FINAL 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 of the Global Harmonization Task Force

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This document was produced by the Global Harmonization Task Force, a voluntary international group of representatives from medical device regulatory authorities and trade associations from Europe, the United States of America (USA), Canada, Japan and Australia.

The document is intended to provide non-binding guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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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. It is expected that the reader is proficient with the requirements of ISO 13485:2003.

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.

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 from the use of a standardized and transparent grading system of QMS nonconformities. This will build the confidence necessary for the potential mutual acceptance of the results of a regulatory audit.

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 intent of this new grading system for regulatory purposes is to support the exchange of audit results 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 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 standardized results.

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 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)

2.2 Nonconformity

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

2.3 Quality management system (QMS)

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

3.0 References

GHTF SG4/N28R4:2008 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 1: General Requirements

GHTF SG4/N30:2010 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy

GHTF SG4/N33R16:2007 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 3: Regulatory Audit Reports

GHTF SG4/N83:2010 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 4: Multiple Site Auditing

GHTF SG4/N84:2010 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 5: Audits of Manufacturer Control of Suppliers

ISO 13485:2003 – Medical Devices –Quality Management Systems - Requirements for Regulatory Purposes

ISO 9000:2005 - Quality Management Systems – Fundamentals and Vocabulary

ISO 17021:2011 – Conformity Assessment – Requirements for bodies providing audit and certification of management systems

ISO 19011:2011 – Guidelines for Auditing Management Systems

4.0 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. The Regulatory Audit Information Exchange Form at the end of this document is a tool used to capture the grading so that it can be utilized in an exchange of information between interested regulatory bodies.

4.1 Writing Nonconformities

Regulatory audits should be performed in accordance with GHTF SG4 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 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 should be an accurate representation of the reviewed records, samples and procedures, as well as interviews conducted.

The nonconformity should[1]:

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

c) identify the specific requirements which have not been met:
   - use the words of ISO 13485:2003
   - document the source of the requirement (e.g. medical device regulations, other applicable standards, procedures or requirements established by the organization, etc.)

Multiple instances 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 (see Appendix A – "NC #2"). Examples of poorly and better worded nonconformities are provided in Appendix A.

[1] ISO & IAF 9001 Auditing Practices Group Guidance on: Documenting a Nonconformity (5 June 2009) www.iso.org/tc176/ISO9001AuditingPracticesGroup

4.2 Grading of Nonconformities

The nonconformity grading for regulatory purposes consists of a two-step approach that leads to calculation of a final grade for each nonconformity (Figure 1 – shaded area):

Step 1 - A Nonconformity Grading Matrix, which provides an initial grade

Step 2 - Additional escalation rules are applied, to determine a final grade

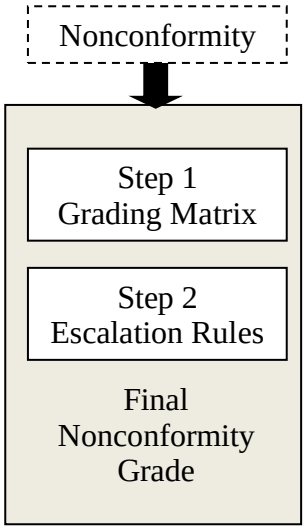

Figure 1: Grading Overview

4.2.1 Step 1 Grading Matrix

As illustrated in Figure 1 above, the Grading Matrix is the first step in grading a nonconformity.

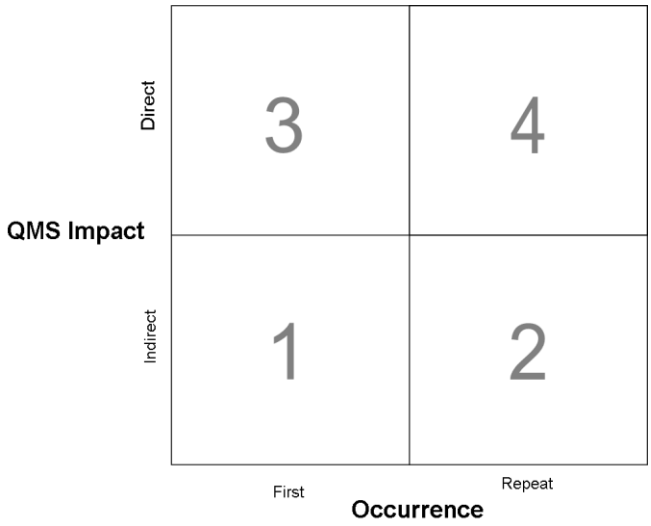

Figure 2: **Grading Matrix**

The Y-axis of the Grading Matrix (Figure 2) 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 13485:2003 clauses 4.1 through 6.3, 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.

