Guidance for Industry and FDA Staff

Total Product Life Cycle: Infusion Pump - Premarket Notification [510(k)] Submissions

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

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Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Alternatively, electronic comments may be submitted to http://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the Federal Register.

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When final, this document will supersede the Guidance on the Content of Premarket Notification [510(k)] Submissions for External Infusion Pumps, issued March, 1993.

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

Written comments and suggestions may be submitted at any time for Agency consideration to the Division of Dockets Management, 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.

Additional Copies

Additional copies are available from the Internet at: http://www.fda.gov/medicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm206153.htm. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 301-847-8149 to receive a hard copy. Please use the document number (1694) to identify the guidance you are requesting.
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Guidance for Industry and FDA Staff

Total Product Life Cycle: Infusion Pumps - Premarket Notification [510(k)] Submissions

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

1. Introduction

FDA has developed this guidance document to assist industry in preparing premarket notification submissions for infusion pumps and to identify device features that manufacturers should address throughout the total product life cycle. The device, as defined in 21 CFR 880.5725, is intended for use in a health care facility to pump fluids into a patient in a controlled manner.¹

The recommendations in this guidance are intended to improve the quality of infusion pumps in order to reduce the number of recalls and infusion pump Medical Device Reports (MDRs). The FDA believes that these recommendations will help mitigate current risks and reduce future risks associated with infusion pumps.

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

2. Background

FDA has seen an increase in the number and severity of infusion pump recalls. Analyses of MDRs have revealed device problems that appear to be a result of faulty design. Between January 1, 2005 and December 31, 2009, FDA received over 56,000 MDRs associated with the use of infusion pumps. Of these reports, approximately 1% were reported as deaths, 34% were reported as serious injuries, and 62% were reported as malfunctions.

¹ This guidance also includes recommendations for prescription infusion pumps intended for use by lay users in the home or elsewhere. For purposes of this guidance, “lay users” or “home users” are users who receive infusion pumps from or on the order of a health care provider and who use the pumps under the supervision of a licensed practitioner in any appropriate setting, including the home.
The most frequently reported infusion pump device problems are: software error messages, human factors (which include, but are not limited to, use error), broken components, battery failure, alarm failure, over infusion and under infusion. In some reports, the manufacturer was unable to determine or identify the problem and reported the problem as “unknown.” Subsequent root cause analyses revealed that many of these design problems were foreseeable and, therefore, preventable.

The FDA has evaluated a broad spectrum of infusion pumps across manufacturers and has concluded there are numerous, systemic problems with device design, manufacturing, and adverse event reporting. FDA has structured this guidance document to address these device problems prior to clearance of the premarket notification and in the postmarket context.

3. Scope
The scope of this document is limited to the following device, as described in 21 CFR 880.5725 and includes the product codes listed in the table.

§ 880.5725 Infusion pump
(a) Identification. An infusion pump is a device used in a health care facility to pump fluids into a patient in a controlled manner. The device may use a piston pump, a roller pump, or a peristaltic pump and may be powered electrically or mechanically. The device may also operate using a constant force to propel the fluid through a narrow tube which determines the flow rate. The device may include means to detect a fault condition, such as air in, or blockage of, the infusion line and to activate an alarm.
(b) Classification. Class II (performance standards).

<table>
<thead>
<tr>
<th>Product code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRN</td>
<td>Infusion pump</td>
</tr>
<tr>
<td>MEA</td>
<td>Patient controlled analgesia (PCA) infusion pump</td>
</tr>
<tr>
<td>MEB</td>
<td>Elastomeric infusion pump</td>
</tr>
<tr>
<td>LZG</td>
<td>Insulin infusion pump</td>
</tr>
<tr>
<td>OPP</td>
<td>Insulin bolus infusion pump</td>
</tr>
<tr>
<td>LZH</td>
<td>Enteral infusion pump</td>
</tr>
<tr>
<td>MRZ</td>
<td>Infusion pump accessories</td>
</tr>
</tbody>
</table>

All product codes classified under 21 CFR 880.5725 are included within the scope of this document, with the exception of the following: gallstone dissolution pump (MHD), ophthalmic infusion pump (MRH), and analytical sampling infusion pump (LZF).

2 A manufacturer who intends to market a device of this generic type must conform to the general controls of the Federal Food, Drug, and Cosmetic Act (the Act), including the premarket notification requirements described in 21 CFR 807 Subpart E, and obtain a substantial equivalence determination from FDA prior to marketing the device. (See also 21 CFR 807.81 and 807.87.) This document supplements other FDA documents regarding the specific content requirements of a premarket notification submission.
This document does not address submissions for Class III infusion pump systems (e.g., implantable programmable infusion pumps (product code LKK) and closed-loop, autonomous infusion pump systems (product codes LHE and LSX)), which require premarket approval. This document also does not address pressure infusors for I.V. bags (as described in 21 CFR 880.5420, product code KZD), extra luminal infusion pumps (as described in 21 CFR 876.5820, product codes FIR and FIH), and withdrawal-infusion pumps (as described in 21 CFR 870.1800, product code DQI).

If you intend to provide or recommend particular disposable functional devices for use with your infusion pump, such as infusion sets or cassettes, you should identify these devices and demonstrate that each is a legally marketed device, whether you or another firm manufactures the device. If these disposable functional devices are included for evaluation in your 510(k), please refer to guidance on those devices, where available. Please note that for purposes of this document, FDA considers the disposable devices to be part of the infusion pump system, and your device should be evaluated as a system.

For purposes of this document, FDA defines the **infusion pump system** to include the:

- Infusion pump;
- Fluid infusion set for the complete fluid pathway from, and including, the drug reservoir or fluid source container (e.g., bag, cassette, vial, syringe), infusion set, extension sets, filters and valves, clamps, up to and including the patient connection;
- Components and accessories (e.g., power cord, wireless controller);
- Network (i.e., any device or system physically or wirelessly connected to the infusion pump);
- Patient;
- Environment of use (e.g., clinical setting, temperature, humidity); and
- User (physician or lay user).

4. **Device Description**

We recommend you identify your device by the regulation and product code described in Section 3, **Scope**. You must provide information on how your device is similar to and/or different from other products of comparable type in commercial distribution, accompanied by data to support the statement, as required by 21 CFR 807.87(f). Side by side comparisons, whenever possible, are desirable.

You should include the following descriptive information about your device:

- A clear statement of the intended use of your device, including:
  - the intended use environment
  - the intended route(s) of administration for infusion
  - any specific uses for the infusion pump (e.g., PCA is a generally accepted specific use);
whether the infusion pump is indicated for the delivery of blood or blood products;
and
whether the infusion pump is contraindicated for a specific use or for the delivery of a
specific therapy.

- If the infusion pump is labeled for use with a specific device, drug, or biologic, you should
  provide information demonstrating that this use is consistent with the FDA approved labeling
  for that device, drug, or biologic.

- For each route of administration identified in your statement of intended use, you should
  identify an FDA approved drug or biologic to demonstrate that at least one such product is
  approved for infusion through the proposed route of administration and at the proposed
dosage.

- If your infusion pump is intended for transport or ambulatory use, you should describe how it
  was designed for mobility, various environmental conditions (e.g., water exposure, altitude,
electromagnetic interference), and ruggedness.

- If your infusion pump is intended for home use, you should describe how the device has been
  designed to be safely and effectively used by the homecare user population, which often have
  limited or no clinical background and may receive limited training with your device.

- You should state if your device is intended to be marketed as stand-alone or as part of a multi-
  parameter module.

- If your infusion pump incorporates or is intended to incorporate radio-frequency (RF) wireless
  technology (e.g., IEEE 802.11, Bluetooth, Zigbee), the description should include information
  about the specific RF wireless technology and characteristics, its use and functions (e.g.,
  remote monitoring or control, software updates), the data to be transmitted including any
  alarms transmitted wirelessly, quality of service (QoS) needed, wireless security protocols,
  and any limitations or restrictions relating to coexistence with other RF wireless technology or
  electromagnetic interference (EMI).

