Medical Devices 101…
and more….

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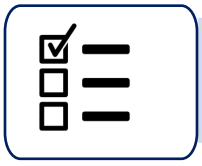
Objectives

Bridging the gaps in the information we utilize today

Sharing the challenges from a broader perspective



Building on the consistencies

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Agenda

Topics:
Opportunities and Challenges
Risk management Best Practices
Risk Management Basics
Risk management Tools
Evolution of the Treatment Environment
Case Studies

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Opportunities & Challenges

Medication Delivery , Diagnostics, and Treatment

- Pre-Filled Syringes, implants, co-packaged delivery systems, and closed loop systems
- Software applications for EMR, "apps" and other digital solutions
- Future state includes novel opportunities for drug delivery – 3D Printing, digital adherence tools, and telemedicine

Increasing Global Regulatory Requirements

- Establishment of new regulatory requirements for medical devices
- Quality & compliance risks increase as regulations evolve
- Advanced and novel devices increase complexity of regulatory applications and reviews

Evolving Regulatory Frameworks to Adapt to New Technology

- Advancements in technology driving new risk (Cybersecurity 3D Printing)
- Revised EU regulations for devices
- ISO 13485: 2016

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Opportunities & Challenges

All Medical Devices have a different Risk Profile

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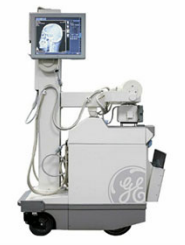
Risk Management Best Practices

Things to Do

- Know your product (Strength, Weaknesses, and Competitor Produ
- Understand product analytics (i.e., Databases, Recalls, Customer Feedback)
- Understand how your product is manufactured and process risks
- Ensure you have the right people evaluating risk while using the right tools at the right stages in the process
- Ensure your post market surveillance activities, compliance, and quality initiatives feed into the development lifecycle



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Risk Management Best Practices

- Begin early in design phase
- Formal review of identified deficiencies
- Clinical evaluation in actual or simulated use environment
- Piloted production, shipping and receiving
- Human Factors for packaging and labeling
- Address end user requirements

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Risk Management Basics

Harm: Injury or Damage to the Health of people, or damage to the property or the environment

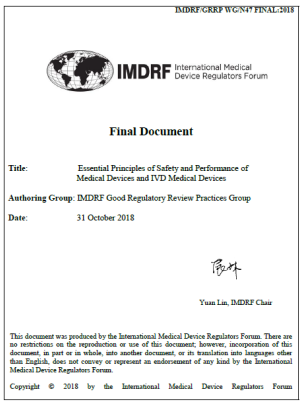
Hazard: The potential source of harm

Risk: The combination of the probability of occurrence of Harm and the severity of that Harm

Risk Analysis: Systematic use of available information to identify Hazards and to identify Risk

Risk Assessment: Overall process comprising a Risk Analysis and a Risk Evaluation

Risk Evaluation: Procedure based on Risk Analysis to determine whether tolerable Risk has not been exceeded



IMDRF/GRRP WG/N4 FINAL:2018

IMDRF International Medical Device Regulators Forum

Final Document

Title: Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

Authoring Group: IMDRF Good Regulatory Review Practices Group

Date: 31 October 2018

Yuan Lin, IMDRF Chair

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Risk Management Basics

Manufacturers should establish, implement, document and maintain a risk management system to ensure the ongoing quality, safety and performance of the medical device and IVD medical device. Risk management should be understood as a continuous iterative process throughout the entire lifecycle of a medical device and IVD medical device, requiring regular systematic updating. In carrying out risk management manufacturers should:

1. Establish a risk management plan
2. Identify and Analyze the known and foreseeable hazards
3. Estimate and Evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse
4. Eliminate or Control the risks
5. Evaluate the impact of information from the production and postproduction phases, on the overall risk, benefit-risk determination and risk acceptability

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Risk Management Basics

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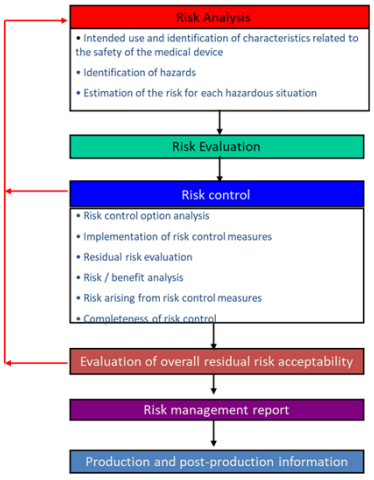

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Risk Management Tools

ISO 31000: Risk Management Guidelines on principles and implementation of risk management

- The risk management framework has been critical in establishing a common methodology and vocabulary. However, in any risk management exercise, "the devil is in the details." The effectiveness of the exercise will depend on the abilities of the responsible individuals to conduct the risk analysis using a range of risk management tools, some of which are detailed in Annex G.6 of ISO 14971
- Because different tools are useful for various types of analysis, many have suggested that an effective risk management program should be built on a combination of tools with complementary capabilities.

