

Sterility Assurance & Quality Risk Management Conference



PDA[®]
Parenteral Drug Association
Midwest Chapter



Do's and Don'ts with Product Risk Management

Thomas M. Heckmann, P.E

October 25, 2023



Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



Agenda

- **Introduction**
- **Risk Management**
- **Some Dos and Do Nots**
with
- **Tales of Weal and Woe**
- **Discussion / Questions**

Disclaimer:

- *Statements and opinions given here are my own, and may not represent the position of Baxter or any other organization*
- *Topics presented are anonymized or available in the public record*
- *Images are used with attribution or are not copyrighted in the public domain*
- *Presentation content not to be reproduced except in entirety*
- *Any case-studies are “Monday-morning-quarterbacking” and based upon incomplete information – not to second-guess behaviors at time or trying to identify culpability, fault, etc. – rather, my intent is to learn from past to help improve safety for everyone in the future*

Introduction





About me

- **Thomas M. Heckmann, P.E.**
- Sr. Principal Engineer, Quality Operations / Element Steward GQR-10, Product Risk Management
- Located in Buffalo-Niagara region of New York
- Serving Baxter since November 2015
- Licensed Professional Engineer (P.E.) since 2003
- Senior Member IEEE
- BS Engineering Physics (Electrical Engineering and Physics) from SUNY at Buffalo
- Prior experience in Research, Product Development, Manufacturing, Forensic Analysis, Laboratory Operations, Global Regulatory Compliance, Quality Management, and 3rd party Quality/Health/Safety/Environmental Certification

Statements and opinions given here are my own, and may not represent the position of Baxter



My Day Job

✓ My Function is Element Owner/Steward for QMS Element 10 – Product Risk Management

✓ Primary responsibilities

An element steward is assigned to each QS element as the lead Subject Matter Expert. Element Stewards are responsible for the following:

- Develop and maintain quality processes and systems that meet customer and regulatory requirements
- Drive consistent deployment of their QS element
- Provide guidance around their QS element
- Ensure alignment throughout the organization through global input/interaction
- Drive continuous improvement and implement best practices
- Ensure process implementation applies a risk-based approach, as appropriate

The Quality System Element develops/revises content with input from global subject matter experts



Sterility Assurance & Quality Risk Management Conference

Steward:

- We cannot have wide open processes leading to wild behavior
- We cannot smother the business with strict administration
- We must curate a middle way with balanced and interconnected processes to allow adaptation and efficiency operation to enable a broad portfolio of safe and approved products

