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Joint Committee on GMP for Dietary Supplements

April 18, 2024

Proposed revision to NSF/ANSI 455-2ARG – *Audit Requirement Guidelines for Good Manufacturing Practices for Dietary Supplements* (455-2ARGi41r1)

Revision 1 of NSF/ANSI 455-2ARG, issue 41 is being forwarded to the Joint Committee for consideration. Please review the proposal and **submit your ballot by May 9, 2024** via the NSF Online Workspace.

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 the language for laboratory requirements for clarity and update the corresponding ARGs.

Background

4.6.13.1 Updated the language by combining with 4.6.16.2
4.6.14 ARG changes:
- Updated language for clarity,
- Moved items to other requirements where they are more appropriate,
- Removed duplicate item already covered in another requirement (e.g. 4.6.14.12 covered in 4.6.8).
- Added definition for scientifically valid method. The standard requires test methods used to be 'scientifically valid' however, it is not defined. To provide guidance, the definition from the American Council of Independent Laboratories (ACIL) is added to the ARG.

4.6.15.8 Rephrased the language to be concise and clearer on intent.
4.6.15.11 Moved from 4.6.16.3

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4.6.16 Updated the language by combining with related 4.6.17 requirement and align with referenced regulation. Updated reference 21 CFR 111.315 to include all items (a,b,c,d,e).
4.6.16.1 Editorial change
4.6.16.2 & 3 Moved to 4.6.13.1 and 4.6.15.11, respectively where they are more appropriate. To keep the numbering, replaced with items moved from 4.6.17.2 and 4.6.14.7
4.6.17 Removed and combined with 4.6.16
4.6.17.1 Removed as it is duplicate of 4.6.8.2
4.6.17.2 Moved to 4.6.16 where it is more appropriate.

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

Freddie Agyin

Chair, Joint Committee on GMP for Dietary Supplements
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.]

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NSF/ANSI Standard
for GMP for Dietary Supplements –

Good Manufacturing Practices for Dietary Supplements

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4 Audit requirements

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4.6 Performance evaluation

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4.6.13 QC laboratory operations and procedures shall be established. [21 C.F.R. § 111.303]

4.6.13.1 *Procedures should be established and being followed for laboratory operations, including sample receipt and handling, tracking, storage, preparation, maintaining sample integrity, results reporting, reference standard programs, and laboratory OOS result investigations.*

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4.6.14 Test methods and examinations used to determine whether specifications are met shall be scientifically valid, and verified as appropriate for their intended use. Test methods and examinations shall include at least one of the following: [21 C.F.R. § 111.75 (h) & 21 C.F.R. 111.320]
— gross organoleptic analysis;
— macroscopic analysis;
— microscopic analysis;
— chemical analysis; or
— another scientifically valid method.

~~4.6.14.1~~ *~~If applicable, in-house analytical test procedures should be scientifically valid and fit for purpose.~~*

4.6.14.1 *A test method is considered scientifically valid if one of the following criteria are met[1]:*

- *The test procedure is a published compendial method from AOAC, USP, or other standard setting organization. These methods should be used within the published scope of method applicability and should be documented in a company Standard Operating Procedure (SOP).*
- *The test method is a fully validated method. This validation should follow published guidelines from AOAC, USP, or other standard setting organization, and the validation study should be documented.*
- *The test method is validated using an "in-house" validation procedure. The validation procedure should be documented in a company Standard Operating Procedure (SOP) and the results of the validation should be documented.*
- *The test method is demonstrated to be scientifically valid and fit for purpose using an in-house protocol. This protocol should be documented in a company SOP and contain the following:*
  - ** Demonstration of method precision*
  - **Demonstration of method accuracy*
  - **Demonstration of the method specificity*
  - **Document range applicable concentrations*
  - **Document matrices used in method performance verification*
- *If the test method in use does not meet the criteria listed above, there should be adequate justification and documentation to explain the reasons.*

[1] American Council of Independent Laboratories, 1300 I Street, NW, Suite 400E, Washington, DC 20005 https://www.acil.org/, https://www.acil.org/resource/resmgr/ess_material/ACIL_Best_Practices_Guideboo.pdf

4.6.14.2 *Method transfer protocols, with pre-determined acceptance criteria, should be defined and followed whenever a test method is to be used that was developed and validated at a different laboratory.*

