Medical Device Single Audit Program:

Nonconformity Grading System for Regulatory Purposes and Information Exchange

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Introduction

- Intended for regulatory authorities and auditing organizations
- Can be utilized for internal or other quality audits
- Standardized nonconformity grading system
  - 5 level system expanding beyond ‘Major’ and ‘Minor’
- Global Harmonization Task Force (GHTF) – “GHTF/SG3/N19:2013 – Quality Management System – Medical Devices – Nonconformity Grading System for Regulatory Purposes and Information Exchange”

Document Link:
https://www.fda.gov/downloads/MedicalDevices/InternationalPrograms/MDSAPPilot/UCM468937.pdf

N19 Definitions

- **Manufacturer**
  - Any natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s). (GHTF SG1/N55:2009)
- **Nonconformity**
  - Non fulfillment of a requirement. (ISO 9000:2005, 3.6.2)
- **Quality management system (QMS)**
  - Management system to direct and control an organization with regard to quality. (ISO 9000:2005, 3.2.3)

N19 Writing Nonconformities

- It is essential that nonconformities are clearly worded with factual and precise language that enables the reader to comprehend the actual non-fulfillment that was detected during the audit. The nonconformity should[1]:

a) Be a statement of nonconformity written in a clear, concise manner:

- Self-explanatory and related to the issue
- Not just be a restatement of the audit evidence, or be used in lieu of audit evidence

b) Be supported by objective evidence:

- Justify the extent of evidence (e.g. number of records)
- What exactly was found or not found, with an example(s)
- Identify the location or basis (source document) for the evidence (e.g. in a record, procedure, interview, or visual observation)

N19 Writing Nonconformities

c) Identify the specific requirements which have not been met:

- Use the words of the ISO 13485 standard
- Document the source of the requirement (e.g. medical device regulations, other applicable standards, procedures or requirements established by the organization, etc.)

[1] ISO & IAF 9001 Auditing Practices Group Guidance on:

Documenting a Nonconformity (5 June 2009)
www.iso.org/tc176/ISO9001AuditingPracticesGroup

N19 Sample Nonconformity Statements

	Nonconformity Statements		
NC #	**Poorly worded**	**Improved wording**	**ISO 13485:2003 Clause**
1	There was no evidence of training to the medical devices directive	The manufacturer did not follow their own training procedure (#14) requiring training on the medical devices directive (93/42/EEC) for internal auditors.	4.2.1
2	Document control was inadequate because of multiple occurrences of obsolete documents being utilized	The following obsolete documents were found to be in use: Obsolete version of procedure XYZ found to be in use in the calibration department Obsolete version of ABC in receiving area was found to be in use Obsolete version of design review procedure PQR was found to be in use in design department	4.2.3
3	The scheduled internal audit must be conducted and the report provided for review.	There was an absence of a documented procedure for conducting internal audits	8.2.2

N19 Grading Nonconformities: Overview

Two-step approach

- Step 1 – Provides an initial grade
- Step 2 – Additional rules applied for final grade

