Volume 1 Issue 2

mi industry news

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Hot Topics

United States Pharmacopeia (USP) Changes

1. An update to Chapter 841 (Specific Gravity) was published in the March/ April 2012 Pharmacopeial Forum 38(2) which states that the use of mass for preparation of solutions is allowed, provided the density is known. This change supports gravimetric addition of the diluent without a need to revalidate the method. The revision is scheduled to be posted USP 36-NF 31 Supplement 1 in early 2013.
2. In addition, USP is considering an update to Chapter 1251 (Weighing on an Analytical Balance).

Why did FDA change their Guideline on Process Validation?

The revision to process validation guideline is based on the FDA's experience since on the topic of Process Validation. The FDA has discovered that drugs with lower quality had been marketed while they had been manufactured under "validated" processes. This led to product recalls and complaints because of inadequate process understanding and process control. This revision is a Life Cycle Approach which is rational and scientific and could help to improve to control quality.

The guidelines are broken down into three main areas:

- Stage 1 is process design, particularly the concept of building in product quality from the outset.
- Stage 2 is process qualification, to make sure it is capable of "reproducible commercial manufacture".
- Stage 3 is continued process verification, in other words assurance that the process remains in a state of control.

Recalls

Biologics

Firm initiated a voluntary recall of biologic product due to a failed periodic stability test for the molecular size distribution test.

Medical Device

1. The button on a device which was used for continuous and intermittent delivery of medicines (such as local anesthetics or narcotics) to or around surgical wound sites and/or to nearby nerves for pre-operative, during a procedure or surgery (perioperative), and for post-operative regional anesthetic and pain management was faulty. Due to this fault, the patient could receive continuous infusion at a rate greater than expected.

2. Firm initiated a voluntary recall of a compounding device because of incorrect key press responses, caused by fluid entry into device keypads, and intermittent electrical failures. Fluids, such as water, cleaning solutions, and nutrition source solutions, may enter into the keypad of the device's control module and may cause it to generate an incorrect device response to an Automix operator's key press. The incorrect key response failure and the intermittent electrical failures could lead to improperly mixed solutions. For critical components large variations in dosing may occur due to this fault.

3. Firm received reports of customers experiencing motor stalls during infusion with the specific pump model. Most of the motor stalls reported have occurred at high infusion rates (typically over 900 ml/hr). However, the firm could not rule out the possibility of motor stall occurrence at lower infusion rates. When a motor stall occurs, the device displays the visual error code with an audible alarm that is followed by a termination of infusion. Termination of infusion, especially in high risk patients, could be detrimental.

There were two additional infusion pump recalls in August 2012.

System errors caused another firm's infusion pump to go into an alarm condition and stop running, which can result in a delay or an interruption of patient therapy.

Infusion pump was voluntarily recalled because a component on the PC unit power supply board could not be programmed and this may cause a delay in patient therapy.

Warning Letters

Laboratory Testing

Firm had not thoroughly investigated the failure of a batch or any of its components to meet its specifications whether or not the batch has already been distributed [21 CFR 211.192].

Product failures were attributed to errors at the contract laboratory. However, the investigation conducted by the contract laboratory facility concluded that there was no laboratory error. Nevertheless, as part of corrective actions, company ceased using the contract laboratory and started conducting sterility testing in house. Product failures continued with in-house sterility testing. The failures were attributed to inadequate aseptic techniques during sterility testing. The causes after investigations were:

1. Potential lack of sterility of the component used to liquefy the sample.

2. The use of cap in order to puncture each ointment tube to obtain product for testing.

3. Microbial contamination from the water in the water bath used to warm the sample prior to the sterility testing. Water bath was not tested as a possible source of microbial contamination

Clean room validation

1. Clean room particle validation contained obsolete plans for test locations in clean rooms.

2. The validation testing was conducted using a validation plan that was not yet approved.

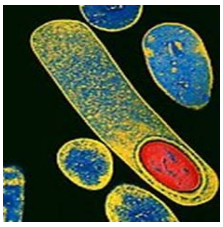
3. Clean room validation plan did not contain any plan for the test locations in clean rooms.

4. The validation testing was conducted using an old clean room validation plan that did not contain the updated test locations for the rooms being validated.

Warning Letters (Continued)

Media Fill

A Bacillus species was identified in the samples incubated for the media fill. The failure was attributed to inadequate aseptic technique by an operator based on the video recording of the media fill operation. However, the Bacillus species identified was an environmental organism that could have been introduced into the aseptic area via multiple sources (e.g., design of the aseptic core, material flow, etc.). The company failed to consider other sources of contamination and considered inadequate disinfection and aseptic training as the possible sources of contamination.



