) Taper for Syringes, Needles, and Certain Other Equipment

15. Intravascular Device-Related Infections Prevention: Centers for Disease Control and Prevention, (Federal Register September 27, 1995)

16. Guidance for Industry and for FDA Staff-Use of Standards in Substantial Equivalence Determinations (March 12, 2000)

17. Guidance on the Recognition and Use of Consensus Standards (February 19, 1998)

The Division of Small Manufacturers Assistance (DSMA) has additional guidance documents that may be relevant, as well as, Facts on Demand, an automated system which allows requests for device-specific guidance documents, 24 hours a day, 7 days a week by calling (800) 899-0381 from a touch-tone phone.

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

J. The FDA Review Process[2]

Administrative Review

Upon submission of a 510(k) to the FDA Document Mail Center (DMC), the submission is date-stamped and assigned a 510(k) number. The DMC identifies and enters into a document system certain data, such as the applicant's phone numbers, etc., and the specific Class assigned to the device (either Class I,II, or III).

The 510(k) is routed to the appropriate review division and an acknowledgment of receipt letter is sent to the applicant.

An initial administrative review is conducted to determine if the 510(k) contains the information required by regulation. If the 510(k) is not administratively complete, FDA may place the submission on hold and send a letter to the applicant explaining the deficiencies. FDA may also resolve the deficiencies by phone with the applicant.

If the 510(k)is administratively complete, FDA places the submission in a queue for scientific review.

There is typically one of three outcomes from the scientific review:

1. FDA determines the device to be substantially equivalent (SE) and sends a letter to the applicant which clears the device for marketing.

2. More information is needed to complete the review. FDA either telephones or sends a letter to the applicant. If FDA telephones, the 510(k) may be placed on administrative hold. If a letter is sent, then either a 30 day limit is placed on the response time, or FDA considers the 510(k) withdrawn because the complexity of the deficiencies precludes resubmission within 30 days.

3. FDA determines the device not substantially equivalent (NSE).

If more information is requested and FDA does not consider the 510(k) withdrawn, the review stops until the information is received. When the applicant resubmits the information FDA places the amended 510(k) in a queue for review.

If the information is not received in the time frame noted in the deficiency letter, or as requested over the telephone, FDA considers the submission withdrawn.

If the information is received, but it is not complete, FDA may find the device NSE, or may ask for more information, and another amendment is required.

[2] This outlines the 510(k) process. For more detailed information, refer to Premarket Notification 510(k) Regulatory Requirements for Medical Devices (HHS Publication FDA 95-4158).

Scientific Review

FDA determines if a new device is substantially equivalent (SE) to a legally marketed device according to Blue Book 510(k) Memorandum #86-3 (available from DSMA).

There are three main questions the FDA reviewer considers when evaluating the information in the 510(k):

1. Does the new device have the same intended use as the legally marketed device that is identified by the applicant?

2. Does the new device have the same technological characteristics (i.e., design, materials, energy source, etc.) as the legally marketed device?

   If not, does evaluation of the new device and/or its technology raise new types of safety and effectiveness questions when compared to the legally marketed device?

3. Are performance data needed to evaluate if the new device is as safe and effective as the legally marketed device, and does the device have new technological characteristics?

   If so, do the data show that the new device performs as safely and effectively as the legally marketed device?

K. Standards Relating to Intravascular Administration Sets

As a result of FDAMA, there are three main ways in which manufacturers may elect to use standards in demonstrating substantial equivalence in 510(k)s. Manufacturers may elect to conform to an FDA-recognized standard and include a declaration of conformity in a 510(k)submission, or manufacturers may include a statement that a device conforms (or will conform before marketing) to an FDA-recognized standard instead of a declaration of conformity; or manufacturers may elect to conform to a voluntary consensus standard that is not recognized by FDA. Unlike recognized standards, however, there is less assurance that a non-recognized standard will be fully acceptable in addressing critical factors supporting substantial equivalence.