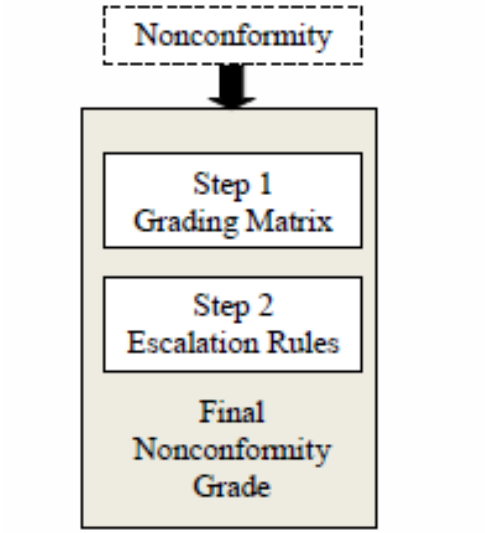


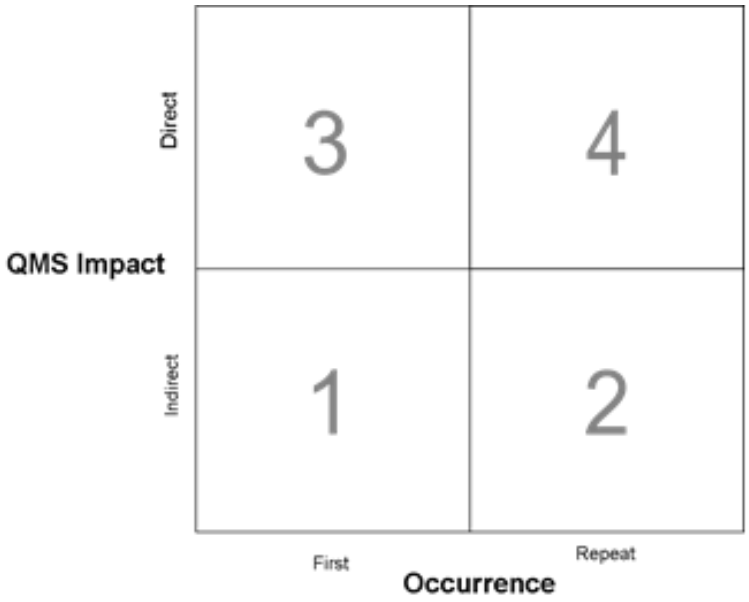
Figure 1: Grading Overview

N19 Grading Matrix: Y-axis

QMS Impact:

- **Indirect Impact:** ISO 13485:2003 clauses 4.1 through 6.3, are seen as “enablers” (making it possible or feasible) for the QMS processes to operate

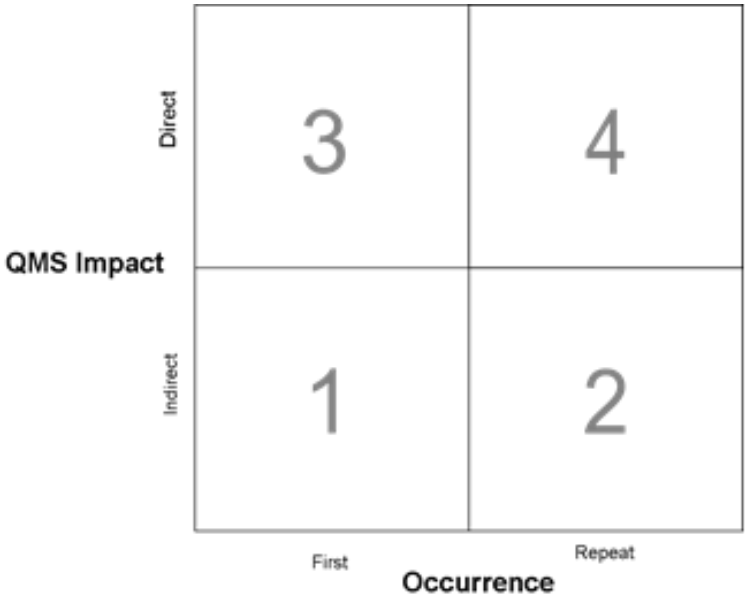
- **Direct Impact:** ISO 13485:2003 clauses 6.4 through 8.5, are seen as having direct influence on design, and manufacturing controls



N19 Grading Matrix: X-axis

Occurrence:

- **First:** Addresses a nonconformity in a particular sub-clause (X.X.X) of ISO 13485:2003 identified for the first time. Defined as not observed in the two previous QMS audits which evaluated the same sub-clause
- **Repeat:** A nonconformity that has been identified within either of two previous QMS audits which evaluated the same sub-clause (X.X.X). Poses an increased risk because it is an indicator that a corrective action has not been adequately taken or implemented



N19 Grading Example

Nonconformity where safety issues raise the grading to Direct Impact:

A manufacturer distributes a product in the European Union, Canada and the US. The manufacturer has a documented procedure for notification of adverse events that meets the criteria of the European regulations, but has no references or requirements for adverse event reporting in the other jurisdictions. The medical device caused an adverse event and the manufacturer followed its procedures related to adverse event reporting. The manufacturer reported the event to the appropriate European Competent Authority and did not consider reporting it to the other jurisdictions. This nonconformity should therefore be assigned to clause 8.5 – Improvement and not to 4.2 Documentation Requirements.