- **Direct QMS impact:** ISO 13485:2003 clauses 6.4 through 8.5, 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.

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.

[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).

- When the nonconformity has the potential to affect safety or performance, it should be written against the specific requirement in ISO 13485:2003 found in clauses 6.4 through 8.5, because it has direct QMS impact.

- When the nonconformity is against the manufacturer's quality manual, procedures or requirements, is not specifically required in ISO 13485:2003 or does not impact safety or performance, then the nonconformity should be assigned to clauses 4.1 through 6.3, because it has indirect QMS impact.

The X-axis of the Grading Matrix in Figure 2 is **Occurrence** and is divided into two categories:

- **First:** The first category addresses a nonconformity in a particular sub-clause (X.X.X)[4] of ISO 13485:2003 identified for the first time. The first time is defined as not observed in the two previous QMS audits which evaluated the same sub-clause.

- **Repeat:** The second category is a nonconformity that has been identified within either of two previous QMS audits which evaluated the same sub-clause (X.X.X). 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.

Nonconformities can often be written up against more than one clause. Therefore, it is the auditor's obligation to determine the impact of the non-conformity 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 in Step 1 are provided below.

- ***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

[4] 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.

followed their 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.

- ***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 13485:2003 clause 7.5 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 - Documentation Requirements for the manufacturer not following their own procedure and not against clause 7.5 – 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 – Production 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.

4.2.2 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:

1. Absence of a documented process or procedure

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.

2. 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 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. It is no longer considered a nonconforming product and the escalation rule will not be applied.

4.3 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" (score of 3) or "indirect impact" (score of 1), as defined above.

B. Repeat nonconformities against the same QMS sub-clause (X.X.X): The auditor should check the previous two audit reports which evaluated the same sub-clause to see if a nonconformity that is identified in the current audit was previously raised. The nonconformity does not have to be identical to the nonconformity in the previous audit, just cited to 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. Each rule below is applied to determine the final grade of the nonconformity.

> **Rule 1 - Absence:** Absence of a documented process or procedure of any requirement, the grade increases by 1.
>
> **Rule 2 - Medical Device:** Release of a Nonconforming Medical Device outside of the controls of the manufacturer's QMS, the grade increases by 1.

The final grade for a nonconformity under this grading scheme will be a number between 1 and 6. However, the grade of "5" was determined to be the maximum, because this represents a significantly high enough risk that some intervention is required. The differentiation between 5 and 6 was not felt to be of benefit in the grading system. Therefore, if a grade of 6 is achieved, the final grade is documented as "5." Refer to Appendix B, example #8.

4.4 Regulatory Audit Information Exchange Form

To enable information exchange between regulators, the following Regulatory Audit Information Exchange Form (Form) is introduced.

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														
2														

Table 1 - Regulatory Audit Information Exchange Form

This Form consists of three sections (see Table 1):

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

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

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 13485:2003 should be identified in the Medical Device Country Specific Regulatory Requirements section of the Form. This area is not graded, but the auditor should reference the specific section of the applicable Regulation or Legislation against which the nonconformity is cited.

4.5 Use of the Regulatory Audit Information Exchange Form

When the Form is exchanged between regulatory authorities, specific information about the audit should be included with the Form. Examples include: date of the audit, scope of the audit, sites audited, auditors' name(s), etc.

The Nonconformity Grading section of the Form is intended to capture the grade of nonconformities against ISO 13485:2003. If a nonconformity is against a ISO 13485:2003 clause, it should at minimum be captured under the Nonconformity Grading section of the Form and graded.

The intent of the Medical Device Country Specific Regulatory Requirements section is to capture additional issues outside the specific requirements of ISO 13485:2003. This section is not graded but the nonconformities are listed by regulatory jurisdictions (covered by the audit) and general regulatory requirements for that jurisdiction. Certain regulatory jurisdictions (such as Canada) may require that nonconformities against country specific regulatory requirements are written against a specific clause in the standard in the Nonconformity Grading section.

Below is a completed Form with some specific examples:

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 organization.	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 process has not been validated, as per procedure DOC12345 but has not resulted in nonconforming 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. Procedure 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				

- Nonconformity #1 – An example of a nonconformity of the QMS from the requirements of ISO 13485:2003.

