XAVIER HEALTH

Senior Leadership

Challenges Involved in Complex Decisions

The Saga Continues …

As part of the investigation (not identified in Session #1 activities), it is determined the event on March 30, 2016 is the first spontaneous adverse event of this nature received for the product (Lot A).

Product, specifically Lot A, is also being used in a clinical trial to support a pediatric (ages 0-12) indication.

To date, there are no related events on Lot B.

Case Study Discussion #2: *Handout*

At Your Table

Compare and Contrast

Your Quality Defect Investigation Processes

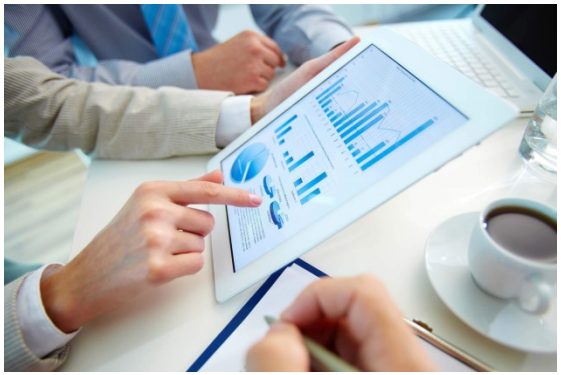
Case Study Additional Information: *Handout*

Expedited investigation revealed…

- Three complaints on Lot A not associated with an adverse event. One of the three was captured as “device does not work”. Another, from a CT site, was associated with a “leaking device”. No complaint samples were returned; both were deemed inconclusive.
- Review of the risk management file demonstrated no failure mode exceeding expected occurrence rates modes
- Review of batch records demonstrated no atypical events
- A visual assessment of retention samples for Lot A was performed with no defects noted

Immediate Reporting Considerations

- Information to consider when making an immediate reporting decision include:
  - *Destination (e.g., CDRH)*
  - *Origin (e.g., domestic or foreign)*
  - *Source (e.g., spontaneous, literature, clinical trial)*
  - *Reporter (e.g., HCP, consumer)*
  - *Serious criteria*
  - *Relatedness to drug*
  - *Listed in label and label type*
  - *Malfunction; yes or no*
  - *Improper Use/Storage*
  - *Reporting (days)*
  - *License (e.g., marketed, investigational)*



- Have a process, procedure and/or organization responsible: Quality Assurance, Regulatory, Safety

Immediate Reporting Examples

USA

- Any event (e.g., complaint) potentially impacting product quality and/or patient safety (e.g., bacteriological contamination), distributed in the US market must be reported to FDA within 3 working days of becoming aware of a problem. For a combination product, if the issue is caused by the device constituent part, 21 CFR Part 803 (Medical Device Reporting) applies.

- Serious AE associated with device malfunction or unknown submitted to CDRH from all countries of origin within 30 days for marketed products.

- Non Serious AE associated with device malfunction (i.e., company identified reportable malfunction) submitted to CDRH from all countries of origin within 30 days for marketed products.

- Similar dynamics associated with investigational devices require 10 day submission to CDRH and CDER when involved in clinical trial.

Immediate Reporting Examples (cont'd)

United Kingdom (UK)

- Serious AE associated with device malfunction or unknown submitted to MHRA from domestic origin within 10 days for marketed products.
- Non Serious AE associated with device malfunction or unknown submitted to MHRA from domestic origin within 30 days for marketed products.
- Death related to drug associated with investigational compound submitted to MHRA from domestic origin within 7 days. Any other serious adverse event; 15 days.

Japan

- Death associated with device malfunction and other serious AE without death and unlisted with device malfunction submitted to PMDA from foreign or domestic origin within 15 days for marketed products.
- Serious AE without death and listed associated with device malfunction and listed submitted to PMDA from foreign or domestic origin within 30 days for marketed products.

Possible Market Actions

1. Recall – removal from market
2. Retrieve clinical trial material, if applicable
3. Recall - Correction
4. Cease manufacturing and distribution of the Product
5. No market or clinical trial action taken, but include mitigation

Case Study Discussion #3: *Handout*

At Your Table

- Establish a final recommendation for senior management regarding regulatory body reporting action.
- Discuss what additional information you wish you had?
- What tool(s) might you use to obtain additional information?