II. Information to be contained in a 510(k) for Intravascular Administration Sets, and Accessories

A. Cover Letter

The 510(k) regulation, 21 CFR Section §807, Subpart E, specifies the required information for inclusion in a 510(k) application. General 510(k) guidance from DSMA explain the basic requirements in detail. As noted in Section I.A., page 4, the applicant should refer to applicable

FDA guidance on the specific device for submission recommendations.

The regulation requires the following information be included in 510(k)s, either in the cover letter or tabulated in the 510[k]:

- common name of the device (classification name)
- proprietary or trade name
- FDA classification (Class I, II, or III)
- establishment registration number (if available)
- device panel code (Pancode)
- device product code (Procode)

See chart (below). The information is from Classification Names for Medical Devices and In Vitro Diagnostic Products (FDA Publication 91-4246).

For regulatory purposes, accessories are classified in the same class as the device for which they are assembled (e.g., a stopcock is the same class as the IV administration set).

Class	Panel	Procode	Common Name
II	80	FMG	I.V. Stopcock Set/Manifold
II	80	FPA	Needleless Access Devices/Systems
II	80	FPA	IV Administration Set
II	80	BRZ	Blood Transfusion Set
II	80	FPB	Infusion Line (in-line) Filter
II	80	FPA	Blood Flow Regulator
II	80	CAK	Blood Transfusion Microfilter
II	80	FPK	Fluid Delivery Tubing
II	80	LHI	I.V. Fluid Transfer Set
II	80	LHI	Vial Adapter

B. Information Required by the Safe Medical Devices Act of 1990

Under the Safe Medical Devices Act of 1990, 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], or (2) a statement that safety and effectiveness information will be made available to interested persons upon request [510(k) statement]. 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).

Specifics regarding the requirements for the 510(k) summary, the 510(k) statement and the Truthful and Accurate Statement may be found in 21 CFR §807.92, §807.93, and §807.87 (k), respectively.

In addition, in accordance with the Center for Devices and Radiological Health (CDRH) policy, a 510(k) submission must include a statement of the device indications for use using a separate sheet of paper.

In sum, provide the following documents in the 510(k) submission:

1. a 510(k) summary (see 21 CFR §807.92) or statement (see Appendix B)

2. the Truthful and Accurate Statement (see Appendix A)

3. an Indications for Use Statement (see Appendix C)

C. Labels and Labeling

General Information

Provide copies of the proposed labels and labeling for the device (may be submitted in draft form).

- 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 the device depends upon labeling that is legible and designed for readability and comprehension. Guidance for writing clear labeling and considerations of human factors are contained in human factors and labeling guidance documents. (Section I.I.,7, page 9). All instructions should be clear and concise, e.g., Do not use with light-sensitive infusate.

Labeling Considerations for Intravascular Administration Sets, Accessories and Needleless Device Features

1. The labeling must meet the requirements of 21 CFR Part 801:

    - Subpart A, §801.4 and §801.5, relative to intended uses and adequate directions for use; and

- Subpart B, §801.109 and §801.116, relative to prescription devices and commonly known directions.

2. FDA recommends that the following items be included in the labeling (some items required by regulation)for IV administration sets and accessories, if applicable:

    a. the identity of the device (type, size/set length in inches or millimeters, inner diameter (ID), outer diameter (OD), drops/ml, priming volume, filter, needle gauge and length and quantity). The description may be in words and/or pictorials;

    b. the statements "single use only, nontoxic, sterile, nonpyrogenic fluid path if package is intact, undamaged and protective caps are secure";

    c. the prescription statement under §801.109(b)(1): "Caution: Federal law restricts this device to sale by or on the order of a physician";

    d. an identification of any dedicated administration set or the specifications and/or specific models of infusion sets which are appropriate for use with specific pumps or other devices;

    e. indications for use including special indications (e.g., pediatric patients);

    f. any precautions and guidance related to the duration of use and frequency of device replacement - include special instructions for needleless components, for administration of lipids, blood and blood products (e.g., 24 hour time limit for use);

    g. any special limitations related to opacity and the types of solutions to be used with the device (e.g., light sensitive solutions, fat emulsions, lipids, blood and blood products, etc.) - the use of diethylhexylphthalate (DEHP) in the fluid pathway of polyvinychloride (PVC) tubing should be identified since leaching of the plasticizer may occur on contact with lipids.

