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Approval Sign-Off Sheet

1. Purpose

This document is intended for regulatory authorities and auditing organizations participating in or utilizing the results of the Medical Device Single Audit Program (MDSAP). It provides guidelines for the use of the document GHTF/SG3/N19:2012: *Quality management system - Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange* for grading nonconformities resulting from MDSAP audits.

2. Scope

The “major” and “minor” classification of nonconformities commonly used in medical device audit and certification schemes does not provide enough detail for global information exchange. However, the terms “major” and “minor” nonconformity are defined in ISO 17021-1:2015 clauses 3.12 and 3.13 and are often utilized in medical device certification programs, including those for regulatory purposes, to assign a priority to the implementation of corrective actions. While the terms “major” and “minor” are not the subject of this document, general correlation between “major” and “minor” nonconformities as defined in ISO 17021-1:2015 and the grading system defined in this document is discussed in section 5.2. The intent of this grading system for regulatory purposes is to support the exchange of information about nonconformities from audit findings that go beyond the binary concept of “major” and “minor” to a 5 level grading system of nonconformities.

The regulatory authorities can determine how the audit information provided in the Regulatory Audit Information Exchange Form will be utilized within their jurisdiction. Regulatory authorities may also choose to consider other data sources in addition to the outcome of the regulatory audits such as product evaluations, recalls, vigilance reports, etc. for regulatory oversight.

3. Definitions/Acronyms

AO: Auditing Organization

RA: Regulatory Authority

4. Authorities/Responsibilities

Auditing Organizations: responsible for oversight of audits that are conducted in accordance with MDSAP, including ensuring adherence to this procedure and all other relevant MDSAP policies and procedures.

Regulatory Authorities: responsible for evaluation of the graded nonconformities and MDSAP audit reports per their legislation.

5. Policy

5.0 General

The following sections introduce a standardized nonconformity grading system for regulatory purposes. To enable consistent grading, guidance has been provided on how to write a nonconformity.

Nonconformities identified during an MDSAP audit must be recorded on the Nonconformity Grading and Exchange (NGE) form (MDSAP AU F0019.2)

5.1 Writing Nonconformities

Regulatory audits conducted under the MDSAP should be performed in accordance with MDSAP AU documents and other applicable regulatory references. The output of those audits may include nonconformities.

In order for the significance of nonconformities to be characterized utilizing the nonconformity grading system described in this document, it is essential that the most specific requirement is correctly identified and used. Nonconformities are to be clearly worded with factual and precise language that enables the reader to comprehend the actual nonfulfillment that was detected during the audit. A nonconformity must assist the manufacturer to identify its cause. The

information presented should be an accurate representation of the reviewed records, samples and procedures, as well as interviews conducted.

The nonconformity should:

a) identify the specific requirements which have not been met:
- use the words of ISO 13485:2016 or of the applicable regulatory requirement
- document the source of the requirement (e.g. medical device regulations, other applicable standards, procedures or requirements established by the organization, etc.)

If several requirements may apply:
- choose the one which will result in the highest grade of nonconformity; and
- give preference to a requirement to implement over a requirement to just document.

b) be a statement of how a requirement is not being fulfilled and written using complete sentences in a clear, concise manner:
- be related to a requirement, not just be a restatement of the audit evidence, or be used in lieu of audit evidence
- be significant and relate to an observed or potential problem with the facility, equipment, processes, controls, products, employee practices, or records. “Potential problems” should have a reasonable likelihood of occurring based upon observed conditions or events.
- contain a statement regarding the product(s) related to the nonconformity using trade name(s) and generic name(s)
- be factual and avoid opinionated or subjective terms

c) be supported by objective evidence:
- the evidence must be directly related to the requirement
- be traceable so it should identify what (source procedure, record, interview, or visual observation), who (using job titles), when and where (location).
- justify the extent of evidence (e.g. number of records) - what exactly was found or not found, with an example(s)

Multiple instances (examples) of non-fulfillment of a requirement should be combined into a single nonconformity unless the instances originate or relate to different aspects of a clause.

