PROPOSED DOCUMENT

Global Harmonization Task Force

**Title:** Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange

**Authoring Group:** Study Group 3

**Date:** 18th April, 2012
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preface</td>
<td>................................................................................................................................. 3</td>
<td></td>
</tr>
<tr>
<td>Introduction</td>
<td>................................................................................................................................. 3</td>
<td></td>
</tr>
<tr>
<td>1.0 Scope</td>
<td>................................................................................................................................. 3</td>
<td></td>
</tr>
<tr>
<td>2.0 Definitions</td>
<td>................................................................................................................................. 4</td>
<td></td>
</tr>
<tr>
<td>2.1 Audit Finding</td>
<td>................................................................................................................................. 4</td>
<td></td>
</tr>
<tr>
<td>2.2 Manufacturer</td>
<td>................................................................................................................................. 4</td>
<td></td>
</tr>
<tr>
<td>2.3 Nonconformity</td>
<td>................................................................................................................................. 4</td>
<td></td>
</tr>
<tr>
<td>2.4 Quality management system (QMS)</td>
<td>................................................................................................................................. 4</td>
<td></td>
</tr>
<tr>
<td>3.0 References</td>
<td>................................................................................................................................. 4</td>
<td></td>
</tr>
<tr>
<td>4.0 General</td>
<td>................................................................................................................................. 5</td>
<td></td>
</tr>
<tr>
<td>4.1 Regulatory Audit Information Exchange Form</td>
<td>................................................................................................................................. 5</td>
<td></td>
</tr>
<tr>
<td>4.2 Writing Nonconformities</td>
<td>................................................................................................................................. 6</td>
<td></td>
</tr>
<tr>
<td>4.3 Grading of Nonconformities</td>
<td>................................................................................................................................. 7</td>
<td></td>
</tr>
<tr>
<td>4.4 Step 1 Grading</td>
<td>................................................................................................................................. 8</td>
<td></td>
</tr>
<tr>
<td>4.5 Step 2 Grading – Escalation Rules</td>
<td>................................................................................................................................. 10</td>
<td></td>
</tr>
<tr>
<td>4.6 Applying the Nonconformity Grading System</td>
<td>................................................................................................................................. 11</td>
<td></td>
</tr>
<tr>
<td>4.7 Use of the Regulatory Audit Information Exchange Form</td>
<td>................................................................................................................................. 11</td>
<td></td>
</tr>
<tr>
<td>5.0 Appendix A: Examples of statements of nonconformities</td>
<td>................................................................................................................................. 13</td>
<td></td>
</tr>
<tr>
<td>6.0 Appendix B: Examples Illustrating use of the Nonconformity Grading System</td>
<td>................................................................................................................................. 14</td>
<td></td>
</tr>
</tbody>
</table>
Preface

This document was produced by the Global Harmonization Task Force (GHTF), a voluntary group of representatives from medical device regulatory authorities and the regulated industry. The document is intended to provide non-binding guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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Introduction

This document is intended for regulatory authorities and auditing organizations. It introduces a standardized Nonconformity Grading System for regulatory purposes with a Regulatory Audit Information Exchange Form providing consistent audit information in order to enable exchange among regulatory authorities. It is expected that the reader is proficient with the requirements of ISO 13485:2003.

Currently, the significance of a nonconformity related to a medical device manufacturer’s Quality Management System (QMS) may vary between regulatory authorities and auditing organizations. All parties will benefit through the use of a standardized and transparent grading system of QMS nonconformities to communicate the findings of a regulatory audit, building the confidence necessary for the potential mutual acceptance of the results of a regulatory audit.

This grading system provides a common risk based approach. The major and minor classification of nonconformities commonly used does not provide enough detail for global information exchange. Therefore the terms major and minor nonconformity will not be defined nor utilized in this document. The purpose of this new grading system for regulatory purposes is intended to support the exchange of audit results that go beyond the binary concept of major and minor to a level grading system of nonconformities.