    h. a step by step procedure for the use of the device. Warnings related to unrestricted flow should be included for administration sets that may be used with an infusion pump without the restricted flow feature - instructions for use with gravity flow should be included;

    i. illustrations, pictures, posters, cards or other visuals that may clarify and reinforce the directions for use;

    j. special patient instructions if indicated for home use (e.g. procedure for contacting healthcare provider);

    k. the manufacturer's and/or distributer's name and address;

l. instructions for discarding a used device;

m. highlighted warning and caution statements (Section I.I.,6, page 9);

n. highlighted instructions for cleaning/disinfecting y-sites and pre-slit septa;

o. the name of specific blunt cannulae for use with split septa.

3. FDA recommends that the shelf or multi-unit container be labeled as follows (some items required by regulation):

a. a description of the contents, in words and/or pictorials;

b. the number of infusion set accessories;

c. instructions for use in each shelf container, or on the unit container;

d. the words "sterile" and "single use;"

e. the manufacturer's or distributer's name and address;

f. the lot designation, the year and month of sterilization; and

g. the recommended storage conditions, if any.

D. Device Description

The applicant should include a complete description of the device, including all sizes and various configurations for all models of the devices. For accessories, describe all variations of the accessory device and how each is incorporated as an integral component of the overall device.

1. General Description

Provide a summary description of the device. Describe its general features and mechanism of operation.

2. Drawings/Pictures/Illustrations

Provide a visual representation of the device (e.g., photographs, detailed drawings with delineated fluid flow path, or engineering drawings with critical dimensions) including any safety features, and accessories, labeled in sufficient detail to facilitate the evaluation of the nature and operation of the device and any safety feature.

3. Intended Use

Provide a statement of the intended use of the device, and proposed claims pertaining to the device. The intended use statement and claims must be consistent with the labeling. The information in the 510(k) should support the intended use statement.

Note: The intended use statement is critical in defining the type and amount of data that are needed in the submission. (For example, claims related to prevention of diseases, reduction/elimination of needlestick injuries, and other benefits should be supported by data).

4. Indications for Use

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

5. Device Specifications and Technical Characteristics

List the specifications and characteristics of the device. State the tolerances for the specifications.

a. Physical Specifications

Provide the following:

- dimensions: inner diameter (ID), outer diameter (OD), length, width, types of configurations, priming volume, residual volume in needleless access ports, and dimensions of other features;
- proximal and distal end configuration: shape, location, and diameter of outlets and side ports;
- connector types, e.g., luer lock, slip fit, etc;
- the color of all components; and
- any unique physical features and specifications of the device not mentioned above.

b. Mechanical Specifications

Provide the following:

- strength of materials (tensile, flexural);

- strength of joints, bonds, connections, hinges, valves, locking mechanisms, etc.;
- tubing elongation;
- connector performance criteria, e.g., to prevent leakage;
- burst pressure;
- puncture/reseal limits of septa;
- durability;
- flow characteristics;
- material hardness;
- crimping/flexion when intended for used with infusion pumps.

c. Biocompatibility Specifications

Provide the biocompatibility category of the device. You may refer to the Blue Book Memorandum #G95-1, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing", ISO-10993 which includes a matrix that categorizes devices based on risk of exposure, and designates the type of testing needed for various medical devices. Intravascular Administration Sets are defined as externally communicating devices with an indirect blood path.

d. Sterilization

(See Appendix E)

6. Materials

Provide a complete listing of ALL device materials (specific trade and scientific nomenclature). This information is particularly essential for fluid pathway, and any metallic materials. The addition of any metallic component to an IV administration set should be brought to the attention of the Agency. Metallic components may have an impact on the safe use of the device in an MRI environment. 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 PVC plasticizers, lubricants, bonding agents, or other additives and their amounts.