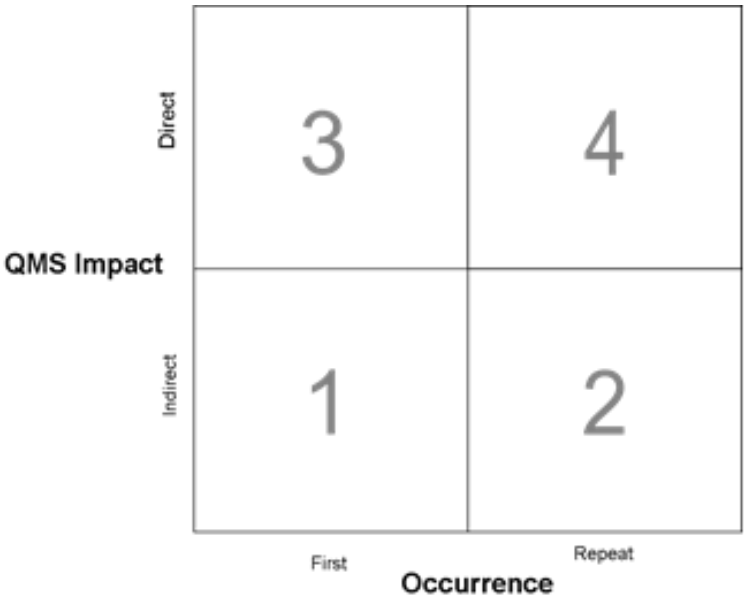
N19 Escalation Rules

The Step 1 grade is increased by 1 for each of the following rules:

- Absence of a documented process or procedure
  - The word “absent” or “absence” should be obviously written within the nonconformity for consistent grading
- Release of Nonconforming Medical Device
  - Results in release of nonconforming device to the market
  - Note: if a nonconforming device is release under concession with adequate technical and scientific justification the nonconformity is resolved and the escalation rule will not be applied

N19 Grading Matrix: Step 1

1. Identify direct impact (score of 3) or indirect impact (score of 1)
2. Evaluate previous two audit reports, check if an identified nonconformity in current audit was previously raised
3. If nonconformity was previously raised, increase grade by 1. Note, it does not have to be identical, just cited to the same QMS sub-clause



N19 Grading Matrix: Step 2

4. Apply Escalation Rules

   - Absence of a documented process or procedure, increase the grade by 1

   - Release of a nonconforming device outside of the controls of the manufacturer's QMS, increase the grade by 1

The final grade will be between 1 and 6. However, the grade of "5" was determined to be the maximum because it represents significant risk that requires intervention. The difference between "5" and "6" was considered nominal, therefore a grade of "6" will be documented as "5"

Nonconformity Grading: Example 1

Step 1						Step 2			
NC #	Description of NC	ISO 13485 Clause	Occurrence	Step 1 Grade	Explanation of Step 1 Grade	Absence of documents	Released Device	Final Grade	Explanation of Final Grade
1	An off-the-shelf software application used to convert and display analytical information for management review purposes has not been validated in accordance with procedure AUP0021. **This is the first occurrence of this nonconformity**	4.1.6	1st	1	Initial grade of 1: Related to an ISO clause before 6.3 and no evidence of prior occurrence	No	No	1	Final grade of 1: No escalation applied. Documented procedures were not absent and there is no evidence of impact against a released product

Nonconformity Grading: Example 2

Step 1						Step 2			
NC #	Description of NC	ISO 13485 Clause	Occurrence	Step 1 Grade	Explanation of Step 1 Grade	Absence of documents	Released Device	Final Grade	Explanation of Final Grade
2	Several cans of epoxy glue in the cold storage room, had expired four months ago. Procedures do not adequately describe storage and expiration management of adhesive used in product assembly. **Further observation confirmed that batch numbers (x, y and z) containing this expired glue is on the market.** This is the first occurrence of this nonconformity.	7.5.11	1st	3	Initial grade of 3: Finding is related to a clause between 6.4 and 8.5. No evidence of this nonconformity in previous audits	No	Yes (+1)	4	Final grade of 4: Escalation rules applied because there was evidence to suggest that released product had been affected. However, there was a documented procedure despite it being inadequate.