4.6.14.3 *Compendial methods should be verified with pre-determined acceptance criteria to show that the methods are competently executed and suitable for use. Documentation of verification should be available and suitable.*

4.6.14.4 *Procedures should define the acceptable criteria for determining non-compendial methods are scientifically valid, ~~e.g., precision, accuracy, repeatability, etc.~~ Guidance can be found within authoritative sources such as USP, ICH or AOAC criteria for method validation.*

4.6.14.5 *Methods should reference the source and lot numbers of reference standards and reagents used. Expiration dates should be indicated.*

4.6.14.6 *~~Methods based on accepted standards (i.e., USP, AOAC, BAM) are recommended.~~ Method references should be provided. Methods published by accepted standard setting bodies (i.e., USP, AOAC, BAM) are recommended.*

~~4.6.14.7~~ *~~Personnel conducting testing and examinations should document at the time of performance the laboratory methods that were used. All test results should be documented.~~*

4.6.14.8 *~~Microbiological specifications should be established as needed; and sampling plans and~~ Suitable ~~t~~Test procedures employed ~~to~~ should ensure that the desired microbiological specifications of the dietary ingredients and other components are met; including the absence of objectionable organisms~~.~~*

~~***4.6.14.9** Skip-lot testing program should have adequate historical data and documented justification available.~~

***4.6.14.10** Positive and negative controls should be in place when conducting microbiological testing.*

~~***4.6.14.11** Products or ingredients that test positive for microbiological contamination (pathogens) should not be reprocessed or released.~~

~~***4.6.14.12** All finished product should be tested per regulations in 21 C.F.R. § 111.75 to assure it meets identity, purity, strength, and composition specs. (e.g., label claim).~~

***4.6.14.13** Methods should be an accurate representation of the ~~actual test~~ testing performed.*

4.6.15 Laboratory facilities used shall be adequate for testing of components, in-process materials, and dietary supplements. [21 C.F.R. § 111.310]

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~~***4.6.15.8** In full operation, there should be adequate personnel to ensure that interruption of critical steps, within testing methods, does not occur in order to accommodate other testing that may be run in parallel.~~ *In full operation, there should be adequate personnel to ensure that testing is not negatively impacted by concurrent volume of testing.*

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***4.6.15.11** Areas for storing reference standards, supplies, and reagents should be adequately controlled and segregated. In some cases, humidity, temperature, light, or other environmental factors may require control.*

4.6.16 Laboratory controls shall be established and ~~have been~~ approved by QC, including use of sampling plans, criteria for establishing specifications, testing methods or examinations, and standard reference materials, and use of test methods and examinations in accordance with established criteria. [21 C.F.R. § 111.315 ~~(a)~~]

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

Commented [ER1]: This suggested change is 455-2i59r1. To vote or comment on this suggested change proceed to the 455-2i59r1 ballot at: https://standards.nsf.org/higherlogic/ws/groups/db501a6e-2381-412f-a5c0-018976f9bc62/ballots/ballot?id=8979

***4.6.16.1** Test procedures and methods should be up to date and should have been reviewed and approved by ~~quality~~ Quality.*

~~***4.6.16.2** Quality should establish processes and procedures for laboratory sample receipt, tracking, storage, sample preparation, sampling plans, as well as maintaining sample integrity.~~

~~***4.6.16.3** Areas for storing reference standards, supplies, and reagents should be adequately controlled and segregated. In some cases, humidity, temperature, light, or other environmental factors may need to be controlled.~~

***4.6.16.2** Sampling plans for obtaining representative samples should be approved by Quality, including any modifications.*

4.6.16.3 *Personnel conducting testing and examinations should document at the time of performance the laboratory methods that were used. All test results should be documented.*

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~~**4.6.17** Parameters shall be set for laboratory controls for sampling plans, criteria for examination and testing methods, and standard reference materials. [21 C.F.R. § 111.315 (b, c, d, e)]~~

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

Commented [ER2]: This suggested change is 455-2i59r1. To vote or comment on this suggested change proceed to the 455-2i59r1 ballot at: https://standards.nsf.org/higherlogic/ws/groups/db501a6e-2381-412f-a5c0-018976f9bc62/ballots/ballot?id=8979

~~***4.6.17.1*** *Finished product assays should be carried out using the marketed form of the final product.*~~

~~***4.6.17.2*** *Sampling plans should be approved by Quality, including any modifications.*~~

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