DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

August 24, 2016

Firm name
Address

LABELING CHANGE REQUEST

Dear X,

The Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) previously requested information from your firm to evaluate a postmarket safety issue associated with the use of syringe infusion pumps cleared under 21 CFR 880.5725 and product code FRN. The safety concern is related to serious clinical consequences from lack of flow continuity resulting in delay of therapy, over-infusion or under-infusion, while infusing at low rates (e.g., less than 5 mL per hour, and especially flow rates less than 0.5 mL per hour). The FDA has determined that lack of flow continuity while infusing at low rates may extend to all programmable syringe pumps capable of delivering at low infusion rates. Serious adverse events have been reported relating to hemodynamic instability, loss of sedation, and increased pain indicators in critically ill neonatal patients. These issues were brought to our attention through Medical Device Reports (MDRs), discussions with clinicians and engineers, and published information[1].

As discussed below, FDA is requesting that additional information be included in the health care practitioner labeling documents to clarify the instructions for use of these devices, and reduce the likelihood and/or the severity of these potentially serious adverse events. Therefore, CDRH requests manufacturers who currently market programmable syringe pumps that are capable of

1 Several published articles were reviewed including, but not limited to:

ECRI Institute. Syringe Pumps- Delay in Drug Delivery May Occur at Low Flow Rates, Putting Patients at Risk. *Medical Device Hazard Report* 2015 October 6.

Peterfreund RA, Philip JH. Critical parameters in drug delivery by intravenous infusion. *Expert Opin Drug Deliv*. 2013; 10(8): 1095-1108.

Sherwin CMT, Medlicott NJ, Reith DM, Broadbent RS, Intravenous drug delivery in neonates: lessons learnt. *Archives of Disease in Childhood,* 2014; 99(6): 590–594.

Van der Eijk AC, van Rens R, Dankelman J, Smit BJ, A literature review on flow-rate variability in neonatal IV therapy. *Pediatric Anesthesia*, 2013; 23(1): 9-21.

delivering at low flow rates review their most recent health care practitioner instructions for use and training materials, and consider including the following information if one or more items are not already addressed and are determined to be applicable:

Syringe Size and Selection

- Warning: Ensure syringe sizes and models are compatible with the syringe pump (refer to page X for more information). Use of incompatible syringes can cause improper pump operation resulting in inaccurate fluid delivery, insufficient occlusion (blockage) sensing, and other potential problems.

- Warning: Use the smallest compatible syringe size necessary to deliver the fluid or medication; this is especially important when infusing high risk or life-sustaining medications at low infusion rates (e.g., less than 5 mL per hour, and especially flow rates less than 0.5 mL per hour). Using a larger syringe when infusing at low rates can lead to inadequate syringe pump performance including delivery inaccuracies, delay of therapy, and delayed generation of occlusion alarms. This is due to the increased friction and compliance of the syringe plunger tip with larger syringes.

Use of Accessory Devices

- Precaution: Use compatible components which have the smallest internal volume or "deadspace" to minimize residual volumes between the syringe and the patient when administering medications or fluids at low infusion rates (e.g., less than 5mL per hour, and especially flow rates less than 0.5 mL per hour). This reduces the amount of time it takes for fluid to reach the patient, maintains delivery accuracy, and reduces occlusion detection times. For example:
    - **Tubing internal diameter**: Small bore or microbore tubing is recommended when infusing at low rates
    - **Tubing length**: Tubing length should be minimized, when possible
    - **Filters**: Internal volume (deadspace) of in-line filters should be minimized
    - **Connection sites**: The number of connection sites such as stopcocks and Y-sites should be limited, and high risk or life-sustaining solutions should be connected as close to the intravenous access site as possible.

- Precaution: Avoid use of manifolds with ports containing high pressure valves. High pressure valves require additional pressure (e.g., 50-200 mmHg) to open and allow fluid flow. These high pressure valves may cause a significant delay in therapy followed by a sudden bolus once the valve is opened, particularly at low infusion rates (e.g., less than 5mL per hour, and especially flow rates less than 0.5 mL per hour).

Starting an Infusion or Changing a Syringe

- Precaution: Manually prime the syringe and tubing to remove all air, before connecting to the pump.

- Warning: **Electronically prime the syringe pump system before starting an infusion or after replacing a near-empty syringe with a replacement syringe.**
    - Verify the fluid flow to the patient is OFF, and if available, use the prime (or purge) function on the syringe pump to remove any mechanical slack in the system.
    - Using the syringe pump's prime (or purge) feature engages the mechanical components of the pump and decreases the syringe's friction and compliance (i.e., stiffness) to minimize startup delays and delivery inaccuracies, especially at low infusion rates.
    - Failure to use the prime (or purge) feature on the syringe pump after every syringe change and/or tubing change can significantly delay the infusion delivery startup time and lead to delivery inaccuracies.