5.2 Grading of Nonconformities

5.2.1 Step 1 Grading – Indirect or Direct QMS Impact

For the purpose of stratification in the grading system, the clauses of the standard are divided into two categories:

- ***Indirect QMS Impact:*** ISO 13485:2016 clauses 4.1 through 6.3 (with the exception of 4.2.3 – Medical device file, which is considered to have Direct QMS impact) are seen as “enablers” (making it possible or feasible) for the QMS processes to operate. These clauses are therefore considered to have indirect influence on medical device safety and performance and are generally analogous to “minor” nonconformities as defined in ISO 17021-1:2015 clause 3.13.

- ***Direct QMS impact:*** ISO 13485:2016 clauses 6.4 through 8.5 (with the exception of 8.2.4 – Internal audits, which is considered to have indirect QMS impact) are seen as having direct influence on design, and manufacturing controls. These clauses are therefore considered to have direct influence on medical device safety and performance and are more likely to be analogous to “major” nonconformities as defined in ISO 17021-1:2015 clause 3.12 when there is a significant doubt that effective process control is in place, or that products or services will meet specified requirements.

Clauses with Indirect QMS impact are graded at this step with a “1”.

Clauses with Direct QMS impact are graded at this step with a “3”.

There are two basic principles that the auditors should follow when writing the statement of nonconformity and assigning a clause number for purposes of utilizing this grading system.

- When an audit observation or audit evidence indicates that more than one applicable requirement has not been fulfilled, the nonconformity must be written against the specific requirement in ISO 13485:2016 found in clauses 4.2.3, 6.4 through 8.5, (if applicable), when the nonconformity does, or has the potential to, affect safety or performance; because it has direct QMS impact.

In general, nonconformities that have the potential to affect safety or performance are comparable to a "major" nonconformity per ISO 17021-1:2015 clause 3.12. These types of nonconformities would require the Auditing Organization to review, accept and verify the correction and corrective actions prior to granting a certification decision in accordance with ISO 17021-1:2015 clause 9.5.2(b).

- When an audit observation or audit evidence indicates that a requirement of the manufacturer's quality manual, procedures or requirements, or is not specifically required in ISO 13485:2016, or does not impact safety or performance, then the nonconformity should be assigned to clauses 4.1 through 6.3 (except 4.2.3, which is considered to have direct QMS impact), and 8.2.4; because it has indirect QMS impact.

Nonconformities can often be written up against more than one clause. Therefore, it is the auditor's obligation to determine the impact of the nonconformity on the QMS and assign the appropriate clause. The QMS impact of the nonconformity will determine whether the resulting clause will be Direct or Indirect. Some examples to help illustrate the grading process for direct versus indirect impact are provided below.

Example 1: Nonconformity where safety issues raise the grading to Direct Impact: A manufacturer distributes a product in Australia, Canada and the US. The manufacturer has a documented procedure for notification of adverse events that meets the criteria of Canada and the US, but has no references or requirements for adverse event reporting in Australia. The medical device caused an adverse event within Canada and the manufacturer followed their procedures related to adverse event reporting. The manufacturer reported the event to Health Canada and the US FDA, but did not consider reporting it to Australia. This nonconformity should therefore be assigned to clause 8.2.3 – Reporting to regulatory authorities and not to 4.2.5 Documentation Requirements.

Example 2: Nonconformity where safety is not an issue that is against a self-imposed requirement in a procedure leads to a starting grade with an Indirect Impact: A manufacturer's procedure for a process revalidation of an injection molding process requires annual revalidation regardless of changes or process deviations. The annual revalidation was not performed; however, there were no changes or process deviations noted. In this example, ISO 13485:2016 clause 7.5.6 does not require annual revalidation. There were no process changes or deviations and there does not appear to be a safety issue. This nonconformity should be assigned to clause 4.2.5 - Documentation

Requirements for the manufacturer not following their own procedure and not against clause 7.5.6 – Validation of processes for production and service provision.