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

1.0 Scope

This document provides a method to present outcomes of regulatory audits that can be used by regulatory authorities for information exchange. It introduces a Nonconformity Grading System for regulatory purposes with a Regulatory Audit Information Exchange Form providing consistent audit information.
The following are not included in the scope of this document:

- How to perform audits and prepare associated reports (see GHTF SG4 documents)
- How the Regulatory Audit Information Exchange Form will be utilized by regulatory authorities

2.0 Definitions

2.1 Audit Finding

Results of the evaluation of the collected audit evidence against audit criteria (GHTF SG4/N28 R4:2008 Part 1: General Requirements, section 6.4)

2.2 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)

2.3 Nonconformity

Non fulfillment of a requirement (3.1.2). (ISO 9000:2005, 3.6.2)

2.4 Quality management system (QMS)

Management system (3.2.2) to direct and control an organization (3.3.1) with regard to quality (3.1.1). (ISO 9000:2005, 3.2.3)

3.0 References


4.0 General

The Regulatory Audit Information Exchange Form is a tool to be used to exchange information about the results of a QMS audit of a medical device manufacturer between interested regulatory bodies. The following sections provide a format for an Exchange Form, and guidance for the wording and subsequent grading of nonconformities.

4.1 Regulatory Audit Information Exchange Form

A Regulatory Audit Information Exchange Form is introduced for the purpose of information exchange between regulators. This report consists of three parts (see Table 1):

1. List of nonconformities from the audit report - It is important to provide sufficient insight into the context and relevance of each nonconformity listed on the exchange form. The list of nonconformities provided in the exchange form should be identical to that provided in the audit report.

2. Details of the calculation of the Nonconformity Grading System - The details of how the final nonconformity grade was obtained for nonconformities specifically against ISO 13485:2003. The use of this section of the exchange form provides transparency in the calculation process.

3. Medical device country specific regulatory requirements - For nonconformities that are raised against specific country regulatory requirements outside of ISO 13485:2003, these should be identified in the third part of the exchange form, to allow regulators to have a complete view of the manufacturer’s state of compliance to local regulatory requirements, as applicable.
### Table 1 – Regulatory Audit Information Exchange Form

<table>
<thead>
<tr>
<th>NC#</th>
<th>Nonconformity</th>
<th>ISO 13485 Clause</th>
<th>Step 1 Grade</th>
<th>Absence</th>
<th>Medical Device Grade</th>
<th>EU</th>
<th>CAN</th>
<th>USA</th>
<th>AUS</th>
<th>JPN</th>
<th>OTHER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>2</td>
<td></td>
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</tr>
</tbody>
</table>

### 4.2 Writing Nonconformities

Regulatory audits should be performed in accordance with GHTF SG4 documents and 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 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 information presented must be an accurate representation of the actual records, samples, procedures or interviews that were audited and provide the auditor’s reasoning for the issuance of the nonconformity.

The nonconformity should:

1. a) be a statement of nonconformity written in a clear, concise manner
   - be self-explanatory and be related to the issue
   - not just a restatement of the audit evidence, or be used in lieu of audit evidence

2. b) be supported by objective evidence, specifically:
   - the evidence - what exactly was found or not found (give an example); justify the extent of evidence (e.g. number of records)
   - source of evidence - the location or basis for the evidence (e.g. in a record, procedure, interview, or visual observation)

3. c) identify the specific requirements which have not been met, specifically:
   - the requirement - using the words of ISO 13485:2003 to help justify the nonconformity

---

Nonconformities relating to the QMS standard (ISO 13485:2003), should be cited against a specific clause or sub-clause of the standard. Multiple instances of non-fulfillment of a requirement (see Appendix A – “NC #2”) should be combined into a single nonconformity unless the instances originate or relate to different aspects of a clause. Examples of poorly worded and better worded nonconformities are provided in Appendix A.

4.3 Grading of Nonconformities

The Nonconformity Grading System for regulatory purposes consists of a two-step approach:

- **Step 1** a Nonconformity Classification Matrix (see Figure 2) provides an initial evaluation.

- **Step 2** additional escalation rules are applied, to determine a final grade for the nonconformity.

The final grade for each nonconformity is then documented in a Regulatory Audit Information Exchange Form for potential sharing of audit information among regulators.

Figure 2: Grading System Overview
4.4 Step 1 Grading

As illustrated in Figure 2 above, the grading of nonconformities is a two step process. Step 1 involves the use of the Nonconformity Grading Matrix.