- Warning: During programming and prior to starting an infusion, verify that the syringe size and model on the syringe pump's display screen matches the syringe size and model loaded onto the syringe pump.

Height and Location of Syringe Pump System

- Warning: Ideally, the syringe pump should be level with distal tip of the catheter (e.g., the site of fluid delivery; if accessing a central line the syringe pump should be at the level of the patient's heart). If the pump height is raised relative to the distal tip of the catheter (e.g., during patient transport), the increase in height of the syringe pump can result in a temporary increase in fluid delivery or bolus until the flow rate stabilizes. Alternatively, if the pump is lowered relative to the distal tip of the catheter, the decrease in height of the syringe pump may result in a decrease in delivery or under-infusion until the flow rate stabilizes.

- Precaution: If using multiple syringe pumps and it is not clinically feasible to have all pumps level with the distal tip of the catheter (or the site of fluid delivery), place the high risk or life-sustaining medications as close to level with the distal tip of the catheter as possible. When infusing multiple high risk or life-sustaining medications, consider placing the ones infusing at the lowest rates as close to the level with the distal tip of the catheter as possible.

- Precaution: Minimize the height difference between the pump and the patient and avoid changes in the height of the pump (e.g., during transport of critically ill patients) to prevent unintended fluctuations in the flow rate.

Occlusion Considerations

- Warning: To minimize the amount of time it takes the pump to recognize an occlusion (blockage) and generate an alarm while infusing at low rates (e.g., less than 5mL per hour, and especially flow rates less than 0.5 mL per hour):
    - Consider the plunger force or occlusion pressure threshold setting and adjust it, as necessary. The lower the plunger force setting or occlusion pressure threshold setting, the shorter the occlusion detection time. However, when infusing viscous or thick fluids (e.g., lipids), the plunger force or occlusion pressure threshold setting may need to be adjusted to reduce false alarms. Please refer to page X for further detail.
    - Use the smallest compatible syringe size necessary to deliver the fluid or medication. This minimizes the amount of friction and compliance (i.e., stiffness) of the syringe plunger tip. Because syringe pumps infuse fluids by precisely controlling the plunger, smaller syringes provide more precise fluid delivery than larger syringes.
    - Use the prime (or purge) feature on the pump when changing a syringe and/or tubing.
    - Use accessory devices, which have the smallest internal volume or deadspace (e.g., use microbore tubing when infusing at low rates, shorter length of tubing, etc.). See page X for further detail.

- Warning: When addressing or clearing an occlusion:
    - **Ensure the fluid flow to the patient is OFF** to prevent administering an unintended bolus. An occlusion may pressurize the infusion tubing and syringe, which can result in an unintended bolus of drug when the occlusion is cleared. In order to prevent this additional bolus, disconnect the tubing, or relieve the excess pressure through a stopcock, if present. The health care professional should weigh the relative risks of disconnection with the risks of an unintended bolus of drug.
    - Be aware that using larger size syringes on a high plunger force setting may produce a larger post occlusion bolus due to excessive syringe plunger tip compliance.

Please refer to FDA's guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device", which provides guidance to 510(k) holders on deciding when to submit a 510(k) for a change to an existing device. For the labeling changes requested above, we do not believe that a new 510(k) is necessary; however, appropriate internal documentation of your decision-making process and the basis for that conclusion should be documented. Although it is not specifically recommended in the guidance, should you believe submission of a new 510(k) is not necessary, please update your existing 510(k) with your revised labeling by submitting an amendment in paper copy and eCopy formats referencing the original 510(k) number to the Document Control Center at the following address:

U.S. Food and Drug Administration

Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Please note. If you choose to modify your labeling to address this issue but plan to deviate from the suggested language above, we are providing you the opportunity to receive FDA feedback on your language prior to your implementation and submission of a new 510(k), or amendment to your existing 510(k). Please contact Kathleen White at Kathleen.White@fda.hhs.gov and CDRHSignalManagement@fda.hhs.gov if you choose to pursue this option.

Please acknowledge receipt of this email within 3 business days by replying to Kathleen.White@fda.hhs.gov and CDRHSignalManagement@fda.hhs.gov. In addition, within 45 days of receipt of this request, please inform us (via the same email addresses) of your plans to address the requested labeling changes, your timeframe for implementing the changes, and your plans for informing users of the changes. As noted above, any new 510(k) submission or amendment to the existing 510(k) must be submitted to the document control center at CDRH in both paper copy and electronic copy (eCopy) format. For more information on eCopies, please see FDA's guidance, "eCopy Program for Medical Device Submissions."

If you have questions about this request, please contact Kathleen White at Kathleen.White@fda.hhs.gov and CDRHSignalManagement@fda.hhs.gov or by telephone at 301-796-5832.

Sincerely,

Aron Yustein, M.D.
Deputy Director and Chief Medical Officer
Office of Surveillance and Biometrics
Center for Devices and Radiological Health