- Provide a detailed description (including, where appropriate, engineering drawings and
  schematics) of the pump components. The components may include:

  - The infusion delivery mechanism
  - The bolus mechanism
  - The drug reservoir
  - Pump tubing and connectors (built-in or external to the pump)
  - A user-interface, consisting of the programming unit, display unit, audio and tactile
    notification units
  - An alarm handler
  - A watchdog timer
  - Power supply
  - Pump battery and circuitry to charge and monitor the battery
  - A drug library or other dose error reduction mechanism
A real time clock (RTC)
On-board memory
Pump log
A communication interface, including network components and interfaces to other
devices and systems

- You should describe any communication between your device and a hospital information
management system or another device.

- You should describe the principle of operation of the infusion pump (i.e., the scientific
principles behind how the device achieves its intended use).

- You should describe the user interface components of the pump, including keypads, control
menus, data entry screens, displays, indicator lights, alarms, auditory and tactile feedback,
infusion sets, cassettes, free-flow prevention mechanisms, tubing, latches, doors or other
components of the physical pump that may be manipulated.

- You should identify and describe all patient interface accessories (e.g., infusion sets or
cassettes, bolus buttons, wireless controllers).

- You should describe how you will market the device (e.g., sterile, single use, home use).

To support substantial equivalence, we recommend that you provide a table comparing your
device to a legally marketed predicate device. This table should include the following:

- The intended use for each device, including the patient population for which the devices are
intended (i.e., neonate, infant, pediatric, adult) and the intended use environment.
- The specifications for the devices (e.g. flow rate accuracy specifications).
- The technological features of the devices (e.g. alarms, flow rate programming, etc.).

You should describe how any differences in technology may affect the comparative safety and
performance of your device.

5. **Risks to Health**

In the table attached as Appendix A, FDA has identified the risks to health generally associated
with the use of the devices addressed in this document. The measures recommended to mitigate
these identified risks are given in this guidance document. If you elect to use an alternative
approach to address a particular risk identified in this document, or if you have identified risks
additional to those in this document, then you should provide sufficient detail to support the
approach you have used to address the risk(s).³

³ The information presented in Appendix A is also presented, in various forms, in Tables 1-8 of
this document. The difference is that Appendix A, “Risks to Health,” presents the information
from a risk perspective; Tables 1-8 present the information from a hazard perspective, each
focusing on one specified hazard category, such as operational or use hazard.
6. **Assurance Case Report**

FDA expects that most new infusion pumps will include new implementations of software or other changes in materials, design, performance, or other features compared to the predicate. FDA therefore expects that most new devices (as well as most changed or modified devices\(^4\)) will have different technological characteristics from the legally marketed predicate device even while sharing the same intended use. Accordingly, under section 513(i)(1)(A) of the Federal Food, Drug, and Cosmetic Act (the Act), determinations of substantial equivalence will rest on whether the information submitted, including appropriate clinical or scientific data, demonstrate that the new or changed device is as safe and effective as a legally marketed device and does not raise different questions of safety and effectiveness than the predicate device.

In making this demonstration of substantial equivalence for your infusion pump, FDA recommends that you submit your information through a framework known as an assurance case or assurance case report. An assurance case is a formal method for demonstrating the validity of a claim by providing a convincing argument together with supporting evidence. It is a way to structure arguments to help ensure that top-level claims are credible and supported. In an assurance case, many arguments, with their supporting evidence, may be grouped under one top-level claim. For a complex case, there may be a complex web of arguments and sub-claims. Although assurance cases have not generally been used in the premarket review of medical devices, they have been used in other industries with safety-critical systems (e.g., nuclear and avionics). FDA believes the methodology will be particularly useful for presenting and reviewing information about infusion pumps.\(^5\)

An assurance case addressing safety is called a safety case. A top-level claim (e.g., “this infusion pump is comparably safe”) is supported by arguments that demonstrate why and how the evidence (e.g., performance data) supports the top-level claim. The arguments in a safety case are typically organized in a hierarchical fashion with multiple layers of sub-claims, each supported by appropriate evidence. The arguments in a safety case are intended to convince a qualified reviewer or reviewers that the top-level claim is valid.

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\(^4\) Based on FDA’s analysis of these devices, FDA expects that most changes or modifications to infusion pumps could significantly affect the safety and effectiveness of the devices and would therefore require submission of a new 510(k). See 807.81(a)(3). Note that any change to a 510(k)-cleared device may render the device not substantially equivalent (NSE). Any such device may thus require premarket approval (PMA) unless the device is reclassified under section 513(f)(2) or (3) of the Act.

To elaborate, the three main elements of an assurance case are:

1. **Claim**: Statement about a property of the system or some subsystem.

2. **Evidence**: Information that demonstrates the validity of the claim. This can include facts (e.g., based on observations or established scientific principles), analysis, research conclusions, test data, or expert opinions.

3. **Argument**: Links the evidence to the claim. Arguments can be deterministic, probabilistic, or qualitative. The argument will describe what is being proved or established (i.e., the claim(s)), identify the items of evidence you are appealing to, and the reasoning (inference, rationale) that the evidence is adequate to satisfy the claim. Arguments may also introduce sub-claims or assumptions which require further exposition, as the preceding examples illustrate.

In this section, FDA has identified some categories of hazards present in an infusion pump system^6 that should be addressed in your assurance case, if they apply to your device. The hazard categories identified in this section are:

**Section 6A**: Operational Hazards  
**Section 6B**: Environmental Hazards  
**Section 6C**: Electrical Hazards  
**Section 6D**: Hardware Hazards  
**Section 6E**: Software Hazards  
**Section 6F**: Mechanical Hazards  
**Section 6G**: Biological and Chemical Hazards  
**Section 6H**: Use Hazards

We recommend that you conduct your own hazard analysis for your particular infusion pump to identify any additional hazards particular to your device. Your premarket notification should clearly describe the method used to analyze the hazards and each hazardous event mitigation. If you elect to use an alternative approach to address a particular hazard, or categorization of hazards, identified in this document, or if you have identified a hazard additional to those in this document, you should provide sufficient detail to support the approach you have used to address that hazard.

In response to a hazardous event, a pump may issue an alarm or a warning signal. Each alarm or warning should be clearly indicated to the user through audio, video and/or haptic feedback. In addition, the alarm or warning should also be recorded by the pump log, along with the appropriate date-time stamp. We recommend that your device meet the requirements of IEC 60601-1-8: Medical electrical equipment – Part 1-8: General requirements for safety – Collateral standard: Alarm systems. In your 510(k) submission, please present data or certification to standards demonstrating that the alarms and warnings for your device meet the requirements of this standard.

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^6 The infusion pump system is defined in the Scope section of this document.

^7 For more information on recognized consensus standards, see [www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm).
**Alarm**

An alarm may be caused due to one or more hazardous events, including, but not limited to:

- Occlusion (supply side and patient side)
- Air-in-line
- Free flow / Improper flow of fluid
- Depleted battery or No power
- Empty reservoir
- No reservoir
- Dose limit / Bolus limit exceeded
- Panel unlocked / door open
- Key pressed alarm
- Power on self test (POST) failure – issued when one of the POST tests fails
- ROM / RAM CRC test failure
- Tone test failure
- Pump mechanism failure
- Watchdog alarm – issued when the watchdog timer expires
- Overheating
- Defective battery
- Drug library mismatch

**Warning**

The pump may issue a warning message when it encounters a less severe hazardous situation. A warning is typically indicated through visual and auditory signals, and does not interrupt the ongoing infusion. Typical warning messages may include:

- Low battery
- Low reservoir
- Infusion set not loaded properly
- Key press required (a key input is required, while the pump is idle for too long)

**Other Safety Mechanisms**

Apart from these responses to hazardous situations, an infusion pump may also have safety mechanisms to prevent or detect anomalies. These may include, but are not limited to:

1. Power on self test (POST) checks – performed during pump startup or initialization
2. Battery test
3. Stuck key test
4. Tone test
5. Pump mechanism failure test
6. Watchdog interrupt tests
7. (Periodic) System checks – including a CPU test and ROM / RAM CRC tests
8. Sensor checks – to check the proper functioning of sensors attached to the pump, if any
9. Dose error reduction checks
Reliability
Reliability includes component and system level analyses. While reliability analysis includes the particular hazard sub-categories referenced below, it also is appropriate at the system level. You should provide an analysis of your infusion pump system reliability. The analysis should include a description of your system’s reliability specification and the reliability activities completed to verify and validate that the specification has been met (e.g., design analysis, test plans, and test reports). As part of the assurance case, the analyses and associated activities may take the form of claims, arguments, or evidence.