E. Descriptive Comparison to a Legally Marketed Device

The applicant must claim substantial equivalence to at least one legally marketed device. FDA recommends that the applicant identify a legally marketed device that is similar in intended use and, where possible, technology. (For example, a needleless device with a pre-slit septum should be compared to a similar legally marketed device with a pre-slit septum). If known, state the 510(k) number(s) for the legally marketed device.

An applicant may claim equivalence to more than one device.

Compare and contrast:

- the design features of the devices;

  Describe how any differences may affect safety and effectiveness. Side by side comparison tables, whenever possible, are desirable (see Appendix D).

- the intended use and all claims of the new device to the legally marketed equivalent predicate device(s);

  Compare and contrast other aspects of labeling (labels, instructions for use, promotional material). To facilitate comparison, also include clear representations of the legally marketed device(s), unless the labeling for the legally marketed device has ample information.

  Note: Previous predicate device labeling may not be current in terms of directions to users.

- all materials used to fabricate the devices; and

  Identify the precise materials used in the legally marketed predicate devices for comparison.

- the specifications.

F. Design Inputs, Verification/Validation Tests, and Test Recommendations

Provide a list of the design inputs used as a basis for the design of the device and the tests used to demonstrate that the device conforms to its specifications.

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

If the inputs or tests 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.

Also, submission of reports of tests generally is not necessary when a comparison of descriptive information alone, such as labeling and specifications, is sufficient to establish substantial equivalence. Differences between the new device and the predicate device may incur a need for data and information related to those differences, if they are significant.

When submitting test reports, provide the test protocol, test sample size justification, pass/fail criteria, basis for criteria, methodology, controls, summary data analysis including statistics, results and conclusions.

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

FDA does not prescribe specific test protocols. This guidance provides an overview of information applicants should consider. Where there is no applicable standard or recognized method to assess an aspect of performance, the applicant may devise a test method that meets the stated test objective or otherwise to demonstrate equivalency with a predicate device.

FDA recommends that performance data for IV devices with safety features be submitted which assesses the safety feature. These data are described below.

G. Specific Information on Tests for Devices with Safety Features

FDA recommends that IV administration sets that include features designed to protect the healthcare worker from accidental sharps injury include data to demonstrate that the feature achieves its intended purpose.

Devices with a safety feature may diminish risks to users but may also increase risks to patients and those who dispose of waste. The applicant should conduct a risk analysis to determine what risks may exist and the means to address those risks and to evaluate the design solution.

FDA recommends that the applicant consider the types of tests described below. Preclinical, animal, and actual clinical use data should be submitted only when requested, or as noted in the discussion that follows.

Engineering Tests

Engineering tests should evaluate the safety feature using worst case simulated static and dynamic forces (noting how the worst case conditions were determined), including failure point of component. Tests should include a dry test condition and wet environment simulating body fluids or fluids being administered. Include the following:

- force to attach and detach connections;

- force to (de)activate the safety feature, (e.g. needleless device);
- number of injection port accesses to failure for needleless port with valves and diaphragms/membranes; and
- pressure and leak tolerance for pre-slit septa under extreme conditions of use when used with specific blunt cannulae.

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 which 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. The applicant should compare the new device to legally marketed devices with this safety feature.

Results from a simulated use test that includes parallel comparison testing with a similar device should be provided. The comparison testing should be designed to mimic the device's use in a clinical setting and 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). Simulated use testing should be conducted 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.

A detailed protocol for the study should be provided to include 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. The methods used to prepare the challenge organism(s), method of device contamination, access procedure, and time and culture procedures should also be included. The protocol should provide a justification for the challenge microorganism(s) used as inoculum, type of environment in which the study was conducted, the positive and negative controls used in the study, and a justification for 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.

An analysis of the study results and conclusions, as well as the actual test data, should be provided.

Simulated Use Test

The 510(k) should include prospective data from tests in which the device is evaluated by health

care professionals who typically use the type of device. In most cases data from a simulated use test will suffice.

Several factors that influence the conduct and content of a simulated or clinical test include:

1. Simulated and clinical use tests are not necessary for devices that are identical to a legally marketed device or have only minor variations (e.g., trade name, exterior markings, color). Minor variations are those which do not affect the safety and effectiveness of the medical device with safety features.