![Nonconformity Grading Matrix]

**Figure 3**: Nonconformity Grading Matrix

The Y-axis of the Nonconformity Grading Matrix is **QMS impact**. It is related to the influence of the QMS clause on medical device safety and performance. It is vitally important to highlight that all the clauses of the standard are equally required if applicable,\(^2\) to effectively establish and maintain a quality management system that will meet regulatory purposes.

For the purpose of improved stratification in the grading system\(^3\), the clauses of the standard are divided into two categories:

- **Indirect QMS Impact**: ISO 13485 sections 4.1 through 6.3, are seen as “enablers” (making it possible or feasible) for the QMS processes to operate. These sections are therefore considered to have indirect influence on medical device safety and performance.

\(^2\) See ISO 13485:2003 clause 1.2

\(^3\) Justification for approach: In order to assist the evaluation of QMS impact for this grading system, it was designed to categorize the QMS requirements contained within ISO 13485:2003 standard at a specific sub-clause level (e.g., 6 vs. 6.2 vs. 6.2.2).

The system was assessed at several different tier levels and it was determined that the QMS impact should be started at the second sub-clause (X.X) level of standard, while the Occurrence should be started at the third sub-clause (X.X.X) level and to allow the subsequent rules to be added for further refinement of the grading system.
• **Direct QMS impact:** ISO 13485 sections 6.4 through 8.5, are seen as having direct influence on design, and manufacturing controls. These sections are therefore considered to have direct influence on medical device safety and performance.

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

• When the nonconformity has the potential to affect safety or performance, the nonconformity should be written against the technical area in the standard found in 6.4 through 8.5.

• When the nonconformity is against the manufacturer’s quality manual, procedures or requirements, etc and is not specifically required in the standard and there is no safety or performance concern, then the nonconformity should be assigned to clause 4.2.1.

The X-axis of the Nonconformity Grading Matrix is **Occurrence** and is also divided into two categories:

• **First:** The first category addresses nonconformity in a particular sub-clause (X.X.X) of the standard identified for the ‘First Time.’ This represents an initial risk.

• **Repeat:** The second category is a ‘Repeat’ nonconformity within the same sub-clause (X.X.X) from the three previous QMS audits (typically this occurs in a 3 year certification cycle). A Repeat nonconformity poses an increased risk because it is an indicator that a corrective action has not been adequately taken or implemented.

Some examples to help illustrate the grading process in Step 1 are:

• **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 their procedures related to adverse event reporting. The manufacturer reported the event to the appropriate European Competent Authority and did not consider reporting to the other jurisdictions. This nonconformity should therefore be assigned to clause 8.5.1 – Improvement /General and not to 4.2.1 Documentation requirements/General.

• **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, since the ISO 13485 standard clause 7.5.2 does not require annual revalidation. There does not appear to be a safety issue, since no changes or process deviations were noted. This nonconformity should be assigned to clause 4.2.1- Documentation require-
• **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 7.5.2 – Validation of processes for product and service provision.

• **Nonconformity to illustrate a Repeat Occurrence:** An initial nonconformity was found in 7.5.2.2 relating to a nonconformity in a sterilization process validation. A subsequent audit found a nonconformity in 7.5.2.1 in an injection molding process validation. Both nonconformities fall within 7.5.2 - 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.

4.5 **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:

1. Absence of a documented process or procedure;
2. Release of a Nonconforming Medical Device

The absence of a documented process or procedure will fundamentally affect consistency and effective implementation of any process.

The word “absent” (or “absence”) should be used in the nonconformity statement when there is no documented process or procedure for the requirement. It is critical that this word be obvious within the nonconformity statement in order to consistently grade the nonconformity.

Similarly, a nonconformity which resulted in the release of a nonconforming medical device to the market is direct evidence of a QMS failure. This rule in the grading system is assessing the QMS nonconformity at a higher risk, because nonconforming product is on the market and outside the control of the manufacturer’s QMS. If a nonconforming medical device is released under concession with adequate technical and scientific justification then the nonconformity has been resolved and is no longer considered nonconforming.
4.6 Applying the Nonconformity Grading System

Step 1 – Using the Nonconformity Grading Matrix

A. Direct or Indirect Impact: When a nonconformity is written and the clause assigned, identify whether it is “direct impact” (therefore score of 3) or “indirect impact” (therefore score of 1), as defined above (see 6.1).