A. Operational Hazards
Operational hazards are those hazards inherently related to the operation of the device. Please refer to Table 1 for examples of operational hazards, the corresponding significant risks to health, and their possible causes.

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s) of Hazard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air in Line</td>
<td>Underdose</td>
<td>Incorrect/incomplete priming processes</td>
</tr>
<tr>
<td></td>
<td>Air Embolism</td>
<td>Broken, loose, or unsealed delivery path</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td>The pump is unable to release gas or air</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The pump is set up with an incompatible infusion set</td>
</tr>
<tr>
<td>Occlusion</td>
<td>Overdose</td>
<td>Delivery path obstructed, e.g., kinked tubes</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>Chemical precipitation inside the delivery path</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td>Bolus occurring after an occlusion</td>
</tr>
<tr>
<td>Free Flow</td>
<td>Overdose</td>
<td>Valves in the delivery path are broken</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>The pump is positioned much higher than the infusion site, causing unintentional drug flow</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The delivery path is damaged, creating a vent on the path that allows unintentional gravity flow</td>
</tr>
<tr>
<td>Reverse Flow</td>
<td>Underdose</td>
<td>The pump is positioned much lower than the infusion site, causing the pump to siphon</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td>The delivery path is damaged, creating a vent on the path that diverts an intentional drug flow from reaching the user</td>
</tr>
<tr>
<td></td>
<td>Exsanguination</td>
<td></td>
</tr>
<tr>
<td>Excessive bolus administration due to too many bolus requests from the user</td>
<td>Overdose</td>
<td>The bolus history records are corrupted, making the user unable to track previously received boluses</td>
</tr>
<tr>
<td>The programmed bolus dose is delivered unevenly over its specified duration</td>
<td>Overdose</td>
<td>Algorithmic errors</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>The pump motor does not operate as intended</td>
</tr>
<tr>
<td>(Drug) Leakage</td>
<td>Underdose</td>
<td>Loose connection between parts of the delivery path</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td>Broken drug reservoir</td>
</tr>
<tr>
<td>The actual flow rate does not match the programmed infusion</td>
<td>Overdose</td>
<td>Air pressure within the pump is much lower than the ambient air pressure</td>
</tr>
</tbody>
</table>

8 The information presented in Tables 1-8 is also presented in Appendix A, “Risks to Health.” While the information in each Table overlaps in part with the information in Appendix A, the scope and perspective of each Table differs: each focuses on a specific hazard category, for example operational or use hazard, rather than on general risks to health that may or may not derive from the specified hazards.
<table>
<thead>
<tr>
<th>rate</th>
<th>Incorrect therapy</th>
<th>Pumping mechanism out of calibration.</th>
</tr>
</thead>
<tbody>
<tr>
<td>The drug reservoir is detached during normal pump use</td>
<td>Underdose</td>
<td>The drug reservoir compartment is broken or opened</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td></td>
</tr>
</tbody>
</table>

We recommend that you demonstrate mitigation of operational hazards in the assurance case report. Any such demonstration should also include some clinical evaluation as appropriate, as described below in Section 7, Clinical Evaluation.

**Flow Rate Accuracy**

Flow rate accuracy tests should represent the intended use of the device.

The studies should be well-designed to meet the stated objectives and should demonstrate that your device successfully performs as intended. This will include rigorous attention to: statistical elements (hypotheses, analyses, sample size and sampling, power, etc.), controls, minimization of bias, test parameters (endpoints), follow-up, evaluation criteria, etc.

The premarket notification should include the following information for each test performed:

1. A detailed description of the test method, including drawings of the test apparatus where appropriate;
2. An explanation of how the test set up simulates actual clinical use;
3. An explicit statement of the acceptance criteria for the test;
4. The results of the test;
5. An analysis of the test results; and
6. An explicit statement of any conclusions drawn from the test.

If the device fails during a test, you should discuss why the failure does not affect the safety or effectiveness of the device. In addition, if you modify the device after the failed test, you should identify and describe each modification and its intended effect, and you should include additional test results to show that the modified device passes the previously failed test.

FDA considers infusion pumps to be part of a system, as defined in the **Scope** section of this document. We recommend that bench tests be conducted with the complete infusion pump system intended to be used with your device. Each available configuration of the system should be tested, though testing of representative configurations may also be acceptable. Where representative tests are provided, you should describe how the collected data are relevant to the untested configurations.
The flow rate accuracy specification for your infusion pump system should be appropriate for the intended use and should be appropriate for the therapeutic range of the fluids intended to be infused by the system. The flow should also be accurate against different head pressures.

For a pump intended to maintain a constant set flow rate per your specifications, the data should demonstrate that the device can maintain a set flow rate over the complete course of the infusion within the designated accuracy. The testing should demonstrate adherence to specifications at the limits of the operational parameters.

For a pump that does not maintain a constant flow rate, test results should be used to generate a representative flow profile. This representative flow profile should be included in the device labeling. Testing should include an assessment of flow rate accuracy at the minimum, intermediate, and maximum flow rates. You should provide a justification for choice of intermediate flow rate.

For pumps that are capable of bolus delivery, test results should demonstrate that the accuracy of the bolus delivery is within specification. Testing should include an assessment of bolus accuracy at the minimum and maximum bolus dose.

Testing should also demonstrate that the device can maintain the specified flow characteristics despite changes in ambient temperature, pressure, or fluid viscosity, which would reasonably be expected to be encountered according to the intended use of the device. The effects of these factors should be discussed quantitatively in the labeling so that the user is made aware of the effects of these factors.

**B. Environmental Hazards**

Environmental hazards are those hazards related to the location in which the device will be used. Please refer to Table 2 for examples of environmental hazards, the corresponding significant risks to health, and their possible causes.

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
</table>
| Failure to operate/ Pump malfunction | Overdose  
Underdose  
Delay of therapy  
Electric shock | Temperature /Humidity/ Air pressure too high or too low |
| The pump is exposed to pathogens, allergens, and other hazardous substances | Trauma  
Infection  
Allergic response | Contamination due to spillage / exposure to toxins  
Battery leak |
| Tampering (for example, by a patient during home use to adjust drug delivery) | Overdose  
Underdose  
Delay of therapy  
Incorrect therapy  
Air embolism | Unauthorized tampering of pump settings  
Panel lock broken or opened during infusion  
Panel/door opened during infusion  
Infusion started when door open |
| Non-human interference | Overdose | Electromagnetic interference (EMI) from cell phones |
We recommend that your device meet the environmental safety requirements of *IEC 60601-1 (1988)*: Medical electrical equipment – Part 1: General requirements for safety, including Amendment 1 (1991) and Amendment 2 (1995) for Type B equipment and *IEC 60601-1 Collateral Standard: Safety requirements for medical electrical systems*. In your 510(k) submission, please present data or certification to standards demonstrating that your device meets the environmental safety requirements.

The environmental hazards for your particular infusion pump may be different from the generic requirements in IEC 60601 series. For example, environmental hazards for a home use pump may be different from a pump intended for use in a healthcare facility. For this reason, we recommend that you comprehensively characterize the environmental hazards for your infusion pump and establish appropriate design requirements to mitigate the hazards.

The device (i.e., the complete system suitable for its intended use) should withstand the mechanical shocks and vibrations expected in the intended environment of use, including: sinusoidal vibration, broad-band random vibration, mechanical shock and free fall. You are responsible for characterizing the use environment and establishing the performance requirements to ensure that your infusion pump consistently operates as intended. For example, drop tests should be representative of falls experienced in the intended environment.

### C. Electrical Hazards

Electrical hazards are those hazards related to the power supply and infrastructure. Please refer to Table 3 for examples of electrical hazards, the corresponding significant risks to health, and their possible causes.