2. In lieu of simulated and clinical use performance data, the applicant may submit published literature on the marketed device and a discussion of the literature. A comparative analysis of intended use and technological features of the new device compared to the legally marketed device as noted in Section II.E., page 16, should provide support for the claim that the devices are identical or have a minor variation. Simulated or clinical use data may be needed if there is insufficient literature or new questions of safety and effectiveness about the proposed new device.

3. There are several types of devices with safety features, and studies should be adapted to the variables associated with the particular device. While some of these devices will reduce/eliminate needlestick injuries, there are other factors to consider and evaluate, such as risk of contamination and human factors.

4. The applicant should consider variables in the patient and health care professional user populations. If the device may be exposed to many conditions of use, tests designed to consider the variables to accurately judge the performance of the device under these conditions should be performed. Training, learning curve, and the experience of users will vary.

5. FDA believes that a prospectively designed study based upon appropriate clinical and statistical considerations, is the most scientifically valid way in which to demonstrate that a device is safe and effective for its intended use.

   Protocols should be devised, whenever possible, based upon statistical considerations, such as sample size, response variables, pass/fail criteria, comprehensive report forms, proper controls, and appropriate statistical test methods. (This guidance is not intended to provide a detailed discussion of statistical considerations).

H. Sample Device

If possible, provide a sample of the device to facilitate evaluation.

I. Safe and Effective Medical Devices with Safety Features

This guidance is one of several actions initiated by FDA to help prevent needlestick injuries and

contamination. FDA has recommended the elimination of needles in IV administration sets. There is a guidance for sharps containers based on OSHA regulations and industry standards and a guidance for medical devices with sharps injury prevention features which may be obtained from DSMA.

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 on page 9), and regulatory agencies when designing devices.

J. Desirable Characteristics of Devices with Safety Features

A number of sources have identified the desirable characteristics of safety devices [OSHA, 1999c; FDA 1992; Jagger er al. 1988; Chiarello 1995; Quebbeman and Short 1995; Pugliese 1998; Fisher 1999; ECRI 1999; NIOSH 1999]. 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 safety feature can be engaged with a single-handed technique and allows the worker's hands to remain behind the exposed sharp.
- The user can easily tell whether the safety feature is activated.
- The safety feature can 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. Also, a safety feature that requires activation by the user might be preferable to one that is passive in some cases. Each device must be considered on its own merit and ultimately on its ability to reduce workplace injuries. The desirable characteristics listed here should thus serve only as a guideline for device design and selection.

K. Future Revisions

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

Appendix A Truthful And Accurate Statement

[Refer to Section §807.85 (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 Section §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 secrets 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)

(Per 21 CFR Section §801.109)

Appendix D Sample Comparison Table

FACTORS	NEW DEVICE	LEGALLY MARKETED DEVICE
Intended use and claims		
Indication for use		
Technological features		
Materials		
Specifications: Physical Mechanical Biological		
Other		

Appendix E Sterilization Information

For a device sold sterile, provide the following information as detailed in the ODE Blue Book Memorandum #K90-1.

1. the sterilization method that will be used.

2. a description of the method that will be used to validate the sterilization cycle, but not the validation data itself. Reference to a standard method (e.g., ANSI/AAMI).

3. the sterility assurance level (SAL) for the device which the firm intends to meet. An SAL of 10^{-6} is required for devices which contact normally sterile areas of the body.

4. a description of the packaging to maintain the device's sterility (This is not to include packaging integrity testing data).

5. if sterilization involves EtO, the maximum levels of residues of ethylene oxide, ethylene chlorohydrin, and ethylene glycol which remain on the device. The levels should be consistent with the draft Federal Register Notice on EtO limits,[1] or with ANSI/AAMI/ISO 10993-7:1995[2] .

6. whether the product is "pyrogen free" and an identification of the method used to make that determination.[3]

7. the radiation dose, if radiation will be used, and if it has been determined. Otherwise, amend the 510(k) file at FDA when the dose has been determined.