Lessons learned: Appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile were not established .Since the same company had media fill failures and sterility test failures, a holistic approach towards microbial contamination was warranted, including comprehensive evaluation of sterile drug operations; including but not limited to a thorough review of material flow, personnel practices, production supervision, operational procedures, quality assurance oversight, training program, room design, equipment suitability, the environmental monitoring program, systems used to investigate contamination events and the clean area classification.

Process Validation

Firm lacked a documented validation plan or procedure for process validation.

As a response to the observation the firm proposed providing a written procedure for retrospective process validation and a validation plan for the device however it did not include any specific plan or evidence addressing global systemic corrective actions for retrospectively validating all of the process.

Vendor Audits

Failure to establish and maintain adequate requirements, including quality requirements, that must be met by suppliers, contractors, and consultants, as required by 21 CFR 820.50(a). The firm did not follow its own procedures for vendor audits; whereby suppliers were not evaluated or included in the firm's approved list of suppliers.

Design Changes

Failure to establish and maintain adequate procedures for the identification, documentation, validation or, where appropriate, verification, review, and approval of design changes before their implementation, as required by 21 CFR 820.30(i).

- Product Design procedure did not include adequate requirements for the identification, documentation, validation/verification, review, and approval of design changes before their implementation.
- Firm lacked change control documents for the implemented design change of the device.
- Product Life Form for design changes lacked an approval signature and date of approval of this change.
- Design changes lacked design review and verification.

Control, Storage and Distribution

Failure to establish and maintain adequate procedures for the control of storage areas and stock rooms for product to prevent mix-ups, damage, deterioration, contamination, or other adverse effects pending use or distribution and to ensure that no obsolete, rejected, or deteriorated product was used or distributed, as required by 21 CFR 820.150(a).

White papers coming soon

Warning Letters (Continued)

Medical Device Product Complaints

Failure to establish and maintain adequate procedures for receiving, reviewing, and evaluating complaints by a formally designated unit, as required by 21 CFR 820.198(a).

The firm's complaint procedure, did not adequately define a complaint or the process of handling complaints as required.

The corrective action in response to the complaint related observations did not indicate that it would investigate prior complaints to see if they were reportable as MDR events. The firm also did not indicate that it would review all other complaints to see if any should have been reported as MDR events.

The reason for not investigating a complaint was stated as device not being returned to the manufacturer.

Failure to maintain adequate records of the investigation by the formally designated unit as identified in 21 CFR 820.198(a) when an investigation is made, as required by 21 CFR 820.198(e). The firm's procedure did not require that complaint investigations include:

- Evaluation to determine whether the complaint represents an event that is required to be reported to FDA (MDR reportable)
- Evaluation of all complaints to determine whether an investigation is necessary.
- Any complaint involving the possible failure of a device, labeling, or packaging to meet any of its specifications.
- Complaint process deficiencies:

1. The date that the complaint was received;
2. The name, address, and phone number of the complainant;
3. Any reply to the complainant; and
4. Uniform and timely complaint processing.

Upcoming Webinars, Seminars & Workshops

Upcoming Webinars

Disinfection & Cleaning Validation for Reusable Medical Devices

September 26th, 2012

1:30 to 3:30 EST

Cleaning Validation-Common Errors

October 16th, 2012

1:30 to 3:30 EST

Common Microbiology and Cell Culture Laboratory Errors

October 26th, 2012

1:30 to 3:30 EST

Pharmacopoeial Antimicrobial Effectiveness Testing

October 30th, 2012

1:30 to 3:30 EST

Rapid Microbiological Methods-Applications and Regulatory Consideration

November 7th, 2012

1:30 to 3:30 EST

USP Sterility Test and Growth Promotion

December 6th, 2012

1:30 to 3:30 EST

Upcoming Workshops

Advanced Course In Fungal Identification Hands-On Training

St. Joseph, MO

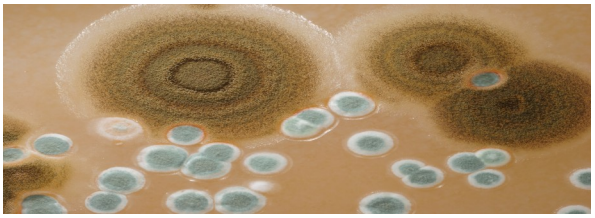
November 7th, 8th &9th, 2012

Cleaning Validation Swab Recovery Studies and Analysis

St. Joseph, MO

October 18th & 19th, 2012

Featured Courses



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