B. Repeat nonconformities against the same QMS sub-clause (X.X.X): The auditor should check the previous three audit reports to see if a nonconformity that is identified in the current audit was previously raised within the same QMS sub-clause (X.X.X). If the nonconformity is a repeat, the grade increases by 1.

Step 2 – Application of Escalation Rules

In this step of grading, the Nonconformity Grading Matrix is no longer used. The rules below are applied to determine the final grade of the nonconformity.

Absence: Absence of a documented process or procedure of any requirement, the grade increases by 1.

Medical Device: Release of a Nonconforming Medical Device outside of the controls of the manufacturer’s QMS, the grade increases by 1.

The final QMS grade could result in a grade of 1 to 5, with 5 being the maximum final nonconformity grade, representing the highest risk of an ineffective QMS. If by applying the grading system, a score higher than 5 is achieved, the score is documented as “5”.

Refer to Appendix B for examples.

4.7 Use of the Regulatory Audit Information Exchange Form

Nonconformities related to medical device country specific regulatory requirements outside of ISO 13485:2003 should be captured on the right side (shaded area) of the Regulatory Audit Information Exchange Form. When the auditor writes a nonconformity it should be either graded under the nonconformity grading section against ISO 13485:2003 or assigned a regulatory requirement citation from a specified regulatory jurisdiction that was not fulfilled. The intent of this exchange form is that a single nonconformity should not be issued under both sections.
Below is a completed Regulatory Audit Information Exchange Form with some specific examples:

- **Nonconformity #1** – An example of a nonconformity of the QMS from the requirements of ISO 13485:2003
- **Nonconformity #2** – An example of a nonconformity of the QMS from additional country specific requirements beyond ISO 13485:2003
- **Nonconformity #3** – An example of a nonconformity outside of the QMS from other medical device country specific regulatory requirements

<table>
<thead>
<tr>
<th>NC#</th>
<th>Nonconformity</th>
<th>ISO 13485 Clause</th>
<th>Step 1 Grade</th>
<th>Absence</th>
<th>Medical Device Grade</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>There is an absence of a Quality Policy in the organization.</td>
<td>5.3</td>
<td>1</td>
<td>+1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>The retention period of training records as specified in procedure XYZ does not meet the minimum retention period of 5 years per Ministerial Ordinance 169.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>The recall of product AB-CXYZ in April 2011 was not reported to the Irish Medicines Board (IMB) as required by procedure QMS123</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Regulatory Audit Information Exchange Form provides a transparent and standardized way of exchanging information between regulatory authorities on the outcome of medical device regulatory audits. The intent is that this Form will be provided to the medical device manufacturer. At minimum a draft of the Form should be provided at the conclusion of the audit. 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 dispute and/or appeals process. The intent is also that the grading and the exchange form be a method to accurately capture the assessment of the audit and to provide uniformity and consistency within the process of grading nonconformities.

The exchange form purposely does not provide a cumulative grade for the overall audit. How the exchange form is utilized is the decision of each regulatory authority for their appropriate assessment based on their own needs or requirements.
### 5.0 Appendix A: Examples of statements of nonconformities

<table>
<thead>
<tr>
<th>NC #</th>
<th>Poorly worded</th>
<th>Improved wording</th>
<th>13485:2003 Clause</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>There was no evidence of training to the medical devices directive</td>
<td>The manufacturer did not follow their own training procedure (#14) requiring training on the medical devices directive (93/42/EEC) for internal auditors.</td>
<td>4.2.1</td>
</tr>
</tbody>
</table>
| 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            |
## 6.0 Appendix B:
Examples Illustrating use of the Nonconformity Grading System