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Risk Management Tools

If the tools are not tailored to the situation, the use of a single or inappropriate tool may give a false sense of security that a risk has been investigated or controlled adequately. Without a thorough analysis, one or more potential hazards may not be identified and managed at the design stage and then may result in an expensive recall or field corrective action

The most commonly used risk management tools in the medical device industry include Preliminary Hazard Analysis (PHA), Failure Mode Effects Analysis (FMEA), Fault Tree Analysis (FTA), Assurance Cases, Hazard Analysis & Critical Control Point (HACCP), and Hazard and Operability (HAZOP).

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Risk Management Tools

Preliminary Hazard Analysis (PHA): a semi-quantitative tool frequently used in early stages. Because relatively little specific information may be available to quantify certain risks at these initial stages, a well-constructed PHA relies on the expertise of the team members and the availability of prior information of hazards or failures in similar systems to presage future situations

Failure Mode Effects Analysis (FMEA): perhaps the most common tool- a bottom-up, matrix-driven procedure used to measure and prioritize individual risks so that the risks can be isolated and considered systematically

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Risk Management Tools

Fault Tree Analysis (FTA): A top-down quantitative or a qualitative approach to model the interrelationships between parts of the system that could cause the system to fail or perform poorly. Its primary goal is to identify all *combinations* of events that can cause a system failure

The safety "assurance case": a top-down approach for medical devices that is often used in conjunction with other approaches such as FTA or FMEA. It is designed to show whether the evidence concerning hazard identification and risk control can logically support the claim that the medical device is reasonably safe for its intended purpose and in its specified environment.

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Risk Management Tools

Hazard Analysis and Critical Control Points (HACCP): Used commonly to assure product safety in the manufacturing stage, by analyzing the chemical, biological, and physical hazards at all stages of production, from the acquisition of raw materials through to the distribution of the finished product

The Hazard and Operability (HAZOP): industry and company experts determine how well production and servicing processes assure that a product adheres to its original design. Historically, the method was applied to processes used in the manufacture or service of medical products but now is often extended to ancillary activities involving suppliers, equipment, and facilities related to the products

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What is a Risk/Benefit Analysis?

Assess the Benefits of Devices

- **Type of benefit(s) -** impact on clinical management, patient health, and patient satisfaction
- **Magnitude of the benefit(s) -** assess benefit according to specific endpoints or criteria
- **Probability of the patient experiencing one or more benefit(s) -** data may show that a benefit may be experienced only by a small portion of patients
- **Duration of effect(s) -** how long the benefit can be expected to last for the patient

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What is a Risk/Benefit Analysis?

Assess the Risks of Devices

- Device-related serious adverse events
- Device-related non-serious adverse events
- Procedure-related complications
- Probability of a harmful event
- Duration of harmful events
- Risk from false-positive or false-negative results for a diagnostic type device

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Evolution of the Treatment Environment

Hospital Environment

- Controlled Environment
- Multiple Support Areas With Expertise
- Trained / Professional

Office Environment

- Controlled Environment
- Limited Support Areas With Expertise
- Trained / Professional

Home Use Environment

- Limited Control of Environment
- Trained / Parent /Guardian
- professional

Inherent Product Risks + Environment + User + ...

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Evolution of the Treatment Environment

Home Environment

- *Lay Person*
- *Single Care Area*
- *Lighting / Distractions*
- *No Standard Practice Guidelines*
- *Product Packaging*
- *Interoperability*
- *Storage*

Inherent Product Risks + Environment + User + ...

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How We Think Products Are Used

Immaculate Environment
- **Adequate Prep areas**

Caregivers
- **Trained**
- **Knowledgeable about the disease**

Adequate Disposal and Storage
- **Safeguarded storage**
- **Organized and easily accessible**

Controlled Environment

Do We Truly Understand How Products Are Utilized?

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How Products are Being Utilized in Some Instances

Immaculate Environment
- **Adequate Prep areas**

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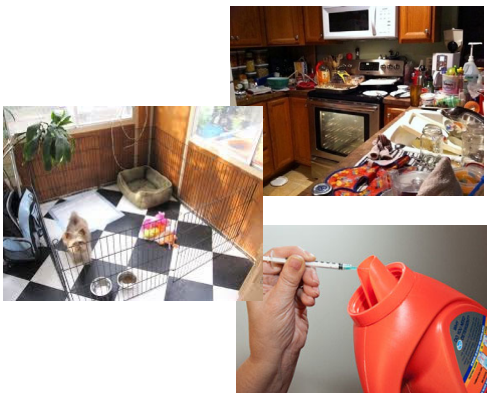
Controlled Environment



Do We Truly Understand How Products Are Utilized?

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CASE STUDIES

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Case Studies

- A grieving mother reported that her child had died after exposure to a fentanyl transdermal patch.
- The mother, who had chronic pain from Crohn's disease, reported that her four-year-old son either had used a discarded patch retrieved from the trash or had opened a wrapper from a box of stored patches and applied a patch to his body.
- His mother found him dead on the floor near an overturned wastebasket that held torn wrappers and disposed patches. It is not known how long the patch had been in place.