N19 Regulatory Audit Information Exchange Form

The form consists of 3 sections:

1. List of Nonconformities – should be identical to those provided in the audit report
2. Nonconformity Grading – based on the grading matrix previously discussed
3. Medical Device Country Specific Regulatory Requirements – nonconformities that are within the manufacturer's QMS but are outside the specific requirements within the clauses of ISO 13485. Note, this area is not graded

N19 Regulatory Audit Information Exchange Form

The form is intended to:

- Provide transparent and standardized way of exchanging information between regulatory authorities on audit outcomes
- Provide input into the grade for the overall audit
- Be provided in draft form to the manufacturer at the closeout meeting

N19 Use of the Regulatory Audit Information Exchange Form

- When the form is exchanged between regulatory authorities, specific audit information should be included such as:
  - Date and Scope of audit
  - Sites audited
  - Auditor's names, etc.
- The Nonconformity Grading section of the Form is intended to capture the grade of nonconformities against ISO 13485

N19 Use of the Regulatory Audit Information Exchange Form

The intent of the Medical Device Country Specific Regulatory Requirements section is to capture additional issues outside the specific requirements of ISO 13485. This section is not graded but the nonconformities are listed by regulatory jurisdictions. Certain regulatory jurisdictions may require that nonconformities against country specific regulatory requirements are written against a specific clause in the standard in the Nonconformity Grading section.

N19 Sample Regulatory Audit Information Exchange Form

List of Nonconformities		Nonconformity Grading					Medical Device Country Specific Regulatory Requirements					
NC#	Nonconformity	ISO 13485 :2003 Clause	Step 1 Grade	Absence	Medical Device	Grade	EU	CAN	USA	AUS	JPN	OTHER
1	There is an absence of a Quality Policy in the organi-zation.	5.3	1	+1		2						
2	Documented procedures for identifying training needs are not established.								21 CFR 820.25		Ord 169 (Article 23 subpart 2)	
3	The injection molding pro-cess has not been validated, as per procedure DOC12345 but has not resulted in non-conforming product being released to the market.	7.5.2	3			3	MDD (93/42/ EEC) (Annex II)					
4	The WIDGET™ device was sold in Canada without a medical device license. Pro-cedure DOC12345 requires that all medical devices class II, III & IV are licensed prior to sale in Canada, according to section 26 of the CMDR. This type of NC was also cited in last year's audit.	4.1	2			2		CMDR section 26				

Grading vs. Defining Nonconformities

Audits are likely to be ‘integrated’, inclusive of both ISO 13485 and regulatory requirements.

ISO 17021-1:2011, 9.1.9.6.3 (note) and 9.1.15 “define” nonconformities as:

- Major: failure to fulfil one or more requirements of the management system standard, or

  a situation that raises significant doubt about the ability of the client's management system to achieve its intended outputs

- Minor: all other nonconformities

Grading vs. Defining Nonconformities

Can’t exactly equate the MDSAP grading with the terms minor and major

AOs previously equated Grades 1, 2, and 3 with “minor” and Grades 4 and 5 with “major”

Changes to the Nonconformity Grading and Exchange Form (NGE) in Fall 2016 have now allowed for the separation of nonconformity identification between certification schemes

MDSAP Audit Results: The Good

If the MDSAP audit results in

- no nonconformities or
- grade 1, 2, or 3 nonconformities

the audit team will likely recommend certification.

Note: a remediation plan (including for each nonconformity: the outcome of the investigation of the nonconformity and its cause(s); the planned correction; and the planned corrective action) is required for all nonconformities. Audit teams only "recommend" certification while the Final Reviewer(s) make the ultimate decision.

