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Joint Committee on GMP for Over-the-Counter Drugs

May 1, 2024

Proposed revision to NSF/ANSI 455-4 – *Good Manufacturing Practices for Over-the-Counter Drugs* (455-4i49r1)

Revision 1 of NSF/ANSI 455-4, issue 49 is being forwarded to the Joint Committee for consideration. Please review the proposal and **submit your ballot by May 22, 2024** via the NSF Online Workspace.

Please review all ballot materials. When adding comments, please include the section number applicable to your comment and add all comments under one comment number whenever possible. If you need additional space, please use the attached blank comment template in the reference documents and upload online via the browse function.

Purpose

The proposed revision will combine and clarify requirements within the standard for ICH 10.

Background

Multiple requirements exist for ICH10 that seem redundant. This issue paper will attempt to clarify or combine requirements to ease the auditing process.

4.2.1 – management commitment; adding all requirements of management.
4.2.2 – management review – removed, already in 4.7.2.
4.2.3 – quality policy moved to 4.2.1 and quality objectives in 4.3.1; removed (it is not a responsibility of management to create quality objectives.

From ICH Q10:
(a) Senior management has the ultimate responsibility to ensure an effective pharmaceutical quality system is in place to achieve the quality objectives, and that roles, responsibilities, and authorities are defined, communicated, and implemented throughout the company.
(a) Senior management should ensure the quality objectives to implement the quality policy are defined and communicated.

Previous 4.2.4 – quality manual; add reference and inclusion of management responsibilities.
Previous 4.2.5 – communication; combine with 4.2.10.

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4.2.10 – communication; remove, combined with 4.2.5.
4.3.2 – managing product life cycle; removed and combined with 4.5.1 – validation.
4.4.1 – add CFR 111 requirement.
4.5.1 – validation; combined with 4.3.2 product life cycle.
4.7.2 – management review; duplicative of 4.2.2, combined reference.

Sec. 211.25 Personnel qualifications.
(c) There shall be an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of each drug product.

If you have any questions about the technical content of the ballot, you may contact me in care of:

Angela Diesch
Chair, Joint Committee on GMP for Over-the-Counter Drugs
c/o Rachel Brooker, Joint Committee Secretariat
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[Note – the recommended changes to the standard which include the current text of the relevant section(s) indicate deletions by use of ~~strikeout~~ and additions by grey highlighting. Rationale Statements are in *italics* and only used to add clarity; these statements will NOT be in the finished publication.]

NSF/ANSI Standard
for GMP for Over-the-Counter Drugs –

Good Manufacturing Practices for Over-the-Counter Drugs

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4 Audit requirements

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4.2 Leadership

4.2.1 ~~Management participates in the design, implementation, monitoring, and maintenance of the company quality system. [ICH Q10]~~ Management responsibilities are defined and include participating in the design, implementation, monitoring, and maintenance of the company quality system, establishing quality policy, committing of resources, advocating continual improvement, conducting management reviews, ensuring communication process exists and other activities to ensure an effective quality system is in place. [ICH Q10 2.1]

~~4.2.2~~ ~~Management reviews shall include, but not be limited to quality system, process performance and product quality; which are to be conducted periodically. The management reviews will be documented. [ICH Q10, 3.2.4]~~

~~4.2.3~~ ~~Management has established a quality policy and quality objectives. [ICH Q10, 2.2]~~

4.2.2 **~~4.2.4~~** The organization shall ~~prepare~~ have a quality manual describing the quality management system, the quality policy, and the organization's commitment to quality management system requirements, management responsibilities and quality risk management. [ICH Q10, 1.8, 2.2]

4.2.3 **~~4.2.5~~** ~~Internal communications assure the flow of appropriate information throughout the organization~~
~~regarding this standard and applicable regulatory requirements. Senior management is notified in the event of critical quality issues. [ICH Q10, 2.5]~~ Appropriate communication processes are documented and implemented within the organization to ensure compliance information flows to every level of the organization, quality issues (GMP deficiencies, regulatory inspections, product defects, etc.) flow to responsible management and critical quality issues (regulatory citations, recalls, etc.) escalate to senior management. [21 C.F.R. § 211.180 & ICH Q10, 2.5]

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~~**4.2.10** Procedures exist for notifying responsible management in a timely manner of regulatory inspections, serious GMP deficiencies, product defects, and related actions. [21 C.F.R. § 211.180 & ICH Q10]~~

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4.3 Planning

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~~**4.3.2** A process for managing the life cycle of products (development, technology transfer, commercial production, product discontinuation) is defined and implemented. [ICH Q10, 3.1]~~

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4.4 Support

4.4.1 Adequate resources (human, financial, materials, facilities, and equipment) are provided to implement, maintain, and improve the quality system. [ICH Q10, 2.4, 21 CFR § 211.25(c)]

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4.5 Operations

4.5.1 Manufacturing processes have been validated utilizing a product lifecycle approach (design, qualification, commercialization and verification, product discontinuation) to produce a product that consistently meets specifications. [21 C.F.R. § 211.100, 21 C.F.R. § 211.110, 21 C.F.R. § 211.111, ICH Q10 3.1 & U.S. FDA Process Validation Guidelines]

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4.7 Improvement

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4.7.2 Periodic management reviews of the quality system~~,~~ and process performance & product quality shall be ~~are~~ conducted~~, with documented~~. Management reviews shall be documented including completion of any identified follow-up actions. [ICH Q10, 2.6, 3.2.4]

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