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overheating</td>
<td>Electric shock</td>
<td>Incorrect or loose interconnections between devices, Supply processor charge too high, Insufficient cooling/faulty heat sink, Unintended magnet quench</td>
</tr>
<tr>
<td>Charge Error</td>
<td>Underdose, Delay of therapy, Incorrect therapy</td>
<td>Battery could not be charged</td>
</tr>
<tr>
<td>Supply Voltage Error</td>
<td>Overdose, Underdose, Delay of therapy, Incorrect therapy, Electric shock</td>
<td>AC supply exceeds limits, Battery voltage exceeds limits, Battery depleted, A-to-D conversion failed</td>
</tr>
<tr>
<td>Battery Failure</td>
<td>Underdose, Delay of therapy, Incorrect therapy</td>
<td>Battery voltage too low, Battery depleted, Battery overcharged</td>
</tr>
<tr>
<td>Leakage Current too high</td>
<td>Electric shock</td>
<td>Inadequate shielding, Short circuit</td>
</tr>
</tbody>
</table>
We recommend that your device meet the electrical safety requirements of IEC 60601-1 (1988): Medical electrical equipment – Part 1: General requirements for safety, including Amendment 1 (1991) and Amendment 2 (1995) for Type B equipment and IEC 60601-1 Collateral Standard: Safety requirements for medical electrical systems.

Electromagnetic compatibility (EMC) is the ability of a device to operate properly in its intended environment of use without introducing excessive electromagnetic disturbances into that environment. IEC 60601-1-2 (2001): Medical Electrical Equipment, Part 1: General Requirements for Safety, 2. Collateral Standard: Electromagnetic Compatibility - Requirements and Tests describes EMC testing and includes both tests for immunity of the device to outside noise and emissions from the device to the outside. In addition to evidence of compliance with this standard you should provide summary information describing what was done and how, the device functions and modes that were tested, pass/fail criteria, reference standards and any deviations or allowances that were taken, any device modifications needed to pass the testing, and appropriate labeling.

If your infusion pump contains any electrical components, you should include in your 510(k) submission a complete description of the EMC characteristics of the device, and the information to verify those characteristics under the following circumstances:

- You should test all devices with the third wire ground connected at the plug end of the power cord.
- We recommend that devices intended for home use should safely function without a protective earth ground as defined in IEC 60601-1-2 (2001), Clause 14.2, class II.


If your submission includes radio frequency (RF) technologies, you should include in your 510(k) submission a complete description of the RF use. While applications of RF wireless technologies might comply with applicable technology standards and Federal Communications Commission rules, medical device safety and effectiveness concerns may remain. For detailed information about possible risks and ways these should be addressed, you may refer to the draft Radio-Frequency Wireless Medical Device Guidance at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077210.htm. Particular points you should address in your 510(k) include: quality of service needed, data integrity, coexistence, security, and EMC. Due to the increased use of RF...
wireless technology that operates in the same frequency range, you should carefully address RF wireless coexistence via testing with other common applications of RF wireless technology that can be expected in the environment of use. The testing should also address the ability of two or more of your infusion devices to operate wirelessly in proximity.

**D. Hardware Hazards**

Hardware hazards are those hazards related to the failure of a hardware component of the device. Please refer to Table 4 for examples of hardware hazards, the corresponding significant risks to health, and their possible causes.

**Table 4 – Hardware Hazard Examples**

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>System failure</td>
<td>Underdose</td>
<td>Malfunctioning component</td>
</tr>
<tr>
<td></td>
<td>Delay in therapy</td>
<td>Synchronization error between pump components</td>
</tr>
<tr>
<td></td>
<td>Incorrect therapy</td>
<td>Watchdog failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reliability specification not met</td>
</tr>
<tr>
<td>Network error</td>
<td>Overdose</td>
<td>Network congestion</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>Communication problem</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td>Loss of (wireless) signal</td>
</tr>
<tr>
<td></td>
<td>Incorrect therapy</td>
<td>Pump not compatible with networked / integrated device</td>
</tr>
<tr>
<td>Memory failure</td>
<td>Overdose</td>
<td>Attempted write to memory failed</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>Critical value data integrity error</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td></td>
</tr>
<tr>
<td>False alarm</td>
<td>Overdose</td>
<td>False watchdog interrupt</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>Device or sensor contaminated</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td>Device or sensor out of calibration</td>
</tr>
<tr>
<td>Failure to alarm</td>
<td>Overdose</td>
<td>Sensor failure</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td></td>
</tr>
<tr>
<td>Incorrect dose value entered</td>
<td>Overdose</td>
<td>Key de-bounce prevention failed</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td></td>
</tr>
</tbody>
</table>

**E. Software Hazards**

Software hazards are those hazards related to improper implementation of the development lifecycle for the software. Please refer to Table 5 for examples of software hazards, the corresponding significant risks to health, and their possible causes.

**Table 5 – Software Hazard Examples**

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data error</td>
<td>Overdose</td>
<td>Failure to backup</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>Data store/retrieval error</td>
</tr>
<tr>
<td></td>
<td>Incorrect therapy</td>
<td>Communication problem</td>
</tr>
<tr>
<td></td>
<td>Delay of therapy</td>
<td></td>
</tr>
<tr>
<td>Software runtime error</td>
<td>Overdose</td>
<td>Buffer overflow/underflow</td>
</tr>
<tr>
<td></td>
<td>Underdose</td>
<td>Null pointer dereference</td>
</tr>
<tr>
<td></td>
<td>Incorrect therapy</td>
<td>Memory leak</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uninitialized variable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Incorrect dynamic libraries</td>
</tr>
<tr>
<td>System malfunction</td>
<td>Overdose</td>
<td>Underdose</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>Corrupted infusion commands</td>
<td>Overdose</td>
<td>Underdose</td>
</tr>
<tr>
<td>Pump could not be silenced</td>
<td>Overdose</td>
<td>Underdose</td>
</tr>
<tr>
<td>Incorrect software version</td>
<td>Overdose</td>
<td>Underdose</td>
</tr>
<tr>
<td>Failure to alarm / False alarm</td>
<td>Overdose</td>
<td>Underdose</td>
</tr>
</tbody>
</table>

Please refer to the *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*, [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089543.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089543.htm), for a discussion of the software documentation that you should provide in the 510(k) submission. We generally consider infusion pumps to be a “Major” level of concern for the purposes of software review.

We encourage you to take advantage of any recognized software standards and provide statements or declarations of conformity as described in FDA guidance, *Use of Standards in Substantial Equivalence Determinations*, [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073752.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073752.htm). Please visit the following website to search for the standards that we have recognized when a medical device contains software, [http://www.accessdata.fda.gov/scripts/cdrh/eventdocs/efStandards/search.cfm](http://www.accessdata.fda.gov/scripts/cdrh/eventdocs/efStandards/search.cfm). We have created a supplemental data sheet for each software standard that we have recognized. The supplemental data sheet includes a table that indicates the documentation that you should include in a submission when you provide a declaration of conformity.

If the device includes off-the-shelf software, you should provide the additional information as recommended in the *Guidance for Industry, FDA Reviewers and Compliance on Off-the-Shelf Software Use in Medical Devices*, [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073778.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073778.htm).

We recommend you describe how your software addresses information security. Information security is the process of preventing the modification, misuse or denial of use, or the unauthorized use of information that is stored, accessed or transferred from your device to an external recipient. We recommend that your device address the following four components of information security described below: Confidentiality, Integrity, Availability, and Accountability (CIAA).
• **Confidentiality** means data, information, or system structures are accessible only to authorized persons, entities and processes at authorized times and in the authorized manner, thereby helping ensure data and system security. (The assurance that no unauthorized users have access to the information.)

• **Integrity** means data and information are accurate and complete and have not been improperly modified.

• **Availability** means data information and information systems are accessible and usable on a timely basis in the required manner. (The assurance that the information will be available when needed.)

• **Accountability** means an authorized user is identified and authenticated before access.

**Dosing Algorithms**
For infusion pumps that contain algorithms intended to provide dosing recommendations, we recommend that you include the following information in your premarket notification:

• The dosing algorithms used within your device.

• For each algorithm identified, you should include the algorithm in symbolic form and define all parameters in each algorithm and identify what parameters can be modified by the end-user.