MEDICATION ERRORS

Fentanyl Transdermal Patches
More Protection Needed for Patients and Their Families

Matthew Grissinger, RPh, FASCP

What Are Some Attributes That Would Need to Be Considered?

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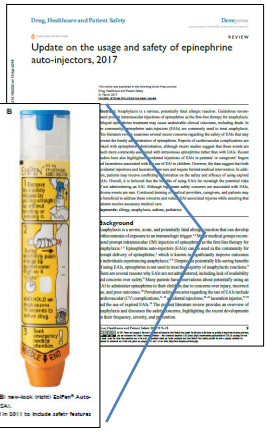
Epinephrine Auto-Injectors

- Life-Sustaining Product
- Redesigned Pens to mitigate Accidental Injection risks
- Unique environments, wide range of patient populations, distractions, and other impending circumstances
- 10% of accidental injections occurred while administering an EAI to another person



Drug, Healthcare and Patient Safety

REVIEW

Update on the usage and safety of epinephrine auto-injectors, 2017

Figure 4 Comparison of the (A) old-look and (B) new-look (right) EpiPen® Auto-Injector (©Viatris Specialty LP, Canonsburg, PA, USA).
Note: The EpiPen Auto-Injector was redesigned in 2011 to include safety features such as the orange needle sheath.

What Are Some Attributes That Would Need to Be Considered?

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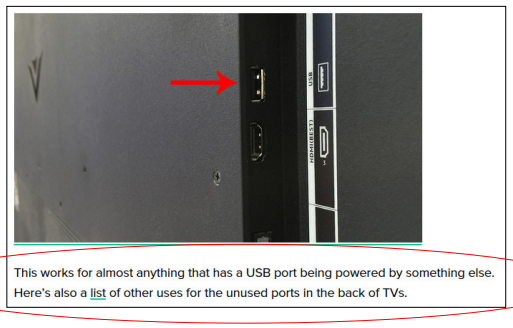
Case Studies

THE BLOG 09/29/2015 03:36 pm ET | Updated Dec 06, 2017

Travel Hacking: Charge Your Phone at a Hotel Without the Wall Plug

By Map Happy



This works for almost anything that has a USB port being powered by something else. Here's also a list of other uses for the unused ports in the back of TVs.

Could This Happen to a Medical Device?

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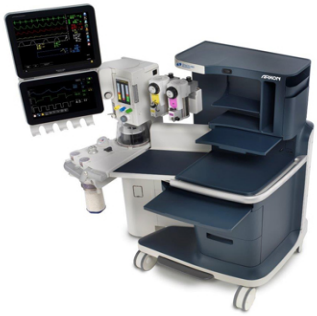
Case Studies

3. SPACELABS ANESTHESIA DELIVERY SYSTEM'S SOFTWARE GLITCH

The FDA on April 16 designated a Spacelabs Healthcare recall of an anesthesia delivery system as Class I.

The Arkon Anesthesia Delivery System is used in hospital operating rooms. The device is actually a Medical Design Excellence Awards finalist for the way it allows anesthesiologists to keep their patients in full view while simultaneously controlling and monitoring gas delivery using their preferred workflow.

Snoqualmie, WA-based Spacelabs in March initiated a voluntary recall of Arkon's with version 2.0 software because the software may cause the system to stop working, requiring manual ventilation of patients and potentially endangering their lives. The error is triggered by the combination of a spirometry loop save and a change in waveform configuration.



The Arkon Anesthesia Delivery System, as shown on Spacelab's website.

There was also potential for the system to stop working if a mobile phone or other USB device is plugged into one of the device's four USB ports for charging, according to the FDA.

April 2014 MDDI **6 Recent Medical Device Failures Catching FDA's Eye**

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PATH FORWARD

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Path Forward

- When tragedy does occur organizations change the behavior as a result of a knee-jerk reaction to prevent this from happening again
- The initial attention to risk management in the wake of a disaster can fade gradually over time
- Consistent behaviors were found in the pharmaceutical, aerospace, & petroleum industries

Harvard Business Review

MANAGING ORGANIZATIONS

Why Organizations Forget What They Learn from Failures

by Francisco Polidoro Jr.

FEBRUARY 05, 2016

Organizations sometimes make catastrophic mistakes. And although they try to learn from these disasters, they tend to make similar mistakes again and again.

Consider NASA, an organization employing some of the nation's brightest minds. In 1986, the space shuttle Challenger exploded – and by now, we all know the story. Some people within the organization had concerns with a component (the O-rings) being affected by low temperatures. However, their views were not taken into account in the decision to launch the shuttle.

This Seems to be Counterintuitive to the Overall Goal of Risk Management

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Path Forward

Many Factors Contribute to a Successful or Non-Successful Development Program

Understand the strength's and weaknesses in your organizations Development culture and process

The utilization of multiple tools will Help mitigate downstream product risk

Realization that the requirements serve a purpose not just a check box to market product

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