TO: Joint Committee on GMP for Over-the-counter drugs

FROM: Angela Diesch, Chair of the Joint Committee

DATE: February 2, 2024

SUBJECT: Proposed revision to NSF/ANSI 455-4 – *Good Manufacturing Practices for Over-the-counter drugs* (455-4i44r1)

Revision 1 of NSF/ANSI 455-4, issue 44 is being forwarded to the Joint Committee for consideration. Please review the proposal and **submit your ballot by February 23, 2024** via the NSF Online Workspace <https://standards.nsf.org/home>.

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 update the standard to align with CFR 211 and ICH Q7.

Background

Sec. 211.46 Ventilation, air filtration, air heating and cooling.

(a) Adequate ventilation shall be provided.
(b) Equipment for adequate control over air pressure, micro-organisms, dust, humidity, and temperature shall be provided when appropriate for the manufacture, processing, packing, or holding of a drug product.
(c) Air filtration systems, including prefilters and particulate matter air filters, shall be used when appropriate on air supplies to production areas. If air is recirculated to production areas, measures shall be taken to control recirculation of dust from production. In areas where air contamination occurs during production, there shall be adequate exhaust systems or other systems adequate to control contaminants.
(d) Air-handling systems for the manufacture, processing, and packing of penicillin shall be completely separate from those for other drug products for human use.

From Guidance for Industry Non-Penicillin Beta-Lactam Drugs: A CGMP Framework for Preventing Cross-Contamination

> *Although FDA has not issued CGMP regulations specific to APIs, the Agency has provided guidance to API manufacturers in the guidance for industry, ICH4 Q7, Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (ICH Q7 guidance). Because some APIs are sensitizing compounds that may cause anaphylactic shock, preventing cross contamination in APIs is as important as preventing cross-contamination in finished products. The ICH Q7 guidance recommends using dedicated production areas, which can include facilities, air handling equipment and processing equipment, in the production of highly sensitizing materials, such as penicillins and cephalosporins.*

Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients Guidance for Industry

D. Containment (4.4)
Dedicated production areas, which can include facilities, air handling equipment and/or process equipment, should be employed in the production of highly sensitizing materials, such as penicillins or cephalosporins. (4.40)

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

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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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4.4 Support

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4.4.32 Adequate ventilation, air filtration and airflow ~~is~~ are provided in all areas of the facility. [21 C.F.R. § ~~211.42~~ 211.46 ICH Q7 4.2, 4.4]

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