Certified Software Solutions Quality Forum
October, 2003 Vol.1 No. 7

Validation Planning Using Safety Risk Management

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This paper will address the topic of validation planning based on information gathered from safety risk management. Safety risk management is becoming increasingly recognized as an important method to support definition of the essential requirements for validation processes and medical device products.

This paper will also highlight and identify where risk management can be applied and suggest approaches to optimize the validation process by using a risk management process. The techniques discussed in this paper are based on industry standard processes and definitions that have been tailored based on our experience with use of these methods for hundreds of processes supporting dozens of pharmaceutical products and medical devices.

Approach

Use of risk management techniques to support regulatory compliance decisions has been endorsed by the FDA as shown in the new approach for the Pharmaceutical CGMP, Guidance for Part 11 Scope and Application, and the Quality Systems Inspection Technique (QSIT) audit methodology.[1,2,3] This paper will discuss a generalized approach to support each of these areas based on a risk management strategy as derived from ISO 14971, Application of risk management to medical devices, and the Good Automated Manufacturing Processes (GAMP) Guide for Validation of Automated Systems.[4,5] This paper will demonstrate how information from risk management can be used logically to plan validation tasks.

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How can Risk Assessments Streamline my Validation Planning?

Risk based methods not only help minimize compliance risk but also provide an excellent tool for achieving business benefits. Use of risk based methods forces a detailed focus on the most critical elements of the process or product and therefore a less detailed focus on other less important functions. This focus has allowed many pharmaceutical companies to reduce the level of validation detail for minor functions while remaining confident that all regulatory and quality/safety related requirements has been thoroughly addressed.

Use of a risk management process can provide significant business and regulatory compliance benefits. Table 1 lists different applications where a safety risk management process can be applied to streamline validation activities and provide increased confidence in product design and manufacturing. It can be seen from this list that the application of risk-based models not only has a very wide scope, but also is heavily endorsed and encouraged by the FDA as well as in regulatory references such as GAMP.

	Application	How Used	Reference
1.	Determines the level of documentation detail required for FDA submissions	Define documentation based on the level of concern or safety risk to a patient	Reviewer Guidance for Computer Controlled Medical Devices[6]
2.	Determine reportable events for Adverse Events Reports	Formal process for evaluation of events to determine if they meet the adverse event criteria	Compliance with the Adverse Event Reporting regulation 21 CFR Part 314.80[7]
3.	Determine reportable events for Medical Device Reports	Defines criteria for evaluating potential for recurrence of an event that could contribute to serious injury or death	Compliance with the Medical Device Reporting regulation, 21 CFR Part 803[8]
4.	Determine Part 11 applicability and requirements	Defines the scope of validation and compliance requirements	Final Guidance for 21 CFR Part 11 Scope and Application[2]

	Application	How Used	Reference
5.	Determine what manufacturing processes and parameters require validation	Defines critical control points to select systems and parameters for validation	Hazard Analysis of Critical Control Points, FDA training program[9]
6.	Determine priority for fixing product/process defects	Defines criteria for prioritizing which outstanding defects must be corrected	GAMP Guide for validation of Automated Systems, GAMP 4[5]
7.	Focus audits on critical systems	Defines most important subsystems to be audited to reduce audit scope	FDA's Quality System Inspection Technique (QSIT)[3]
8.	Determine level of detail for functional requirements and design	Defines functions that should be supported by more detailed definition and test activities	GAMP Guide for validation of Automated Systems, GAMP 4[5]
9.	Determine requirements for supplier audits	Defines criteria for which suppliers should be audited	GAMP Guide for validation of Automated Systems, GAMP 4[5]
10.	Determine regulatory requirements for public health protection	Use of a risk based orientation for the development of new Pharmaceutical CGMPs	FDA's Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach[1]

Table 1 Safety Risk Analysis Methods

A risk assessment can also be used to identify the level of validation required based on established requirements and safety risks. This requires the validation team to consider and identify safety considerations prior to creating validation protocols. Identification of the following elements will help streamline validation tasks:

- Identification of hardware components where failures can lead to an unsafe product.
- Identification of processing algorithms that are safety related (i.e.).
- Identifications of sensors, alarms, and interlocks where

failure could result in the inability to detect or prevent a bad product or operator injury.

- Identification of operator input data or command sequences that can lead to an out of specification product.
- Identification of "critical control points" that capture out of range conditions that could lead to a safety related failure.

How do I Implement Risk Management Based Validation?

The standard flow of safety risk analysis is Risk Analysis, Risk Evaluation, Risk Control and Change Control (as discussed in Quality Forum #6, December 2002, Safety Risk Management, by Chad Osborne and Dan Olivier. www.certifiedsofteware.com/qualityforum /qualityforum.htm). Risk Management can identify failure conditions, and fail safe responses. This can directly influence testing strategy, protocols and activities. This mode can also assist in the definition of specific data to be entered during testing and the expected results for each entry, as well as in the identification of normal, boundary and out of range conditions that need to be verified and validated. It also gives focus to parameters that have safety consequences, and defines acceptance criteria identified in the risk identification process.

The risk control phase includes the definition of the safety requirements and requires verification that the controls are effective in achieving the target level of safety. This means that the defined safety requirements must be verified and/or validated in accordance with established procedures. Based on the results of the verification/validation phases, it may be appropriate to reassess the estimated risk and confirm the accuracy of the estimated probabilities of occurrence and detectability of fault conditions.

It should be noted however that the "intended use" of the product must be defined before any risk analysis can be conducted. The definition of the intended use is necessary to define the product labeling to specify performance limits. Adequacy and completeness of the customer labeling in terms of Cautions and Warnings is essential to provide for customer protection, to satisfy regulatory requirements, and to reduce civil liability. Again the intended use correlates directly to the validation process. The intended use will give further focus to validation efforts reducing the number of unnecessary test cases.

Summary

The benefits obtained from the use of risk management methods are becoming increasingly acknowledged by medical and pharmaceutical manufacturers as well as by regulatory bodies such as the FDA. Optimal use of these methods will provided an excellent strategy to streamline validation activities for products as well as processes and also offers a technique that can instill increased confidence in the safety of established products and processes. Familiarity and competence in the conduct of risk management techniques is increasingly becoming a critical skill for quality and regulatory professionals.

References:

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