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QSIT What is it?

An overview, by Susan Brown

It's the Quality Systems Inspections Technique (QSIT) brought to you by the FDA's Center for Devices and Radiological Health (CDRH). CDRH's Quality Systems Inspections Reengineering Team, composed of personnel from the Office of Regulatory Affairs (ORA) and CDRH's Office of Compliance (OC), has developed a new method of inspecting device manufacturers for compliance with the Quality System Regulation (QSR) (21 CFR 820). A draft QSIT Inspection Handbook was issued in October 1998.

Over four years ago, resource concerns at CDRH prompted an evaluation of the current inspectional process. The reengineering team's three goals were to decrease inspection time, increase focus, and move towards global harmonization. Industry input was solicited early on with field and industry experts developing an inspectional model which was reviewed at an Open Public Meeting in the spring of 1998.

The October 1998 draft QSIT Inspection Handbook has since been used to inspect forty-two firms in three districts for QSR compliance. The firms ranged in size from nine to five hundred employees, had an annual dollar volume of from 25K to 50M, and covered fourteen product categories including *in vitro* diagnostic products.

A survey analysis of this pilot study showed that both FDA investigators' and industry's assessment is that the team's goals were being achieved. More efficient in-plant inspections were conducted over approximately five days as compared to the current ten to fifteen. The inspection emphasized key elements of the QSR and thus key elements of a firm's quality system resulting in more focused inspections. Those firms that had previously experienced inspections by notified bodies or foreign agencies found that the QSIT approach was more similar to those organizations' methods. The "Report on the Quality System Inspection Technique Study", April 26, 1999, is available on CDRH's web site.

Based on the theory that there are seven subsystems in a quality system, QSIT focuses on the top four of these subsystems as the primary indicators of compliance with the QSR. A gap analysis performed on QSIT demonstrated that all the requirements of the QSR were covered by organizing inspections around this set of four subsystems.

Seven Quality Systems Subsystems	Four QSIT Handbook Sections
1. Corrective and Preventive Actions (CAPA)	1. Management Controls
2. Design Controls	2. Design Controls
3. Production and Process Controls	3. Corrective and Preventive Actions (CAPA)
4. Management Controls	4. Production and Process Controls
5. Records/Document/Change Controls	
6. Materials Controls	
7. Facility and Equipment Controls	

In what the FDA describes as a "top-down" approach for evaluation of a company's quality system, each of the four principal subsystems is examined as a system first, followed by an analysis of raw data, e.g. records.

The QSIT Inspection Handbook lists between six and fifteen "inspectional objectives" for the review of each subsystem. Each subsystem evaluation consists of a review of whether a firm has procedures in place and appears to meet the requirements, and a closer review of a sampling of records to verify that the requirements have been implemented in actual practice. Flow diagrams provide an overview of how the inspection of each subsystem should occur.

A "narrative", organized by inspectional objectives, describes how to achieve each inspectional objective and reflects the questions contained within the flow diagrams. Inspectors are not bound to every sentence in the narrative but rather encouraged to inspect subsystems with the narrative guidance in mind. In order to facilitate record review and maintain a timely pace, sampling plans instructions and tables are included for the sampling of records.

When making arrangements for pre-announced inspections, investigators will be asking for a copy of the firm's Quality Policy and high level Quality System Procedures including Management Review Procedures, Quality Plan or equivalent documents.

An investigator's prior review of these documents, which will be returned at the time of the inspection, should facilitate the inspection. Firms are not required to supply requested pre-inspection documents. An inspection still officially begins on site with the presentation of FDA Form 482.

The reversal from a bottom-up approach to a top-down approach, the use of sampling plans for records review, and the pre-inspection activities are the major changes in how an inspection is organized. The shift to a top-down

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technique and the emphasis on the four quality subsystems better reflect the content and emphasis of the revised device GMPs, the QSRs which have been in effect since June 1997. The shift in focus of the inspection was reflected in the distribution of FDA Form 483 observations as indicated in the table at right.

Top ten 483 items

	Previous 13 months, current technique	Pilot study QSIT
Management	None	40%
CAPA	50%	30%
Production and Process Controls	30%	20%
Records	20%	10%

Management Controls and CAPA are of particular interest to the FDA and will receive much attention during an inspection.

An inspection is to begin and end with an evaluation of the Management Control subsystem. The objective is to determine whether management with executive responsibility provides adequte resources, assures that the quality system is functioning properly, monitors the system, and makes necessary adjustments. Prior to review of any subsystem, investigators are to interview the Management Representative "to obtain an overall view of the subsystem as well as a feel for management's knowledge and understanding of the subsystem." The FDA believes that all product, process, design and CAPA problems can be tied to management and intends to have more dialogs with appropriate management representatives. Management Controls are seen as encompassing all subsystem controls.

The evaluation of the CAPA subsystem, in the top-down method, is to be focused on checking the system for systemic deviations from the regulations rather than hunting for minor specific deviations (individual product problems). Acknowledging that nonconformances happen, the investigator is to check whether a firm has a system to catch them and what they did about them. The FDA considers the CAPA to be one of the most important quality system elements. It is seen as directly linked to all subsystems serving as the central hub of a quality system. Within the records of CAPA reside all the quality data.

Production and Process Controls evaluation for the ability to produce product according to specifications includes selecting a process with CAPA indicators of process problems. A separate section of the handbook addresses evaluation of Sterilization Controls; the approach is the same as described for the four subsystems. An evaluation of the Design Control subsystem is to be performed on a single design project from development through transfer.