• For each algorithm identified, you should include clinical data or other justification (i.e., via scientific literature) for why you believe your algorithm is appropriate for your intended patient population.

• Each algorithm should be verified and validated in your software documentation to show that the calculations made by the dose calculator are correct. You should include data demonstrating that the algorithms implemented in your software are calculated correctly.

**F. Mechanical Hazards**
Mechanical hazards are those hazards related to the mechanical design of the device by the user. Please refer to Table 6 for examples of mechanical hazards, the corresponding significant risks to health, and their possible causes.

**Table 6 – Mechanical Hazard Examples**

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unable to set dose, start/ stop/ reset pump, silence alarm</td>
<td>Overdose Underdose Delay of therapy Incorrect therapy</td>
<td>Broken part (e.g., broken keypad)</td>
</tr>
<tr>
<td>Incorrect dose value entered</td>
<td>Overdose Underdose Delay of therapy</td>
<td>Key stuck / depressed</td>
</tr>
</tbody>
</table>
Incorrect therapy

We recommend that you consider the mechanical safety requirements of IEC 60601-1 (1988): *Medical electrical equipment – Part 1: General requirements for safety*, including Amendment 1 (1991) and Amendment 2 (1995) for Type B equipment and IEC 60601-1 Collateral Standard: *Safety requirements for medical electrical systems*. FDA recommends that you evaluate the potential mechanical hazards that your infusion pump system may experience and appropriately mitigate those hazards. We recommend testing your infusion pump system to verify and validate that the system maintains safe and effective operation during and after experiencing foreseeable mechanical hazards. We recommend that you provide this information in your 510(k) submission.

### G. Biological and Chemical Hazards

Biological and chemical hazards are those hazards related to the materials of construction, cleaning substances, and infusates. Please refer to Table 7 for examples of biological hazards, the corresponding significant risks to health, and their possible causes.

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
</table>
| The pump is exposed to pathogens, allergens, and other infectious substances | Infection | Inadequate device cleaning
| Infusion site infection | Device contaminated by blood/leaking fluid
| | Failure to flush
| | The pump is connected to non-sterile infusion sets or reservoir.
| | Packaging of the pump is damaged prior to its use
| | The user is allergic to the infusion set or infusion set adhesive
| | The user fails to rotate infusion sites as recommended
| Chemical precipitation inside the delivery path | Infection | Inadequate device cleaning
| Allergic response | Drug not compatible with device materials.
| Incorrect therapy | |
| Physical damage to pump | Overdose | Inadequate device cleaning or disinfection
| Underdose | |
| Delay of therapy | |
| Incorrect therapy | |
| Loss of drug potency | Incorrect therapy | Incompatible device materials
| | Temperatures exceeds drug specifications
| Toxicty | | Materials of construction are not biocompatible
| | Drug leaches chemicals from device

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2. FDA recommends that you evaluate the potential mechanical hazards that your infusion pump system may experience and appropriately mitigate those hazards. We recommend testing your infusion pump system to verify and validate that the system maintains safe and effective operation during and after experiencing foreseeable mechanical hazards. We recommend that you provide this information in your 510(k) submission.

3. **G. Biological and Chemical Hazards**

4. Biological and chemical hazards are those hazards related to the materials of construction, cleaning substances, and infusates. Please refer to Table 7 for examples of biological hazards, the corresponding significant risks to health, and their possible causes.

5. Table 7 – Biological and Chemical Hazard Examples

6. | Hazard | Corresponding Risk(s) to Health | Potential Cause(s) |
7. | --- | --- | --- |
8. | The pump is exposed to pathogens, allergens, and other infectious substances | Infection | Inadequate device cleaning
9. | Infusion site infection | Device contaminated by blood/leaking fluid
10. | | Failure to flush
11. | | The pump is connected to non-sterile infusion sets or reservoir.
12. | | Packaging of the pump is damaged prior to its use
13. | | The user is allergic to the infusion set or infusion set adhesive
14. | | The user fails to rotate infusion sites as recommended
15. | Chemical precipitation inside the delivery path | Infection | Inadequate device cleaning
17. | Incorrect therapy | |
18. | Physical damage to pump | Overdose | Inadequate device cleaning or disinfection
19. | Underdose | |
20. | Delay of therapy | |
21. | Incorrect therapy | |
22. | Loss of drug potency | Incorrect therapy | Incompatible device materials
23. | | Temperatures exceeds drug specifications
24. | Toxicty | | Materials of construction are not biocompatible
25. | | Drug leaches chemicals from device

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Biocompatibility

Infusion pumps include parts that contact the patient. You should evaluate the biocompatibility of materials in the components which have direct or indirect contact with the patient and report the results in your 510(k) submission. When addressing biocompatibility, we recommend referring to the Blue Book Memo, Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080735.htm. When conducting the biocompatibility tests, you should select tests appropriate for the duration and level of contact with your device. For the purpose of assessing biocompatibility, we recommend considering infusion pumps to have prolonged duration due to the potential for cumulative use of the device and its replacements. We recommend considering the components which contact the patient as surface contacting components with skin contact. Testing should include irritation/intracutaneous reactivity, sensitization, and cytotoxicity. The tests may differ if your device has fluid path contacting materials.

If you use materials in your device that are identical to your predicate device and have the same type and duration of patient contact, you may identify the predicate device in lieu of performing biocompatibility testing. FDA recognizes that it is difficult to document that materials in your device and a predicate device are identical with respect to composition and manufacturing processes. Therefore, if you have documentation to support the identical nature of the materials, we recommend the following statement for biocompatibility certification of previously used materials:

The [polymer/metal/ceramic/composite name] [component name] of the [subject device name] is identical to the [component name] of the [predicate device name] as it was approved in [PMA/510k/IDE number, approval date] in formulation, processing, and sterilization, and no other chemicals have been added (e.g., plasticizers, fillers, color additives, cleaning agents, mold release agents, etc.).

Sterilization

You should provide the appropriate documentation recommended by the FDA Guidance, Sterility Review Guidance available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072783.htm.

Reuse

Infusion pumps and accessories intended for multiple patient reuse should include instructions for cleaning and disinfecting the device between uses in the device labeling. Also, where appropriate, consider specifying in your submission and labeling the number of times the device can be reused, with supporting information (see Shelf Life, below).

If you clean or high level disinfect the device, you should provide validation to demonstrate that such cleaning or high level disinfection is adequate. You should also demonstrate that after cleaning or high level disinfection the device performs as intended.

Numerous infusion pumps are used in the home environment. You should provide in the
labeling cleaning agents/products that are readily available to the average home-based user along with instructions for cleaning the device.

In order to demonstrate that you meet the device’s performance specifications after cleaning or disinfection, you should provide bench data before and after an appropriate number of cleaning or disinfection cycles per your labeling. To demonstrate that your labeled cleaning or disinfection methods achieve their objective, we recommend referring to the *FDA Guidance, Labeling Reusable Medical Devices for Reprocessing* available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080268.pdf for additional information and labeling recommendations.

**Shelf Life**

If your particular infusion pump contains sterile components or materials that could degrade over time, we recommend that you include a shelf life on the packaging.

We recommend that you provide data to demonstrate that the sterility and performance of your particular infusion pump maintain their specifications throughout the time period specified by your shelf life. If accelerated test methods are utilized, we recommend that you provide information validating that the test methods accurately simulate real-time conditions for your device.

**Drug or Biologic Stability and Compatibility**

For each route of administration included in your indications for use, we recommend that you identify at least one FDA approved drug or biologic that is approved for delivery through an infusion pump for that route of administration. You should include a copy of labeling for each drug or biologic identified.

If your infusion pump includes a reservoir, we recommend that you provide stability and compatibility data for each drug or biologic that you have identified above, which assesses the stability and compatibility for the recommended use period and conditions included in your labeling. In addition to demonstrating that the drug or biologic retains its specifications, we recommend that you include a safety evaluation of any leachables, extractables, impurities and degradants. Analytical methods should be used to identify and quantify impurities, degradants, leachables and foreign particulates in the effluent.