Evaluating the Options

Contains Nonbinding Recommendations
Draft – Not for Implementation

Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions

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Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on June 16, 2016.

http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm506679.pdf

Benefit Considerations

- Type of benefits
- Magnitude of benefits
- Likelihood of patient experiencing one or more benefits
- Duration of effects
- Patient preference on benefits
- Benefit factors for healthcare providers or caregivers
- Medical necessity

Risk Considerations

- Risk categories
- Risk severity
  - Device related deaths and serious injuries
  - Device related non-serious adverse events
  - Device related events without reported harm
  - Duration of harm
- Likelihood of Risk
  - Likelihood of nonconformity
  - Likelihood of harmful event/exposure to nonconformity
  - Number of patients exposed
- Additional Risks
  - Nonconforming product risks
  - Duration of exposure to the population
  - Patient tolerance of risks
  - Risk factors for healthcare providers or caregivers

Assessing Decisions Based on Benefit-Risk Assessment Outcome

Factors:

- Uncertainty
- Mitigation
- Detectability
- Failure Mode
- Scope of the Device Issue
- Patient Impact
- Preference for Availability
- Nature of Violations/Non-Conforming Product
- Firm Compliance History

Identify & Assess Each Option

OPTION 1: XXX

FACTORS	STAKEHOLDER CONSIDERATIONS							
	CEO	Shareholder	Patient	Physician	Brand	Employees	Finances	FDA
Risk								
Benefit								
Timeline								
Resources								
Cost								

Compare & Rank the Options

Critical Decision Points	OPTIONS					
	1	2	3	4	5	
	Recall – Removal from Market	Retrieve clinical material	Recall - Correction	Cease mfg. and distribution	Mitigation only – no market or clinical trial action	Preferred Option Ranking
Key differences						
Primary Benefit						
Key Risks						
Probability of Success						
Cost implications						
PREFERRED OPTION						