Nonconformity where safety is an issue, that is against a self-imposed requirement based on a standard leads to a starting grade of a Direct Impact: A manufacturer is utilizing standard ISO 11137-1 for validating their radiation sterilization process and the standard requires quarterly dose audits. This was not performed as required by the standard. In this example, there is a safety issue since the standard requires quarterly dose audits to assure product sterility. Therefore, this nonconformity should be assigned to clause 7.5.7 – Particular requirements for validation of processes for sterilization and sterile barrier systems

Nonconformity to illustrate a Repeat Occurrence: An initial nonconformity was found in 7.5.6 relating to a nonconformity in a coating process validation. A subsequent audit found a nonconformity in 7.5.6 in an injection molding process validation. Both nonconformities fall within 7.5.6 - Validation of Processes for Product and Service Provision. Therefore, the subsequent occurrence should be categorized as a Repeat Occurrence to the X.X.X level of the appropriate clause.

NOTE: If the scenarios are altered within the examples it must be recognized that the conclusions may change.

5.2.2 Step 2 Grading – Escalation Rules

The resultant grading from Step 1 is carried forward to Step 2, which is a rules-based escalation process to address areas of higher risk that have a potential to affect product safety and performance. Under this grading system the Step 1 grade is increased by 1 for each rule:

The MDSAP form developed to record nonconformities (MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form) presents the grading as the result of 4 independent criteria:

- Impact on the QMS (direct: 3 or indirect: 1)
- Repeat nonconformity (yes: 1 or no: 0)
- Combination of the absence of a documented process or procedure and failure to implement (yes: 1 or no: 0)
- Release of nonconforming devices (yes: 1 or no: 0)

1. *Impact on the QMS*

See section 4.2.1 - Step 1 Grading – Indirect or Direct QMS Impact of this document.

2. *Repeat nonconformity*

This category is for a nonconformity that has been identified during any audits within the previous 3 years. Such a nonconformity poses an increased risk because it is an indicator that a corrective action has not been adequately taken or implemented.

The “two previous QMS audits which evaluated the same sub-clause” was selected because:

- in order to assess the risk of repeat occurrence accurately, it is important to assess comparable nonconformities;
- historical data beyond the two previous QMS audits may not represent the current state; and
- review of more audit reports may be counterproductive for an efficient grading system. However, it is important to ensure that the audits reviewed for the Occurrence assessment, have at a minimum evaluated the same sub-clause.

Occurrence in this document is directed at the frequency of a nonconformity cited from one audit to the next performed by the same auditing organization. It is not the occurrences of examples within a given sample size that the auditor may take to determine if a nonconformity exists during an audit.

Auditors should refrain from issuing a new (repeat) nonconformity for a similar finding that was observed at a previous audit if the device organization is implementing the timetabled actions that had been proposed by the device organization, and accepted by the AO. If an auditor can demonstrate that previously proposed actions are not effective, considering new occurrences of the nonconformities, then a nonconformity may be issued for an ineffective corrective action system.

Note: see also MDSAP AU P0019 on how to handle nonconformities previously recognized by the device organization and under process of remediation.

3. *Combination of the absence of a documented process or procedure and the failure to implement a requirement*

The absence of a documented process or procedure will fundamentally affect consistency and effective implementation of any process. The use of this escalation criteria should be limited to situations where there is a combined failure to document **and** implement a requirement.

Documenting a process or procedure aims at ensuring the consistent and effective implementation of the corresponding activities. However, failing to document a procedure or process does not systematically lead to noncompliant implementations of that activity, and conversely, documenting a procedure or process does not always ensures it will be implemented accordingly. However, where an organization fails to 1) document a procedure or process that ISO 13485:2016 or an applicable regulatory requirement require to be documented and 2) implement the corresponding activities in ways that comply with these same requirements, then the grading of the nonconformity shall be escalated.