As noted in the labeling recommendations of this document (Section 10), you should identify the particular drugs or biologics that you have evaluated for use with your device.

**H. Use Hazards**

Use hazards are those hazards related to the use of the device and are found within the interaction between the device and the user. Please refer to Table 8 for examples of use hazards, the corresponding significant risks to health, and their possible causes.

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Corresponding Risk(s) to Health</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>User does not understand how to initiate pump operation</td>
<td>Delay of therapy</td>
<td>User interface design is confusing. User confused by pump operation, IFU insufficient or lacking, training</td>
</tr>
<tr>
<td><strong>The pump is programmed incorrectly</strong></td>
<td><strong>Overdose</strong>&lt;br&gt;<strong>Underdose</strong>&lt;br&gt;<strong>Delay of therapy</strong>&lt;br&gt;<strong>Incorrect therapy</strong></td>
<td>User believes “piggy back” is accounted for in set up but it is not.&lt;br&gt;The instructions for use are confusing for the user.&lt;br&gt;The user specifies incorrect configuration parameters (blood glucose reading, drug concentration, etc.).&lt;br&gt;The user accidentally touches the pump console, presses the wrong key or key “bounces” when hit, changing or mistakenly programming pump settings.</td>
</tr>
<tr>
<td><strong>Infusion stopped prematurely</strong></td>
<td><strong>Underdose</strong>&lt;br&gt;<strong>Delay of therapy</strong></td>
<td>The user forgets to resume the pump after suspending it.</td>
</tr>
<tr>
<td><strong>The user fails to detect or understand pump notifications</strong></td>
<td><strong>Overdose</strong>&lt;br&gt;<strong>Underdose</strong>&lt;br&gt;<strong>Delay of therapy</strong>&lt;br&gt;<strong>Incorrect therapy</strong></td>
<td>Background noise or nuisance alarms cause user to fail to detect or to ignore them.&lt;br&gt;The user muffles the pump’s speaker or other audio devices, either intentionally or unintentionally.</td>
</tr>
<tr>
<td><strong>Wrong medication or concentration is delivered</strong></td>
<td><strong>Incorrect therapy</strong>&lt;br&gt;<strong>Delay of therapy</strong></td>
<td>User selects and sets up pump with incorrect medication or incorrect concentration.&lt;br&gt;Medication is correct but user selects incorrect concentration or delivery rate for that medication.</td>
</tr>
<tr>
<td><strong>Physical set up, such as routing of tubing or selection of appropriate tubing set is incorrect</strong></td>
<td><strong>Overdose</strong>&lt;br&gt;<strong>Underdose</strong>&lt;br&gt;<strong>Delay of therapy</strong></td>
<td>User believes infusion is occurring but it is not.&lt;br&gt;User is required to perform excessive programming task sequences or perform them repeatedly.&lt;br&gt;User is confused about pump set-up, troubleshooting, or operation tasks.&lt;br&gt;Physical set-up of pump components is difficult.</td>
</tr>
<tr>
<td><strong>User “works around” or “bypasses” software limits on drug/dose parameters.</strong></td>
<td><strong>Overdose</strong>&lt;br&gt;<strong>Underdose</strong></td>
<td>Software configuration, possibly user-defined configuration, is not applicable to current treatment and user is compelled to “work around” or “bypass it”.&lt;br&gt;“Work around” or “bypass” requirements are required so often the user does not attend to displayed limits.</td>
</tr>
<tr>
<td><strong>User ignores or misinterprets software-generated “warnings”</strong></td>
<td><strong>Overdose</strong>&lt;br&gt;<strong>Underdose</strong>&lt;br&gt;<strong>Incorrect therapy</strong></td>
<td>Warnings are displayed so often that user ignores them.&lt;br&gt;Warning statements are not sufficiently informative, meaningful or appropriate for the condition.</td>
</tr>
<tr>
<td><strong>User misinterprets or misunderstands pump status or operational mode</strong></td>
<td><strong>Overdose</strong>&lt;br&gt;<strong>Underdose</strong>&lt;br&gt;<strong>Incorrect therapy</strong>&lt;br&gt;<strong>Delay of treatment</strong></td>
<td>Pump operates differently than expected.&lt;br&gt;Pump operational mode indications are absent or not communicated effectively.&lt;br&gt;Display characters not distinguishable.</td>
</tr>
<tr>
<td><strong>The pump is disconnected</strong></td>
<td><strong>Underdose</strong>&lt;br&gt;<strong>Delay of therapy</strong>&lt;br&gt;<strong>Exsanguination</strong></td>
<td>The user’s motions cause the pump to be disconnected from the user.</td>
</tr>
<tr>
<td><strong>Excessive bolus administration due to too many bolus requests from the user</strong></td>
<td><strong>Overdose</strong></td>
<td>The user forgets previously received boluses, and requests for unnecessary boluses without consulting with bolus history records.</td>
</tr>
<tr>
<td><strong>(Drug) Leakage</strong></td>
<td><strong>Underdose</strong>&lt;br&gt;<strong>Trauma</strong>&lt;br&gt;<strong>Allergic response</strong></td>
<td>The user does not follow instructions to disconnect the pump.</td>
</tr>
<tr>
<td><strong>The drug reservoir is detached during normal pump use</strong></td>
<td><strong>Underdose</strong>&lt;br&gt;<strong>Delay of therapy</strong></td>
<td>The user’s motions cause the reservoir to be disconnected.</td>
</tr>
</tbody>
</table>
Human Factors

Reports of device-related incidents and recalls have shown that patterns of use errors resulting from flaws in the design of the pump’s user interface have led to patient harm. The term *user interface* denotes all components of the pump with which the user interacts, such as keypads and control buttons, indicators, auditory and visual alarms, warning and other messages to users, the design of control and display screens, software components that control display and input screens and numerical values.

Use hazards are failures arising from use of pumps. They are a unique form of hazard in that use-related hazards can exist even if a pump operates according to specifications. They generally do not involve specific failures due to faulty mechanical, electrical or software components that are previously known or reasonably anticipated.

To address use hazards, human factors evaluations should start early in the design process and should occur iteratively. These evaluations are also known as formative studies. The formative assessments are useful for discovering previously unknown use problems. They are also useful for determining aspects of use that are most relevant in the design process and will achieve an understanding of the user requirements. The formative human factors assessments should be structured such that tasks, or use scenarios, are prioritized according to relative risk. Identification of a use risk should result in the development of a risk mitigation and subsequent validation of that mitigation.

Following the formative stage of human factors, FDA recommends that you conduct a summative human factors study, with the intent to validate the results of the formative studies. The summative study should include subjective and objective assessment of user performance under simulated conditions. The summative study should also record and analyze anticipated and unanticipated use errors.

Quantified success and failures rates may be useful indicators of use difficulty or interface deficiencies. However, quantified success criteria alone are generally not sufficient to validate use safety. Measures consisting solely of numerical ratings of overall preference, comparison to other devices, or general usability (e.g. “easy to use” vs. “difficult to use”) will not generally suffice. Further inquiry and descriptive analysis may be needed. We therefore recommend that failures be described in terms of the nature of the user interaction involved and the outcome of the failure. This typically requires subjective assessment of use and possibly interviews with participants. Test participants should be asked to describe difficulties or confusion they might have experienced when using the pump for specific critical tasks or scenarios of use as well as for overall use of the pump. Studies that do not consider risk associated with the use of the pump are generally not adequate. Numerical acceptance criterion values for performance “success/failure” should be used with caution and are generally not helpful for summative evaluations. For example, although a 90% success rate on a given task appears to be a “high” success rate, it implies a 10% failure rate which must then be accounted for in terms of the impact these failures would have on the safety of the pump. Use errors that represent use hazards should be mitigated and the mitigation should also be verified to demonstrate its effectiveness. Postponing mitigation of use safety hazards, or mitigating through labeling or training, are generally not acceptable.
Simulated use should be as natural and free from instruction and cuing of the users as possible. The participants involved in the simulated use testing should represent the intended users of your pump. Employees are not representative users. In addition, if a pump is intended to be used in the home by lay users, we will expect that simulated use be conducted with users representing the home use population with realistic levels of training. Simulated use testing should seek to identify and understand the cause of use errors. “Experimental artifact” might be the cause of some errors but these errors should be understood and described. The cause of performance failures, such as the source of confusion experienced by the user, should be determined for any other performance errors or “failures” involving the use of the pump and should be included in the summary report for human factors/usability testing.


