Product Risk Management

Agenda

- General Risk Concepts
- Medical Device Risk Management
  - International Standards
  - FDA Regulations and Guidance
- Drugs and Biologics Risk Management
  - International Guidance
  - FDA Guidance

General Concepts

- Old art / young science
- The art is the process of making good decisions with available data
- Science is based on probability and statistics
- Risk is a modern term and concept
General Risk Concepts

- Business process risk began with insurance of shipping and Lloyd’s of London 1696
- Business Risk related to financial aspects

Standards

Voluntary and Consensus Standards

Voluntary Standards

- Member National Committees appoint official delegates to standards development committees
- Draft Standards are voted by National Committees for adoption
- ANSI is appointed by NIST to coordinate the development of voluntary standards

Voluntary Standards

- AAMI accredited by ANSI to develop voluntary standards for medical devices
- AAMI works with IEC and ISO committees to develop international standards

AAMI=Association for the Advancement of Medical Instrumentation (Non-profit trade association)
ANSI=American National Standards Institute (Non-profit organization)
NIST=National Institute of Standards and Technology (US Government agency)
Medical Device Risk Management

International Organization for Standardization

- In 1946, delegates from 25 countries met in London and decided to create a new international organization, of which the object would be "to facilitate the international coordination and unification of industrial standards"
- TC 210 Quality management and corresponding general aspects for medical devices

International Electrotechnical Commission

- IEC was officially founded in June 1906, in London, England
- Purpose-standardization of the nomenclature and ratings of electrical apparatus and machinery
- Consists of over 80 Technical Committees
- TC 62-Electrical equipment in medical practice

ISO/IEC TC210 SC 62 JWG1

- International risk management standard joint project of ISO and IEC
- ISO/IEC 14971 Medical devices — Application of risk management to medical devices
- First Edition released in 2000
- Second Edition to be released this year
ISO Definitions

- Risk-combination of the probability of occurrence of harm and the severity of that harm
- Harm-physical injury or damage to the health of people, or damage to property or the environment
- Hazard-potential source of harm

ISO 14971 Risk Management Process

- Risk analysis
  - Intended use/intended purpose identification
  - Hazard identification
  - Risk estimation
- Risk evaluation
  - Risk acceptability decisions
- Risk control
  - Option analysis
  - Implementation
  - Residual risk evaluation
  - Overall residual risk acceptance
  - Communication of residual risk
- Production and post-production information
  - Post-production experience
  - Review of risk management experience

Other International Standards

- IEC 60601-1-6:2004 -- Medical electrical equipment, Part 1-6: General requirements for safety - Collateral standard: Usability

**Will be a major impact to medical devices
Other International Standards

- ISO 14155-1 and -2 Clinical Trials standards (require risk management)
- ISO 13485 Quality System standard (requires a risk management process)

Global Harmonization Task Force

- GHTF
- Conceived in 1992 in an effort to respond to the growing need for international harmonization in the regulation of medical devices.
- Representatives from national medical device regulatory authorities and the regulated industry.

GHTF

- The purpose of the GHTF is to encourage convergence in regulatory practices related to ensuring the safety, effectiveness / performance and quality of medical devices, promoting technological innovation and facilitating international trade.


- This document is intended to assist medical device manufacturers with the integration of a risk management system or risk management principles and activities into their existing quality management system by providing practical explanations and examples.
- Discusses risk management related to medical device safety, rather than financial or other business risks.
CDRH

QS 21 CFR 820 regulation requires:
- Risk based decisions
- Risk analysis
QS 21 CFR 820 regulation does **NOT**:
- Require a risk management system as defined in ANSI/AAMI/ISO 14971
- Require ANSI/AAMI/ISO 14971

European Community

- Medical Device Directive requires device meet the “Essential Requirements” of the directive in order to place device on the market
- Essential Requirements focus on device risk