This escalation rule applies even in case where the process is generally documented but entirely fails to address the requirements from a jurisdiction entirely and there is evidence that the implementation of the process failed to meet the requirements of that jurisdiction.

This escalation rule may be invoked in cases where the documented procedure entirely fails to address the topic, or only addresses an applicable regulatory requirement by referencing the regulation. However, it would not be invoked when a procedure addresses the topic but incompletely or lacking details.

4. *Release of a Nonconforming Medical Device*

A nonconformity which resulted in the release of a nonconforming medical device to the market is direct evidence of a QMS failure. This escalation criteria is grading the QMS nonconformity at a higher risk, because nonconforming product is on the market and outside the control of the manufacturer's QMS.

This type of direct evidence of QMS failure and release of nonconforming products to the market is analogous to a "major" nonconformity per ISO 17021-1:2015 clause 3.12 and would require that the Auditing Organization review, accept and verify the correction and corrective actions prior to granting a

certification decision in accordance with ISO 17021-1:2015 clause 9.5.2(b)..

If a nonconforming medical device is released under concession with adequate technical and scientific justification, then the nonconformity has been resolved. It is no longer considered a nonconforming product and the escalation rule will not be applied.

5.3 Applying the Nonconformity Grading System

While it is possible to have the sum of the steps in grading equal a “6” if the nonconformity is a direct QMS impact and all the escalation rules apply, the final grade for a nonconformity under this grading scheme will be a number between 1 and 5. A “5” will be the highest grade.

The grade assigned to each nonconformity should not be changed as a result of any correction(s) or corrective action(s) taken by the manufacturer, but may be amended as a result of the auditing organization’s documented appeals process (ISO 17021-1:2015, clause 9.7). After the auditing organization has completed the audit process, the final MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form should be provided to the manufacturer. The intent is also that the grading and the NGE form be a method to accurately capture the assessment of the audit and to provide uniformity and consistency within the process of grading nonconformities.

5.4 MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form

The MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form is used for information exchange between auditing organizations and regulatory authorities, as well as between regulatory authorities.

Form MDSAP AU F0019.2 can strictly be used as a tool to exchange information with the Regulatory Authorities about the nonconformities issued and their status at the time of the submission. In such case the response of the Audited Facility’s organization to the nonconformity is not recorded in the form. The Auditing Organization using this option needs to record the back and forth with the Audited Facility’s organization using their own tools. Otherwise, the form can also be used to also record the Audited Facility’s response to the nonconformity.

Nonconformity Reports and NGE forms should be actively updated until the effectiveness of the corrections and corrective actions proposed by the audited facility or organization has been verified.

Upon request from an MDSAP Regulatory Authority, the Auditing Organization is expected to provide updated nonconformity reports within 10 calendar days. It is not necessary for Nonconformity reports to be closed at the time they are shared with the Regulatory Authorities.

Form MDSAP AU F0019.2 purposely does not provide a cumulative grade for the overall audit. How the Form is utilized is the decision of each regulatory authority for their appropriate assessment based on their own needs or requirements.

MDSAP AU G0019.4 - Guidelines NC Grading Exchange Form explains the features of Form MDSAP AU F0019.2 - MDSAP Nonconformity Grading and Exchange Form and clarifies how the form is used.

6. Forms

MDSAP AU F0019.2 – Nonconformity Grading and Exchange (NGE) form

7. Reference Documents

GHTF/SG3/Nl9:2012: Quality management system - Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange

MDSAP AU P0019 - Medical Device Regulatory Audit Reports Policy

MDSAP AU G0019.4 - Guidelines NC Grading Exchange Form

MDSAP AU P0027 - Post Audit Activities and Timeline Policy

8. Document History

VERSION NO.	VERSION DATE	DESCRIPTION OF CHANGE	AUTHOR NAME/PROJECT MANAGER
001	2021-09-01	Initial Release	Kimberly Lewandowski-Walker, US FDA

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