7. **Clinical Evaluation**

In addition to performing a simulated study of human factors (described above in Section 6H), FDA recommends that you conduct a clinical evaluation of your infusion pump to evaluate device performance, possible use error and other human factors, where appropriate. The clinical evaluation should seek information pertaining to user perception of difficulties with pump use. It should be carefully designed to assess critical tasks or use scenarios where use error is most likely. As part of this evaluation, you should document and evaluate previously unanticipated use errors if they occur. In addition to assessing the number of failures, you should determine the cause of each failure and examine all adverse events associated with use error. You should also examine all operational hazards that may occur. Please see Section 6A, Operational Hazards, and Section 6H, Use Hazards, for additional information. You should provide the analysis and results in your pre-market notification as part of the assurance case report.

Clinical evaluations are recommended for:

- New devices,
- A major change or modification in the intended use of the device (e.g., different use environments, different disease states, different patient populations),
- Modifications intended to correct problems with the design of the user interface.

If you make a modification that affects usability as it relates to safety, then you should either perform a clinical evaluation or justify in writing to FDA why you believe that a clinical evaluation is unnecessary. This justification should be sent to FDA prior to submitting your 510(k) premarket notification to prevent any delay in the review of your submission.

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9 For more information on the regulatory implications of making changes to your cleared device, see the opening of Section 6, Assurance Case Report, and footnote 4.
FDA has determined that a clinical evaluation of an infusion pump is a significant risk investigation as defined in 21 CFR 812.3(m), and as such, is not exempt from the requirement to submit an investigational device exemption (IDE) application (21 CFR 812.2(b), 812.20(a)(1)). Any clinical evaluation must therefore be conducted under an approved IDE. Sponsors of such studies must not begin their clinical evaluations until FDA has approved the IDE application (21 CFR 812.20(a)(2), 812.42), and they must comply with the following:

- IDE regulations (21 CFR Part 812)
- Regulations governing institutional review boards (IRB) (21 CFR Part 56)
- Informed consent (21 CFR Part 50)

As part of the report of prior investigations (21 CFR 812.27), the IDE application must include results from a simulated human factors study conducted under controlled conditions and bench tests. See Section 6H, Use Hazards for further detail.

FDA encourages sponsors to use pre-submission interactions to obtain informal guidance regarding product and protocol development prior to submission of an original IDE application. FDA comments provided to sponsors during the pre-IDE process are informal input, intended to facilitate open communication between the sponsor and the Agency. Pre-submission interactions for an infusion pump may address all aspects of the IDE or 510(k), or can focus on particular areas, such as engineering testing, simulated human factors studies or clinical evaluation protocols. You should clearly identify any questions or particular items you would like to have addressed as part of the pre-submission interaction.

Information regarding the pre-IDE program is found in the following guidance:

FDA guidance documents regarding IDE submissions are found at:

## 8. Risk Management

Many decisions made during the design and development phase bear on the safety and effectiveness of the device. FDA has an interest in reviewing such design decisions, and those decisions should be documented in the design history file. FDA recommends that your 510(k) submission include a risk management report and the other documents identified below to demonstrate that the results of risk management activities were incorporated into the device design. These documents should be incorporated into the assurance case as arguments or evidence, where appropriate (see Section 6, Assurance Case Report).

### Risk Management Report

Your submission should include a risk management report, summarizing the results of risk management activities pertaining to safety and effectiveness of the device.
The risk management report may be submitted in any reasonable format. For example, the information may be presented in tabular or narrative format, and risk levels may be expressed quantitatively or qualitatively as appropriate. The format you choose will probably be dictated by your firm’s risk management process.

**System Architecture**

Your submission should describe the major components of your system, and indicate how the functional requirements are allocated among them. This may be as simple as a block diagram listing the major functions performed by each system component, and how they are integrated into one system.

**Design Requirements Documents**

FDA recommends that submissions include documents resulting from the design input process that define the inputs (i.e., functional, performance, and interface characteristics) of your system in engineering terms. Your firm may refer to these documents as “system specifications,” “design requirements,” “requirements specifications,” or by other names. In many cases, there will be several such documents, covering the major hardware and software components of the system.

Each submission should also document how the design outputs meet the design inputs. The submission should list the design changes (if any) that were made to the device during the design phase, and how the change affected the device design (i.e., inputs and outputs). The documents provide objective evidence that appropriate risk control measures have been incorporated into the device design, that the device design adequately accounts for the intended use environment, and that technical characteristics of the device critical to clinical performance are adequately described.

In some cases, an FDA investigator might ask to review these same documents during a quality system inspection. The quality system inspector aims to assess the adequacy of your quality system and the extent to which your firm is following its documented quality system processes.

**9. 510(k) Pre-Clearance Inspection for Infusion Pump**

FDA may conduct a Pre-Clearance Inspection for infusion pump manufacturers.

FDA finds that there is a substantial likelihood that failure to comply with the Quality System Regulation (part 820) for these products will potentially present a serious risk to human health. Therefore, future 510(k) submissions for the infusion pumps covered by this guidance may be subject to pre-clearance inspections in accordance with section 513(f)(5) of the Act (21 U.S.C 360c(f)(5)).

Since 2003, FDA has seen a dramatic increase in the number of Class 1 recalls associated with infusion pumps. FDA has also seen significant increase in the number of Medical Device Reports (MDRs) and complaints from consumers submitted to the FDA associated with infusion pumps. These recalls and MDR reports suggest that infusion pump manufacturers may not be in control of the quality system that they had implemented at their facility. Subsequent FDA inspections have identified Quality System regulation deviations in these situations. As a result, FDA has pursued further regulatory action against infusion pump manufacturers.
trends of increasing recalls, MDRs, and regulatory actions, FDA believes that the preclearance inspections may be necessary to reduce serious adverse events associated with the use of these devices.

In determining whether a pre-clearance inspection is needed, FDA may consider, among other factors, whether:

- It is a new device;
- An inspection of the facility has not taken place within the last two years;
- An inspection has occurred within two years, but did not cover a similar process and product;
- An inspection has occurred within two years and the district decision was voluntary action indicated (VAI) or official action indicated (OAI); or
- The device was changed and a new 510(k) submitted to address infusion pump failures.

When a pre-clearance inspection is needed, FDA intends to perform a Level 2 Comprehensive Inspection per FDA’s Compliance Program Guidance Manual 7382.845, Inspection of Medical Device Manufacturers. This inspection will include review of your Medical Device Reporting procedures and processes.

10. Labeling

The premarket notification must include labeling in sufficient detail to satisfy the requirements of 21 CFR 807.87(e). The following suggestions are aimed at assisting you in preparing labeling that satisfies the requirements of 21 CFR Part 801.10

We recommend that you provide clear and concise instructions for use that delineate the technological features of the specific device and how to use the device on patients. Instructions should provide device specific educational material for local institutional training programs designed to familiarize medical personnel and lay users with the features of the device and how to use the device in a safe and effective manner.

We recommend instructions for use be evaluated by representative users to determine if critical aspects of pump use and maintenance are clearly and completely communicated. The results should be part of your submission.

**Directions for Use**

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Although final labeling is not required for 510(k) clearance, final labeling must comply with the requirements of 21 CFR Part 801 before a medical device is introduced into interstate commerce. In addition, final labeling for prescription medical devices must comply with 21 CFR 801.109. Labeling recommendations in this guidance are consistent with the requirements of Part 801.
As a prescription device, under 21 CFR 801.109, the device is exempt from having adequate directions for lay use. Labeling must, however, include adequate information for practitioner use of the device, including indications, effects, routes, methods, frequency and duration of administration, and any relevant hazards, contraindications, side effects and precautions, as described in 21 CFR 801.109(d).

