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 455-4ARG - *Audit Requirement Guidelines for Good Manufacturing Practices for Over-the-counter drugs* (455-4ARGi9r1)

Revision 1 of NSF 455-4ARG, issue 9 are 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 <www.standards.nsf.org>.

Please note that this is an ARG ballot only. ARG guidelines are denoted in italics and only the italic language is open for comments. While this ballot may include some suggested changes to the standard this ballot is NOT on those changes. They are only included so that you can see how those suggested changes impact the ARG. If you have any comments on the included standard changes you MUST make those comments on that issue paper's ballot. The link to the ballot is included in the comments in the ballot. Any comments on the suggested standard changes shown in this ballot will be considered nongermane and will not be addressed.

When adding comments, please use the comment template provided in the reference documents and upload it online via the browse function.

Purpose

The proposed revision will update ARG to include details from CFR211 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

789 N. Dixboro Road, Ann Arbor, Michigan 48105-9723 USA
T +1 734 769 8010 | F +1 734 769 0109 | www.nsf.org

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:

Angela Diesch
Chair, Joint Committee on GMP for Over-the-counter drugs
c/o Rachel Brooker
Joint Committee Secretariat
Tel: (734) 827-6866
Email: rbrooker@nsf.org

[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.]

*****This is an ARG ballot only. ARG guidelines are denoted in *italics* and only the italic language is open for comments. While this ballot may include some suggested changes to the standard, this ballot is NOT on those changes. They are only included so that you can see how those suggested changes impact the ARG. If you have any comments on the included standard changes you MUST make those comments on that issue paper's ballot. The link to the ballot is included in the comments below. Any comments on the suggested standard changes shown in this ballot will be considered nongermane and will not be addressed.*****

NSF/ANSI Standard
for GMP for Over-the-counter drugs –

Good Manufacturing Practices for Over-the-counter drugs

•
•
•

4 Audit requirements

•
•
•

4.4 Support

•
•
•

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]

*****The suggested change above is NOT part of this ballot.*****

4.4.32.1 *HVAC systems shall provide controlled air to production, storage and testing areas. HVAC system design and installation shall be specific to the products produced and prevent cross contamination.*
4.4.32.2 *Excessive powder buildup from powdered products shall be minimized by air extraction.*
4.4.32.3 *Powder collection fines and or vacuum fines shall not be recycled unless validated as acceptable for the manufacture of product.*
4.4.32.4 *Dust collection systems shall be part of cleaning schedule. Dust hoods or hoses directly above or adjacent to product shall be maintained clean at all times and not provide a source of cross contamination.*
4.4.32.5 *Engineering diagrams of all GMP HVAC systems shall be maintained and under change control.*
4.4.32.6 *HVAC qualification and validation studies have been completed, maintenance procedures in place, and changes to the HVAC systems with GMP impact are under change control.*

4.4.32.7 *Air filtration systems, including prefilters and particulate matter air filters are used when appropriate on air supplies to production areas. [21 CFR 211.46 (c)]*
4.4.32.8 *Equipment for adequate control over air pressure, micro-organisms and dust is provided when appropriate for the manufacture, processing, packing, or holding of a drug product. [21 CFR 211.46 (b)]*
4.4.32.9 *Air-handling systems for the manufacture, processing, and packing of highly sensitizing materials (that may cause anaphylactic shock) such as penicillin should be completely separate from those for other products.*

-
-
-