More efficient in-plant inspections performed using QSIT can be partially attributed to the predictability designed into the process. This predictability, promoted by the checklists and flow diagrams, aids investigators and thus industry in managing their time. A firm should be able to determine which of its policies and procedures will be evaluated. However, it will not be able to predict which quality data (records) will be selected for reviewing the rigor of its systems.

The intention of QSIT is to encourage inspection by quality subsystem review and to discourage investigators from starting an inspection by looking at individual records first. However, the old saw about teaching old dogs new tricks leaps irresistibly to mind. ORA is currently developing training programs for investigators and compliance officers. Time will tell.

As audit and management review systems are linked to CAPA records, will actions items identified become 483 observations? The FDA states that training is to emphasize noting inadequacies to the system, that is to the CAPA system, not the problem identified. If a firm recognizes its problems and is correcting and/or preventing their recurrence, the system is working.

The QSIT Handbook, available on the FDA website, can be used by firms in evaluating their own quality system. Ultimately though, compliance to the QSR is the statutory requirement and the FDA will still be on the lookout for nonconforming product.

Nationwide implementation of the new QSIT inspectional method is happening this year with a 1999 edition of the handbook. This next edition contains additions covering Medical Device Reporting (MDR), Corrections and Removals, and Tracking. Current methods may still be employed for for-cause inspections, follow-up inspections and other objectives as needed.

References:

– QSIT Inspection Handbook, October 1998 Draft
– Report on the Quality System Inspection Technique (QSIT) Study, April 26, 1999
– FDA Video Conference Series: The New Quality System Inspection Techniques

For more information:

– Visit website: www.fda.gov/cdrh/gmp/
– Quality Systems Inspections Reengineering Team, Rockville, MD. Phone: (301) 594-4616 Internet: TRW@CDRH.FDA.GOV

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Risk Management in Programmable Electronic Medical Devices

Part 2 of 2

By Gary Seeger

In the last issue of this newsletter, Part 1 of this article presented the more general requirements of IEC 601-1-4 for medical electrical equipment incorporating programmable electronic subsystems including Documentation, the Risk Management Plan, the Development Life Cycle, and the Risk Management Process itself.

In this issue, I discuss the complementary aspects of IEC 601-1-4 including Personnel Qualification, Requirement Specification, Architecture, Design and Implementation, Verification, Validation, Modification, Assessment, and FDA Congruence.

Personnel Qualification

The design and modification of a programmable electrical medical system must be considered as an assigned task in accordance with 4.18 (Training) of ISO 9001.

Requirement Specification

There must be a Requirement Specification for each programmable electrical medical system and each of its subsystems. The Requirement Specification must detail the functions that are risk related including functions that control risks arising from environmental conditions, causes elsewhere in the device, and possible malfunctions.

For each of these functions, the Requirement Specification must give the level of safety integrity necessary to control the risks. Requirement Specifications are often referred to as Hardware Requirement Specifications and Software Requirements Specifications.

Architecture

The Architecture must satisfy the requirement specification. The Architecture for the programmable electrical medical system and each of its subsystems must be specified. Where appropriate, the specification must include requirements for the following items:

– Allocation of risk control measures to subsystems and components.
– Redundancy.
– Diversity.
– Failure rates and modes of components.
– Diagnostic coverage.
– Common cause failures.
– Systematic failures.
– Test interval and duration.
– Maintainability.
– Protection from human intentional or unintentional causes.

Design and Implementation

The design must be decomposed into subsystems, each having a design and test specification, where appropriate.

Where appropriate, requirements are specified for the following items:

– Software development methods.
– Electronic hardware.
– Computer aided software engineering (CASE) tools.
– Sensors.
– Actuators.
– Human interfaces.
– Energy sources.
– Environmental conditions.
– Programming language.
– Third party software.

Verification

Verification of the implementation of safety requirements must be carried out. A verification plan must be produced to show how the safety requirements for each Development Life Cycle phase will be verified and a reference to the methods and results of the verification must be included in the Risk Management Summary.

Validation

Validation that safety requirements are met must be carried out. A validation plan must be produced to show that the correct safety requirements have been implemented. The leader of the validation team carrying out the validation must be independent of the design team. The professional relationships of the members of the validation team with members of the design team must be documented in the Risk Management File and no member of a design team may validate his own design.

These relationships are often documented in the product Design and Development Plan and/or the Company Organization Chart. A reference to the methods and results of the validation must be included in the Risk Management File.

Modification

If any or all of a design results from modification of an earlier design, the IEC 601-1-4 standard may be applied as if the modification is a new design or the continuation of the previous design under appropriate modification/change procedures. All relevant documents in the Development Life Cycle must be revised, amended, reviewed, and approved under a document control scheme in accordance with 4.5.2 (Document Control) of ISO 9001, or equivalent.

Assessment

Assessment must be carried out to ensure that the programmable electrical medical system has been developed in accordance with the requirements of IEC 601-1-4 and recorded in the Risk Management File. The assessment may be carried out by internal audit in accordance with 4.17 (Internal Audit) of ISO 9001.

FDA Congruence

Although the United States Food and Drug Administration does not formally mandate conformance to IEC 601-1-4, the May 29, 1998 FDA "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" does include a *"Section 4. Risk Management Activities During the Software Life Cycle."*

A careful reading of this section of the FDA Guidance clearly demonstrates that the FDA expectations for risk management closely parallel the requirements of IEC 601-1-4. In fact, the FDA Guidance presents a Figure 4 on page 21 entitled "Risk Management Process (Adapted from ICE 60601-1-4)."

Most manufacturers of programmable electronic medical systems deliver products into both the domestic and European markets. The effective inclusion of the IEC 601-1-4 requirements into a company's Design Control process should satisfy both the MDD and FDA requirements for programmable electrical medical systems.

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