Labeling in compliance with the requirements in 21 CFR 801.109 will generally include:

- The prescription statement required under 801.109(b)(1).
- Indications for use, including use environment.
- The intended route(s) of administration for infusion as indicated in the statement of intended use.
- Cleaning and disinfection instructions for reusable infusion pumps and accessories. If the pump is used in the home, please identify cleaning and disinfection agents available to the general public that are suitable for device reuse (cleaning and disinfection).
- Alarm limits and ranges.
- Default settings.
- A complete representation of the user interface including detailed depiction of screens and data fields and how they will be used to accomplish all clinical applications and possible configurations of the pump.
- An identification of any dedicated administration set or the specifications and/or specific models of infusion sets that are appropriate for use with this pump.
- Reservoir volume, flow rates and profiles, flow rate accuracy, residual volume, and the operational conditions (e.g., temperature, pressure, fluid viscosity, electromagnetic interference) under which these are valid.
- A detailed description of start-up error and the effects on flow rate accuracy.
- A description of any effects on accuracy that will occur due to changes in infusion rate or bolus delivery, such as when titrating medications.
- A description of the fluid(s) to be administered by the pump as indicated in the statement of intended use found in the labeling of the device, with a listing of contraindication of fluids (e.g., blood products, enteral feedings and lipids, cytotoxic drugs) that are not compatible with the infusion pump.
- Comprehensive directions for preparation and use for all functions of the device.
- Description of all warning and alarm features and recommended actions should an alarm occur.
• For infusion pumps containing a reservoir contacting the fluid being infused, include information regarding the stability and compatibility of those fluids with your device. All recommendations regarding the fluids should be consistent with the manner in which FDA has approved those products. An example of the labeling statement is described below:

Example The following [fluid(s)] have been tested by [pump manufacturer name] and found to be safe for use in the [pump name]:

Fluid A
Fluid B
Fluid C

Before using different [fluid(s)] with this pump, check the [fluid(s)] label to make sure it can be used with the pump.

• Warning statements on your device regarding the safety of use during diagnostic procedures, such as magnetic resonance imaging (MRI), x-ray, computed tomography (CT), or ultrasound.

• Labeling should include all recommended information related to EMC, including reference to the appropriate standard, such as IEC 60601-1-2.

• For devices with RF wireless technology capabilities, the labeling should include information about the exact RF wireless technology incorporated or able to be used with your device. The information should contain specifics about the technology (e.g., IEEE 802.11 b), the frequency of operation and range, quality of service required for the claimed functions, data integrity, recommended security measures for the RF wireless technology (e.g. WPA2), coexistence and any limitations (e.g. distance between RF devices, EMC limitations).

**Home Use Labeling**

We recommend all infusion pump labeling specify the environment in which the pump is intended to be used. Infusion pumps that are intended for use in the home setting should also include instructions for use suitable for the lay user, who is to receive the device from or on the order of a health care provider and use the device under the supervision of a licensed practitioner.\(^{11}\) These instructions for use should contain the information recommended above. Home care pumps should have your toll free phone number for customer support on the device in the event the device labeling is misplaced or lost.

If home use is not identified in the labeling of your infusion pump but we determine that your infusion pump is reasonably likely to be used in the home and could cause harm when

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\(^{11}\) As described elsewhere in this section, these infusion pumps are prescription devices under 21 CFR 801.109. See footnote 1 for a discussion of lay users.
used in the home, we may require a statement in the labeling that provides appropriate
information regarding use of the device in the home. Section 513(i)(1)(E)(i).

11. Postmarket Surveillance of Infusion Pumps

Manufacturer Reporting Requirements

The Medical Device Reporting (MDR) regulation (21 CFR Part 803) requires a manufacturer
of a medical device to submit reports to the FDA whenever they become aware of information
that reasonably suggests that a device they market may have caused or contributed to a
reportable death or serious injury, or has malfunctioned and the malfunction would be likely
to cause or contribute to a reportable death or serious injury should it recur.

The MDR regulation also includes reporting and record keeping requirements for medical
device user facilities (e.g., hospitals, nursing homes) and importers of medical devices, as well
as adverse event record keeping requirements for medical device distributors.

Manufacturers (21 CFR Part 803.3), including foreign manufacturers, of medical devices are
required to:

- Submit MDR reportable events involving their medical devices as described in 21 CFR
  Parts 803.10(c) and 803.50;
- Submit 5-day reports as described in 21 CFR Part 803.53;
- Submit supplemental reports as described in 21 CFR Part 803.56;
- Develop, maintain, and implement written procedures for the identification and
evaluation of all medical device events to determine whether the event is MDR
reportable as described in 21 CFR Part 803.17;
- Conduct an investigation of each event and evaluate the cause of the event as described
  in 21 CFR Part 803.50(b)(3), and
- Establish and maintain complete files for all complaints concerning adverse medical
device events as described in 21 CFR Part 803.18.

The MDR report (FDA Form 3500A) must contain all the information described in 21 CFR
Part 803.52 that is reasonably known to the manufacturer (21 CFR 803.50(b)). Information
reasonably known includes any information that:

- Can be obtained by contacting a user facility, importer, or other initial reporter;
- Is in the possession of the manufacturer; or
- Can be obtained by analysis, testing, or other evaluation of the device.

The FDA Form 3500A, instructions for completing specific items on the form, and the coding
manual can be found at:

### Common Infusion Pump Reportability Questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
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<tbody>
<tr>
<td>Do I need to submit an MDR report for malfunctions that result in delay of drug therapy?</td>
<td>If the information reasonably suggests that your device may have caused or contributed to a death or serious injury or has malfunctioned and would be likely to cause or contribute to a death or serious injury if it were to recur, then this is considered a reportable event.</td>
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<tr>
<td>We have a fail safe feature in our infusion pumps. Since we have this feature in our pumps when there is a device malfunction, would I have to submit an MDR report?</td>
<td>The fact that you have a fail safe feature does not eliminate your obligation to review the information you have received and assess this information for MDR reportability.</td>
</tr>
<tr>
<td>How much effort should a firm take to obtain additional information and/or the device?</td>
<td>MDR files must contain an explanation of why any information required by the MDR regulation was not submitted or could not be obtained. The results of the evaluation of each event must be documented and maintained in your MDR event file. There is no specified number of attempts a manufacturer must make to obtain information. However, you do need to demonstrate a reasonable or “good faith” effort.</td>
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<tr>
<td>How much detail do I need to use to describe the event?</td>
<td>You are encouraged to provide all information known about the event, including how the device was involved, nature of the problem, required patient treatment, patient outcome or final condition, and any environmental conditions that may have influenced the event.</td>
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**Attached**

Appendix A: “Risks to Health” Chart

### APPENDIX A: RISKS TO HEALTH

<table>
<thead>
<tr>
<th>Risks to health</th>
<th>Mitigation</th>
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<tbody>
<tr>
<td>Overdose</td>
<td>Section 6A. Assurance Case Report: Operational Hazards</td>
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<tr>
<td></td>
<td>Section 6B. Assurance Case Report: Environmental Hazards</td>
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<td></td>
<td>Section 6C. Assurance Case Report: Electrical Hazards</td>
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<td>Section 6D. Assurance Case Report: Hardware Hazards</td>
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<td>Section 6E. Assurance Case Report: Software Hazards</td>
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<td></td>
<td>Section 6F. Assurance Case Report: Mechanical Hazards</td>
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<tr>
<td></td>
<td>Section 6G. Assurance Case Report: Biological and Chemical Hazards</td>
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<tr>
<td>Incorrect therapy (the user either receives the wrong drug, or the correct drug with a wrong dosage or infusion rate)</td>
<td>Section 6A. Assurance Case Report: Operational Hazards</td>
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<tr>
<td>Air embolism</td>
<td>Section 6A. Assurance Case Report: Operational Hazards</td>
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<tr>
<td>Allergic response</td>
<td>Section 6A. Assurance Case Report: Operational Hazards</td>
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<td>Section 6A. Assurance Case Report: Operational Hazards</td>
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<tr>
<td>Exsanguination</td>
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<td>Section 6G. Assurance Case Report: Biological and Chemical Hazards</td>
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<tr>
<td>Section 7. Clinical Evaluation</td>
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<tr>
<td>Section 8. Risk Management Report</td>
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<td>Section 10. Labeling</td>
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