References

1. FDA Proposed Rule, 43 FR27482 (June 23, 1978), Maximum Residue Limits for Ethylene Oxide, Ethylene Chlorohydrin, and Ethylene Glycol.

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

3. FDA Guidelines on Validation of the Limulus Amebocyte Lysate (LAL) Test as an End Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices.

Appendix F Intravascular Administration Set Checklist

510(K)#_____ Sponsor:_____

Date:_____ Reviewer:_____

Cover Letter

Critical Elements			**COMMENTS**
	YES	NO	
..trade name	___	___	_____
..common name	___	___	_____
..classification name	___	___	_____
..classification panel	___	___	_____
..procode/class	___	___	_____
..establishment reg. #	___	___	_____
..purpose of submission	___	___	_____
..contact: _____			
..telephone/fax: _____/_____			

Administrative Requirements	**YES**	**NO**
..Indications for Use	___	___
..Truthful and Accurate Statement (21 CFR 807.87)	___	___
..510(k) Summary (21 CFR 807.92) OR	___	___
Statement (21 CFR 807.93)	___	___

Labeling	**YES**	**NO**	
..identity of the device	___	___	_____
..intended use	___	___	_____
..type, size/set length, ID, OD, drops/ml, priming volume, filter, needle gauge, length, quantity.	___	___	_____
..single use only	___	___	_____
	YES	**NO**	
..sterile/non-toxic	___	___	_____

..nonpyrogenic fluid path	___	___	_____
..prescription statement	___	___	_____
..frequency of replacement	___	___	_____
..directions for use	___	___	_____
..special limitations	___	___	_____
..promotional materials	___	___	_____
..plasticizer	___	___	_____
Description of Device	**YES**	**NO**	
..narrative description	___	___	_____
..photographs/drawing and/or labeled diagrams	___	___	_____
..sample provided	___	___	_____
Intended Use	**YES**	**NO**	
..clear statement	___	___	_____
Physical Specifications	**YES**	**NO**	
..dimensions and volumes	___	___	_____
..proximal and distal end configuration	___	___	_____
..connector type	___	___	_____
..color (purpose)	___	___	_____
..opacity	___	___	_____
..markings and scales	___	___	_____
..special features	___	___	_____
Mechanical Specifications	**YES**	**NO**	
..strength of materials	___	___	_____
..stress characteristics	___	___	_____
..fluid flow rate	___	___	_____
..identify lubricant, if applicable.	___	___	_____
Material Specifications			
Tests	**YES**	**NO**	
..tensile strength	___	___	_____
..burst test	___	___	_____

..leakage test	___	___	_____
..security of attachments	___	___	_____
..hardness	___	___	_____
..%tubing elongation	___	___	_____
..crimping/flexing w clamp	___	___	_____
..cyclic performance w pump	___	___	_____

Sterilization Information	**YES**	**NO**	
..method	___	___	_____
..validation method	___	___	_____
..SAL	___	___	_____
..packaging	___	___	_____
..EtO residuals	___	___	_____
..pyrogen free method	___	___	_____
..radiation dose	___	___	_____

Biocompatibility Tests-- Refer to FDA Modified ISO-10993	**YES**	**NO**	
..cytotoxicity	___	___	_____
..sensitization	___	___	_____
..intracutaneous	___	___	_____
..systemic toxicity	___	___	_____
..hemocompatibility	___	___	_____
..other	___	___	_____

DESCRIPTIVE COMPARISON TO A LEGALLY MARKETED DEVICE

	YES	**NO**	
..identified appropriate legally marketed device(s)	___	___	_____
..side by side comparison	___	___	_____
..features	___	___	_____

	YES	**NO**	
..intended use(s)	___	___	_____
..labeling	___	___	_____
..all materials	___	___	_____
..technological aspects	___	___	_____

..specifications (as above)	___	___	_____
..performance	___	___	_____
..how differences may affect safety and effectiveness	___	___	_____

Performance data	**YES**	**NO**	
..risk analysis, if appropriate	___	___	_____
..engineering	___	___	_____
..microbial challenge, if appropriate	___	___	_____
..simulated use study	___	___	_____
..actual use study	___	___	_____

.