



# The CDRH Recall Health Hazard Evaluation Process

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# CDRH's mission is:

Getting safe and effective devices to market as quickly as possible...



... while ensuring that devices currently on the market remain safe and effective.

# Center Responsibilities Include:

- Classify recall risk
- Provide scientific input for scientific decision-making
- Classify recalls
- Issue FDA Public Health Notifications
- Advise firms on execution of recall
  - Review “Dear Dr.” letters
  - CAPA’s



# Recalls- 2008

- In 2008, the number of recalls increased to 831
- Increase related to:
  - Product software
  - Devices containing tainted heparin

# IVD

- OIVD- problems with software are the third most-common IVD recall issue
- Many of the software problems could be avoided if companies performed proper real-world testing and improved validation activities
- Examples:
  - Lab information systems
  - Clinical information systems
  - Glucose meters- track and download data

# CDRH

- 11 Class 2 Recalls related to Heparin
  - Oxygenators
  - Catheters
  - Chest tubes
- IVD
  - Blood collection tubes
  - Blood gas capillary tubes
  - Heparin-lock syringes
  - Acetaminophen and other reagents

# HHE's are Conducted:

- When a device is recalled
- No appropriate precedent is available
- Likely Class I or high Class II recall
- Unique scientific or public health issues

HHE assumes no  
corrective action will  
be taken by the firm



# Assessing Likelihood

- It is often difficult to estimate frequency of defect and injury
- Information is limited and evaluation may be best estimate
- Past experiences with similar devices defects, and adverse event reports help clarify extent of risk

# Factors to Consider:

- Intended use
- Single vs. multiple-use
- User population
- Benefit/risk profile of product
- Technical characteristics of device
- Cause of failure
- Impact of device/failure on health

# Risk Assessment is Not Lowered because:

- Number of failures is within usual rate for device (if a specific corrective cause known)
- User error is cited as cause of problems
- Lack of injuries/deaths reported

FDA may assume the “worst case” if information is incomplete



It is important that HHE's are as accurate and timely as possible



The Medical Officer (OC; OIVD) is responsible for the clinical risk assessment when an HHE is conducted.

The Medical Officer also shares responsibility for the accuracy of background sections of form.

The Medical Officer may request an HHE Committee if one would be helpful, such as:

- Providing additional technical insight
- Broaden Medical expertise
- Expected high profile situation
- Major enforcement actions anticipated

# Defining the Risk

- Technical assessment of the defect defines likelihood of device failure
- Clinical understanding of product defect and real life situations clarifies risk
- Lack of reported injuries does not mean lower risk or recall classification

# Defining the Risk (cont.)

- Evaluation is conducted assuming no corrective action by firm
- Mitigating circumstances may be taken into account
- If information is incomplete may need to assume higher risk
- Look at population at greatest risk

FDA does not assume that the user will detect the problem before harm is done.

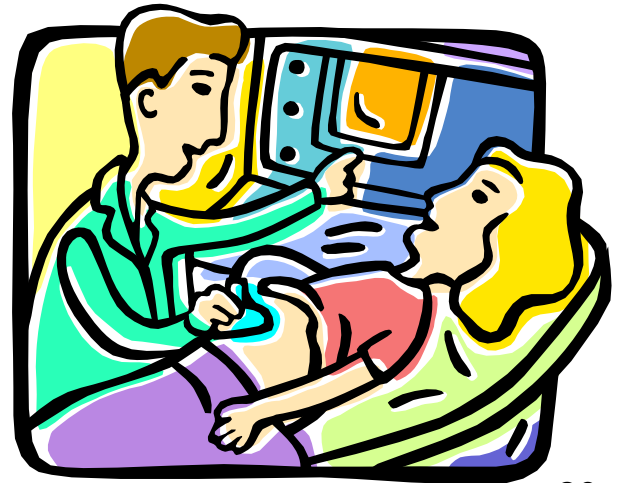
- Devices may not be examined or tested by the user
- IVD controls may not detect the problem
- Alarms may be misunderstood or ignored.

# Factors to Consider

- Intended use
- Single vs. multiple-use
- User population
- Benefit/risk profile of product
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Risk should be determined for the population at greatest risk. This may include children, pregnant women, seniors, critically ill patients or patients with specific medical conditions.



# Pediatric Population

If pediatric use and/or indication must consider:

- Size differences
- Metabolic differences
- Growth and development
- Human factors
- Behavioral and cognitive capabilities
- Implanted devices and surgical procedures
- Diagnostic tests and radiological devices

# When Completing the HHE

- Think broadly when identifying and assessing device defects.
- Assume the “worst case” if information is incomplete.
- Note any assumptions made during the assessment.