- Nonconformity #2 – An example of a country specific regulatory requirement that is a nonconformity within the manufacturer's QMS but more specific than the requirements of the clauses of ISO 13485:2003.

- Nonconformity #3 – An example of a nonconformity within the QMS that is also against a country specific regulatory requirement. In this case, the nonconformity could also be written against the EU Medical Device Directive.

- Nonconformity #4 – An example of a nonconformity to a country specific regulatory requirement that is also cited under section 4.1 of ISO 13485:2003. In this case, Canada requires all nonconformities be written against ISO 13485:2003.

The 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 after following standard auditing procedures where potential nonconformities are routinely discussed throughout the audit

and at the closing meeting of the audit (ISO 19011:2011, clause 6.4.9). It is recommended that a draft of the Form be provided at the closing meeting of the audit for sake of transparency.

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 17021:2011, clause 9.7). After the auditing organization has completed the audit process, the final Form should be provided to the manufacturer. The intent is also that the grading and the 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 Form 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.

5.0 Appendix A: Examples of statements of nonconformities

	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

6.0 Appendix B: Examples Illustrating Nonconformity Grading

	STEP 1				STEP 2			
Example of Nonconformity	**ISO 13485 Clause**	**Occurrence**	**STEP 1 Grade**	**Explanation of STEP 1 Grade**	**Absence**	**Medical Device**	**Final Grade**	**Explanation of Final Grade**
1. 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.	5.4.1 (indirect)	Repeat (2010, 2011)	2	This is a repeat NC. Therefore, it leads to a NC grade of 2.	NO	NO	2	This is not an absence of a QMS requirement. There is a documented procedure however the manufacturer could not provide objective evidence that it was being followed. As a result of this NC it is unlikely that a nonconforming product was placed on the market. Therefore the initial grade does not change.
2. Management reviews are held quarterly per procedure number DOC12345. However, there is no documentation of the third quarter management review meeting for 2010.	5.6.1 (indirect)	First NC	1	This is a first NC, leading to a NC grade of 1.	NO	NO	1	This is not an absence of a QMS requirement. As a result of this NC it is unlikely that a nonconforming product was placed on the market. Therefore the initial grade does not change
3. 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).	6.2.2 (indirect)	Repeat NC	2	This is a repeat NC. Therefore, it leads to a NC grade of 2.	YES	NO	3	The absence of a QMS requirement increases the initial grade by 1, making the final grade as 3.
4. 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 subclause in a previous QMS audit (2010).	7.4.1 (direct)	Repeat NC	4	This is a repeat NC. Therefore, it leads to a NC grade of 4.	NO	NO	4	This is not an absence of a QMS requirement. There is no evidence of nonconforming product being placed on the market. Therefore the initial grade does not change.
5. 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 subclause in a previous QMS audit (2010).	7.4.1 (direct)	Repeat NC	4	This is a repeat NC. Therefore, it leads to a NC grade of 4.	NO	YES	5	Non conforming product was placed on the market as a result of this QMS nonconformity. This increases the initial grading by 1, to a final grade of 5.

	STEP 1				STEP 2			
Example of Nonconformity	**ISO 13485 Clause**	**Occurrence**	**STEP 1 Grade**	**Explanation of STEP 1 Grade**	**Absence**	**Medical Device**	**Final Grade**	**Explanation of Final Grade**
6. 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^{0}C per procedure (#12345).	7.5.5 (direct)	First NC	3	This is a first NC, leading to a NC grade of 3.	NO	NO	3	The initial grade does not change.
7. There is an absence of a Quality Policy.	5.3 (indirect)	First NC	1	This is a first NC, leading to a grade of 1.	YES	NO	2	There is an absence of a QMS requirement. Therefore, the initial grade increases by 1 to a final grade of 2.
8. There was an absence of the requirement for Design verification in the manufacturer's 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).	7.3.5 (direct)	Repeat NC	4	This is a repeat NC. Therefore, it leads to a NC grade of 4.	YES	YES	5	This is an absence of a requirement and non conforming product was placed on the market. Therefore the grade would be 4+2=6. However, since the maximum grade can only be 5, it will be recorded as 5.
9. There was no evidence of design validation as per procedure DOC12 for device model XXX. The product was shipped to five customers.	7.3.6 (direct)	First NC	3	This is a first NC, leading to a grade of 3.	NO	YES	4	Non conforming product was placed on the market as a result of this QMS nonconformity. This increases the initial grade by 1, to a final grade of 4.