Case Study Discussion #3 (cont'd): *Handout*

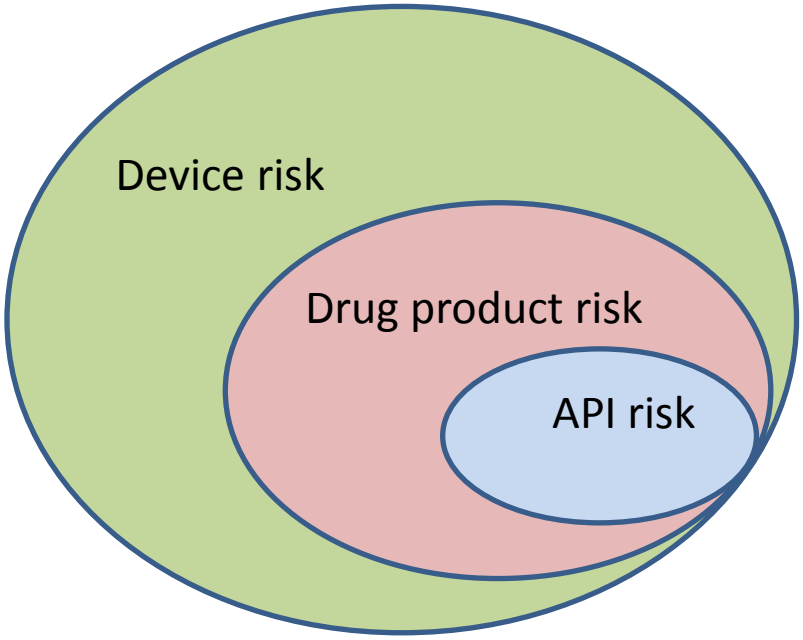
At Your Table

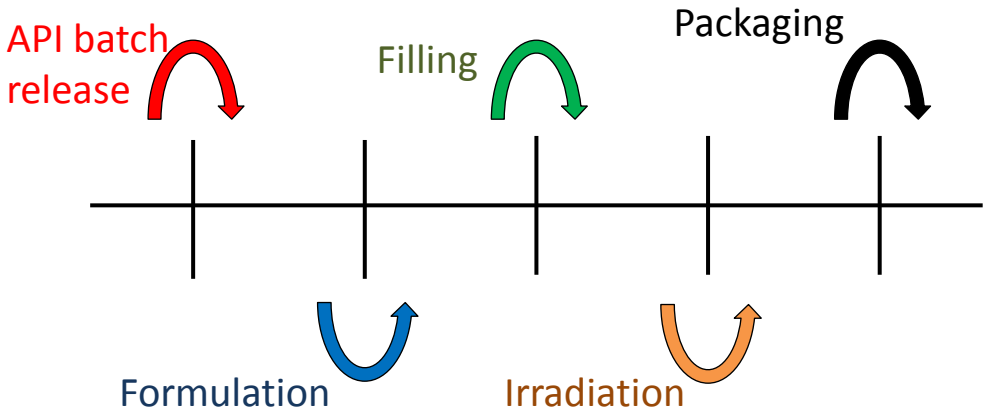
Create a visual of how you might describe the risks that have been discussed to this point in the case study.

Case Study Risks: A Visual …

Case Study Risks: A Visual (cont'd) …

How do these visuals capture the risks we've talked about so far?