There are no quantitative rules to define “Reasonable Probability” vs. “Remote”



# Examples of Serious Injury:

- A fractured bone, loss of digit or tooth
- Infections such as hepatitis or pneumonia
- Diminished hearing or vision that (without correction) affects daily life
- Infertility
- Abnormal blood levels requiring hospitalization
- Chronic pain

# For HHE purposes risk/injury may include:

- Significant psychological distress
- Errors or delays in patient management
- Need for additional surgery/future surgery as a result of device malfunction
- Need for medical intervention as a result of device malfunction

# Common Problems with HHE's

# Form Not Properly Completed

- Write up is too brief
- Lack of explanation
- Unclear comments
- Hand written / illegible
- Lack of clinical input

# Problems with Content

## Inconsistencies within form

- Comments in different sections don't agree
- Boxes checked don't agree with written comments
- Final assessment does not reflect health consequences described

# More Problems with Content

- Scope of consequences included is very incomplete
- Risk assessment lowered based on proposed fix or actions by firm
- Risk assessment lowered due to small number of devices involved
- Failure to consider risks from re-surgery
- Failure to clarify key assumptions made

# Description of Health Consequences Does Not Match Hazard Assessment

**A. Describe the Immediate and Long Range Health Consequences (Injuries or Illnesses) That May Result from Use of or Exposure to the Defective Device. (Include Known Off Label Uses)**      Joint mobility limitation, need for secondary surgical procedure.

**Check All that Might Occur:**

Population at Greatest Risk	Overall Population Using Device	
<input type="checkbox"/>	<input type="checkbox"/>	Life-threatening (death has or could occur)
<input type="checkbox"/>	<input type="checkbox"/>	Results in permanent impairment of body function or permanent damage to a body structure.
<input type="checkbox"/>	<input type="checkbox"/>	Necessitates medical or surgical intervention.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Temporary or reversible (without medical intervention).
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Limited (transient, minor impairment or complaints).
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	No adverse health consequences.

# Example:

## Heparin-Related Risk Assessment

Heparin-related risk assessment:

- Clinical studies evaluating relationship between oversulfated chondroitin sulfate (OSCS) contamination and clinical performance for select chemistry analytes

Analyte	Study Range	Without OSCS	With OSCS
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Cl (mmol/L)	103 – 118	108.1 ± 3.5	108.4 ± 3.6
Chol (mg/dL)	134 – 275	194.5 ± 32.1	195.0 ± 32.3
CK (U/L)	43 – 398	130.6 ± 89.2	130.0 ± 89.4
Creat (mg/dL)	0.8 – 1.3	1.00 ± 0.13	0.99 ± 0.13
CKMB* (U/L)	1 – 10	3.6 ± 2.7	3.5 ± 2.6
Fe (µg/dL)	22 – 190	92.6 ± 34.9	92.5 ± 34.6
Ferritin (ng/mL)	5.8 – 506.9	43.27 ± 79.67	43.81 ± 81.88
Free T4 (ng/dL)	0.58 – 1.66	0.927 ± 0.200	0.927 ± 0.195
GGT (U/L)	10 – 78	26.1 ± 14.8	25.8 ± 15.0
Glob (g/dL)	2.5 – 4.2	3.03 ± 0.35	3.03 ± 0.37
Glu (mg/dL)	59 – 274	97.9 ± 33.5	98.3 ± 33.9
HDL (mg/dL)	20 – 104	54.7 ± 16.6	54.6 ± 16.8
LDH (U/L)	317 – 726	459.3 ± 79.4	457.4 ± 81.1
Mg (mg/dL)	1.7 – 2.4	2.13 ± 0.14	2.13 ± 0.14
Phos (mg/dL)	2.5 – 5.0	3.61 ± 0.63	3.61 ± 0.64
K (mmol/L)	3.6 – 4.7	4.28 ± 0.27	4.26 ± 0.26
Mg (mg/dL)	1.7 – 2.4	2.13 ± 0.14	2.13 ± 0.14
Na (mmol/L)	140 – 156	146.7 ± 3.1	146.8 ± 3.2

Analyte	CAL	Mean Bias (95% Limits)	Clinical Equivalence (yes or no)
ALB	± 5%	0.1 (-0.3, 0.5)	Yes
ALKP	± 10%	0.1 (-0.4, 0.6)	Yes
ALT	± 10%	-0.6 (-2.9, 1.6)	Yes
AST	± 10%	-0.4 (-1.0, 0.2)	Yes
Amy	± 10%	0.5 (-0.4, 1.5)	Yes
BUN	± 3 mg/dL	0.1 (0.0, 0.2)	Yes
Ca	± 0.4 mg/dL	0.02 (-0.01, 0.05)	Yes
Chol	± 5%	0.3 (-0.1, 0.7)	Yes
Cl	± 3 mmol/L	0.3 (0.1, 0.6)	Yes
CO2	± 10%	-0.7 (-1.5, 0.2)	Yes
Creat	± 0.3 mg/dL	-0.01 (-0.02, 0.00)	Yes