GHTF Design Risk Management

CDRH

Device Implementation

Product Risk Management Process

Pre-Launch

1. Risk Management
2. Risk Assessment Tool
3. Risk Mitigation

Post-Launch

1. Risk Management
2. Risk Mitigation

Risk Analysis

<table>
<thead>
<tr>
<th>RiskID</th>
<th>Contributing Factors</th>
<th>Risk level before applying risk control (A)</th>
<th>Risk level after applying risk control (B)</th>
<th>Risk Control Measure (C)</th>
<th>RiskID</th>
<th>TestID</th>
<th>Status</th>
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<td>Unknown errors</td>
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<td>0.5</td>
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<td>3.2</td>
<td></td>
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Implementation of risk management principles and activities within a Quality Management System-GHTF Study Group-3, 2005

Evaluating Risk

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<thead>
<tr>
<th>Probability of Harm</th>
<th>Level of Security</th>
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<tbody>
<tr>
<td>Negligible</td>
<td>Significant 1</td>
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<tr>
<td>Marginal</td>
<td>Significant 2</td>
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<tr>
<td>Critical</td>
<td>Significant 3</td>
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<tr>
<td>Catastrophic</td>
<td>Intolerable 0</td>
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</table>

<table>
<thead>
<tr>
<th>Probability of Harm</th>
<th>Level of Security</th>
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</thead>
<tbody>
<tr>
<td>Frequent</td>
<td>Significant 1</td>
</tr>
<tr>
<td>Probable</td>
<td>Significant 2</td>
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<tr>
<td>Occasional</td>
<td>Significant 3</td>
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<tr>
<td>Remote</td>
<td>Intolerable 0</td>
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<tr>
<td>Improbable</td>
<td>Intolerable 0</td>
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<tr>
<td>Incredible</td>
<td>Intolerable 0</td>
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</tbody>
</table>
Drugs and Biologics Risk Management

ICH
- International Conference on Harmonization
- Founded in 1990 by representatives of the regulatory agencies and industry associations of Europe, Japan and the USA
- Topics selected for harmonisation would be divided into Safety, Quality and Efficacy

Terms of Reference of ICH
- #6-To facilitate the dissemination and communication of information on harmonised guidelines and their use such as to encourage the implementation and integration of common standards

International Conference on Harmonization
ICH HARMONISED TRIPARTITE GUIDELINE QUALITY RISK MANAGEMENT Q9*
Finalized Nov. 2005 at Step 4

This guideline provides principles and examples of tools of quality risk management that can be applied to all aspects of pharmaceutical quality including development, manufacturing, distribution, and the inspection and submission/review processes throughout the lifecycle of drug substances and drug (medicinal) products, biological and biotechnological products, including the use of raw materials, solvents, excipients, packaging and labeling materials.

*Refers to ISO 14971 medical devices risk management standard
CDER and CBER Activities

- In PDUFA III, FDA agreed to satisfy certain performance goals. One of those goals was to produce guidance for industry on risk management activities for drug and biological products.

CDER and CBER Guidance

- Premarketing Risk Assessment
  March 2005
  Risk assessment consists of identifying and characterizing the nature, frequency, and severity of the risks associated with the use of a product. Premarketing risk assessment represents the first step in this process.

- Development and Use of Risk Minimization Action Plans
  March 2005
  RiskMAP means a strategic safety program designed to meet specific goals and objectives in minimizing known risks of a product while preserving its benefits.
Postmarketing safety data collection and risk assessment based on observational data are critical for evaluating and characterizing a product’s risk profile and for making informed decisions on risk minimization.

References

- MDDI January 2006 “The Role of Risk Management in the New IEC 60601-1” by Harvey Rudolph and Charles Sidebottom
- MDDI March 2004 “Medical Devices- The Use and Misuse of FMEA’s as a Risk Analysis Tool” by Michael Schmidt
- MDDI May 2005, “Develop Defensively: Control Risk and Predict Results” by Stan Telson

- www.ich.org
- www.ghtf.org
- www.aami.org
- www.iso.ch
- www.iec.ch
- www.fda.gov
- www.devicelink.com (MDDI)
Questions

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