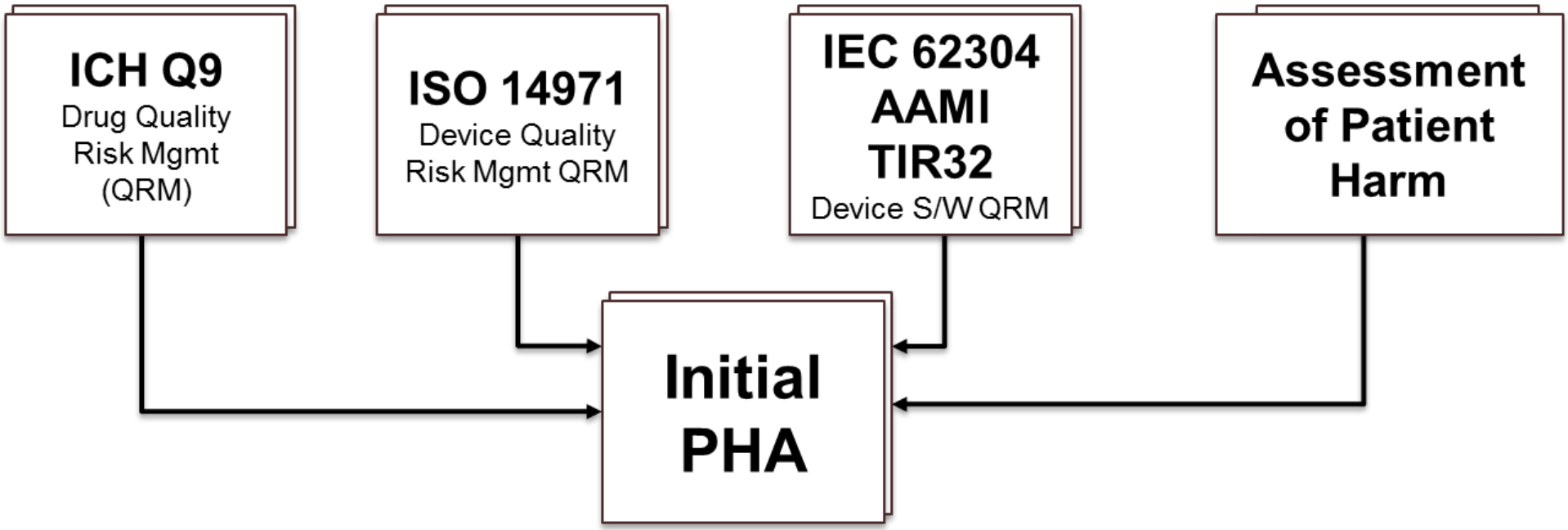




= Specifications met; approval to forward process

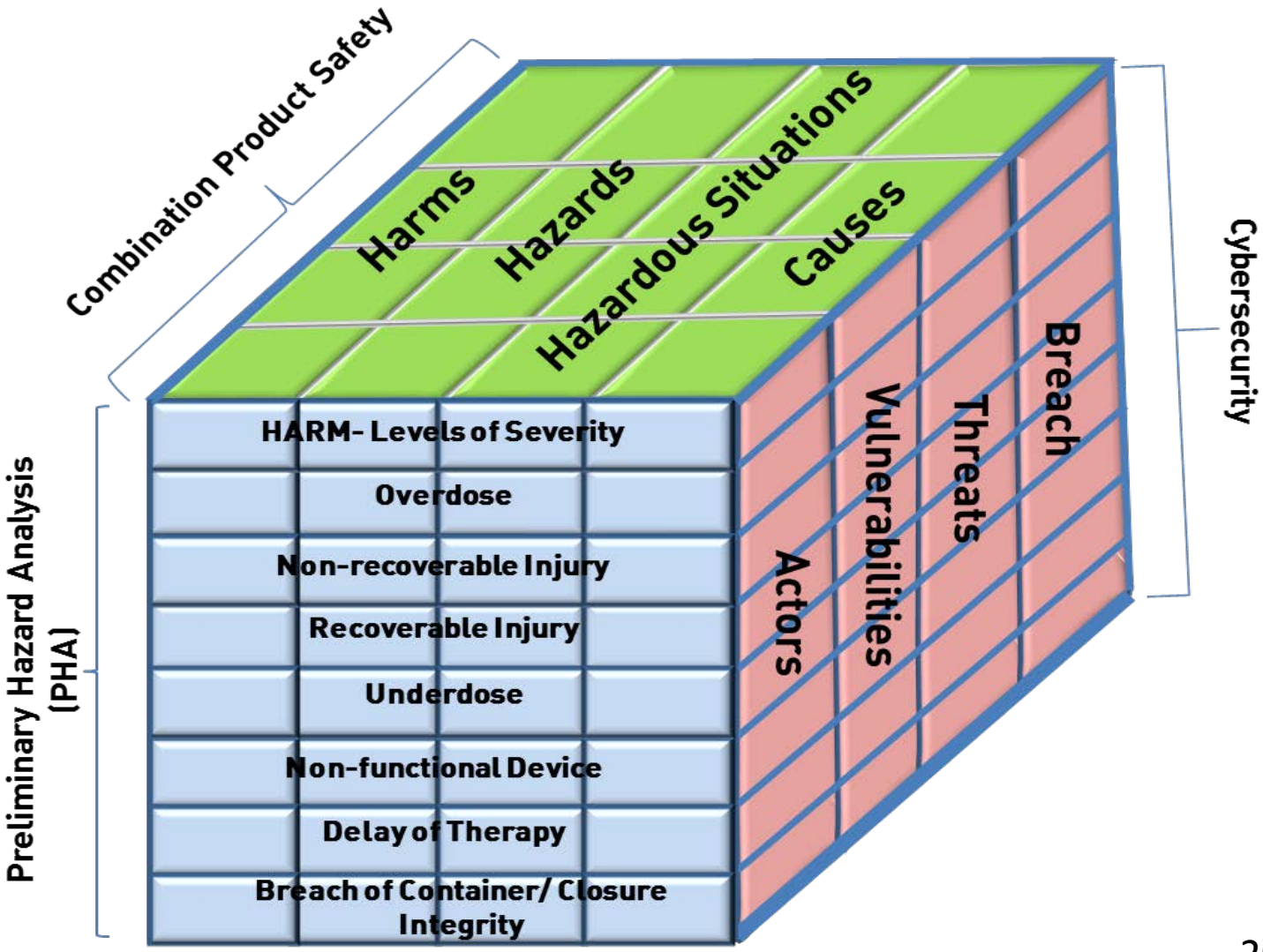
Case Study Risks: A Visual (cont'd) …

What about this visual?



Case Study Risks: A Visual (cont'd) …

What about this visual?



Case Study Risks: A Visual (cont'd) …

What about this visual?