MDSAP Audit Results: The Bad

If the MDSAP audit results in

- *numerous 1, 2, or 3 nonconformities or
- up to two grade 4 nonconformities,

the audit team will recommend certification, pending the submission and acceptance of evidence of implementation of the remediation actions.

*At the discretion of the audit team

MDSAP Audit Results: The Ugly

If the MDSAP audit results in

- one or more grade 5 nonconformities,

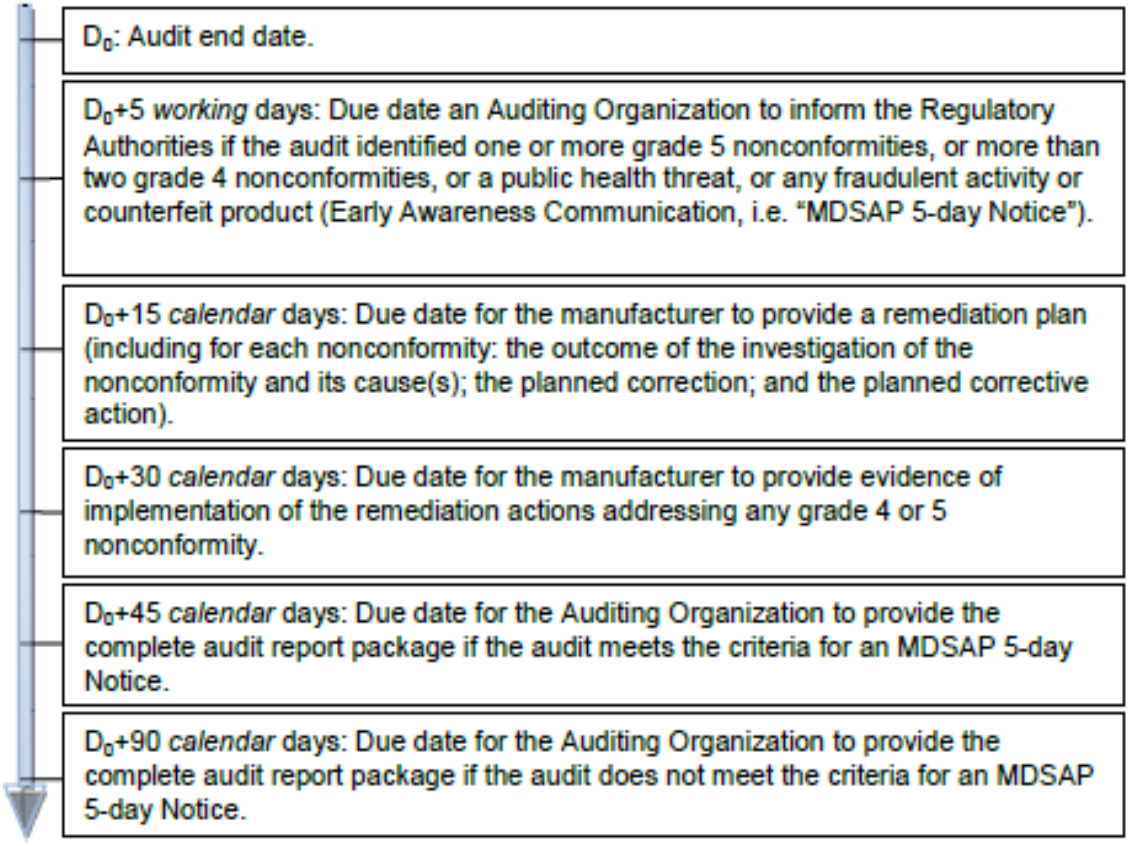
- more than two grade 4 nonconformities, or

- if there is evidence of a threat to public health threat, fraudulent activity, or counterfeit product.

the audit team will not recommend certification -> triggers a Early Awareness Communication (i.e. “MDSAP 5-day Notice”) and will lead to a Special Audit (Unannounced)

MDSAP Reporting Timeline

MDSAP AU P0027.004 Post Audit Activities and Timeline Policy



Thank you

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