<table>
<thead>
<tr>
<th>Example of Nonconformity</th>
<th>ISO 13485 Clause</th>
<th>Occurrence</th>
<th>STEP 1 Grade</th>
<th>Explanation of STEP 1 Grade</th>
<th>STEP 2</th>
<th>Final Grade</th>
<th>Explanation of Final Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is no objective evidence of the establishment of quality objectives for 2011, as required in the auditee's Quality Manual. The same non conformity was cited during the audit of 2010.</td>
<td>5.4.1 (indirect)</td>
<td>Repeat (2010, 2011)</td>
<td>2</td>
<td>This is a repeat NC. Therefore, it leads to a NC grade of 2.</td>
<td>NO</td>
<td>NO</td>
<td>2</td>
</tr>
<tr>
<td>Management reviews are held quarterly per procedure number DOC12345. However, there is no documentation of the third quarter management review meeting for 2010.</td>
<td>5.6.1 (indirect)</td>
<td>First NC</td>
<td>1</td>
<td>This is a first NC, leading to a NC grade of 1.</td>
<td>NO</td>
<td>NO</td>
<td>1</td>
</tr>
<tr>
<td>Competence, Awareness and Training processes are absent from the QMS. Documented evidence for training could not be provided. This NC was also raised in a previous QMS audit (2009, 2011).</td>
<td>6.2.2 (indirect)</td>
<td>Repeat NC</td>
<td>2</td>
<td>This is a repeat NC. Therefore, it leads to a NC grade of 2.</td>
<td>YES</td>
<td>NO</td>
<td>3</td>
</tr>
<tr>
<td>Suppliers are not adequately controlled as per procedure DOC1234. Supplier X of was replaced with Supplier Y on 1st May 2011 without approval. This is the second NC issued against the same sub-clause in a previous QMS audit (2010).</td>
<td>7.4.1 (direct)</td>
<td>Repeat NC</td>
<td>4</td>
<td>This is a repeat NC. Therefore, it leads to a NC grade of 4.</td>
<td>NO</td>
<td>NO</td>
<td>4</td>
</tr>
<tr>
<td>Suppliers are not adequately controlled as per procedure DOC1234. Product XX was shipped on 2nd of September 2011 and was nonconforming due to an uncontrolled specification change made by the supplier. This is the second NC issued against the same sub-clause in a previous QMS audit (2010).</td>
<td>7.4.1 (direct)</td>
<td>Repeat NC</td>
<td>4</td>
<td>This is a repeat NC. Therefore, it leads to a NC grade of 4.</td>
<td>NO</td>
<td>YES</td>
<td>5</td>
</tr>
<tr>
<td>Example of Nonconformity</td>
<td>ISO 13485 Clause</td>
<td>Occurrence</td>
<td>STEP 1 Grade</td>
<td>Explanation of STEP 1 Grade</td>
<td>Absence</td>
<td>Medical Device</td>
<td>Final Grade</td>
</tr>
<tr>
<td>--------------------------</td>
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</tr>
<tr>
<td>There was no evidence of a record for control of storage conditions for a medical device with a 24 month shelf life that requires storage at 2-8°C per procedure (#12345).</td>
<td>7.5.5 (direct)</td>
<td>First NC</td>
<td>3</td>
<td>This is a first NC, leading to a NC grade of 3.</td>
<td>NO</td>
<td>NO</td>
<td>3</td>
</tr>
<tr>
<td>There is an absence of a Quality Policy.</td>
<td>5.3 (indirect)</td>
<td>First NC</td>
<td>1</td>
<td>This is a first NC, leading to a grade of 1.</td>
<td>YES</td>
<td>NO</td>
<td>2</td>
</tr>
<tr>
<td>There was absence of the requirement for Design verification in the manufacturers QMS. As a result design changes to device model XXX were not verified prior to the product release to the market. This is the second NC issued against the same sub-clause in a previous QMS audit (2010).</td>
<td>7.3.5 (direct)</td>
<td>Repeat NC</td>
<td>4</td>
<td>This is a repeat NC. Therefore, it leads to a NC grade of 4.</td>
<td>YES</td>
<td>YES</td>
<td>5</td>
</tr>
<tr>
<td>There was no evidence of design validation as per procedure DOC12 for device model XXX. The product was shipped to five customers.</td>
<td>7.3.6 (direct)</td>
<td>First NC</td>
<td>3</td>
<td>This is a first NC, leading to a grade of 3.</td>
<td>NO</td>
<td>YES</td>
<td>4</td>
</tr>
</tbody>
</table>