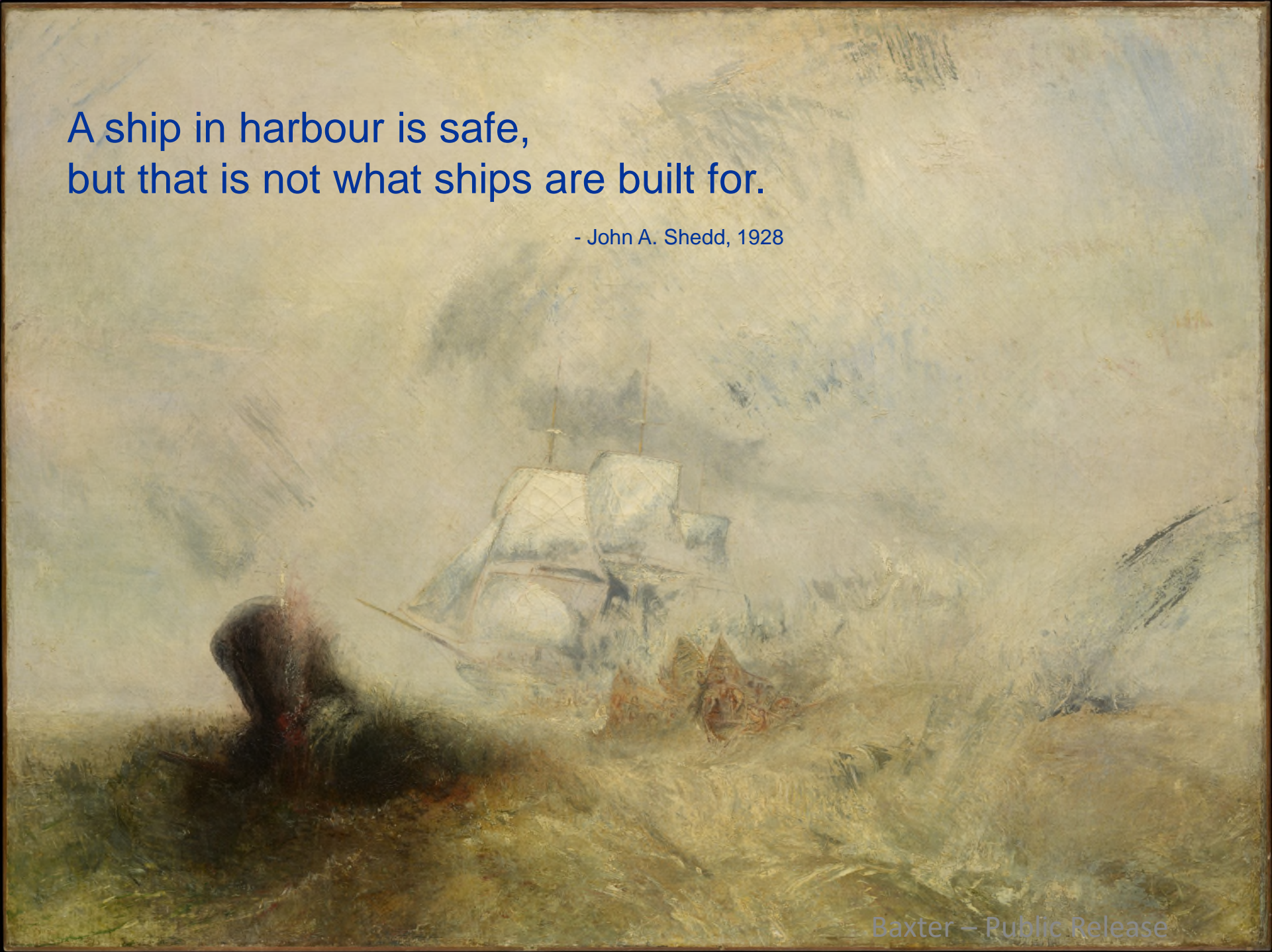




Risk Management

A ship in harbour is safe,
but that is not what ships are built for.

- John A. Shedd, 1928



1845 "Whalers" by
Joseph Mallord
William Turner

Metropolitan
Museum of Art
(United States)

Royalty Free Image
from useum.org



What kind of Risk are we talking about?

The **product** must be of **benefit** when **weighed** against the **risks**.

Medical
Products

Medical
Benefit

Judged by
Persons
qualified by
education
and
experience

Considering the
residual risks
(acceptable
only after
mitigations
reduce risks as
far as possible)

Or else the product cannot be put on the market!



Evolution of Safety Standards

- BASIC SAFETY – Straightforward – Follow Code
 - Fire
 - Electric Shock
 - Mechanical Injuries (sharp points/edges)
 - Toxins
 - High Temperatures, High Pressures
 - Other Energy (Lasers, Audio levels)
- ESSENTIAL PERFORMANCE – Tricky
 - Need to cause 'harm' to cure
 - Innovation needed
 - “Compliance is checked by inspection of the Risk Management File”



Risk Management in Standards

- ✓ Example: IEC 60601-1 Medical Electrical Equipment – Part 1: General requirements for basic safety and essential performance
- ✓ Risk Management is used throughout the standard
 - “*the Risk Management File*” is used 226 times in consolidated version; discounting redline (duplicates), and information, around 100 uses
 - “*Compliance is checked by inspection of the Risk Management File*”, 30 times in the Blackline version
 - Typical entries:

12.1 Accuracy of controls and instruments

When applicable, the MANUFACTURER shall address in the RISK MANAGEMENT PROCESS the RISKS associated with accuracy of controls and instruments.

Compliance is checked by inspection of the RISK MANAGEMENT FILE.

11.6.8 * Compatibility with substances used with the ME EQUIPMENT

When applicable, the MANUFACTURER shall address in the RISK MANAGEMENT PROCESS the RISKS associated with compatibility with substances used with the ME EQUIPMENT. Such RISKS may be addressed through the application of appropriate ISO or IEC standards (giving the presumption of acceptable RISK according to 4.2) such as ISO 15001 [70] for components that contain oxygen at pressures greater than 50 kPa or through the MANUFACTURER’S own testing and RISK CONTROL measures.

Compliance is checked by inspection of the RISK MANAGEMENT FILE.



Common Sense?



- “Isn’t Risk Just Common Sense?”



Do Remember that Risk Management Files Must Communicate Risks to Stakeholders

Risk Files must 'Tell the Story' of Safety

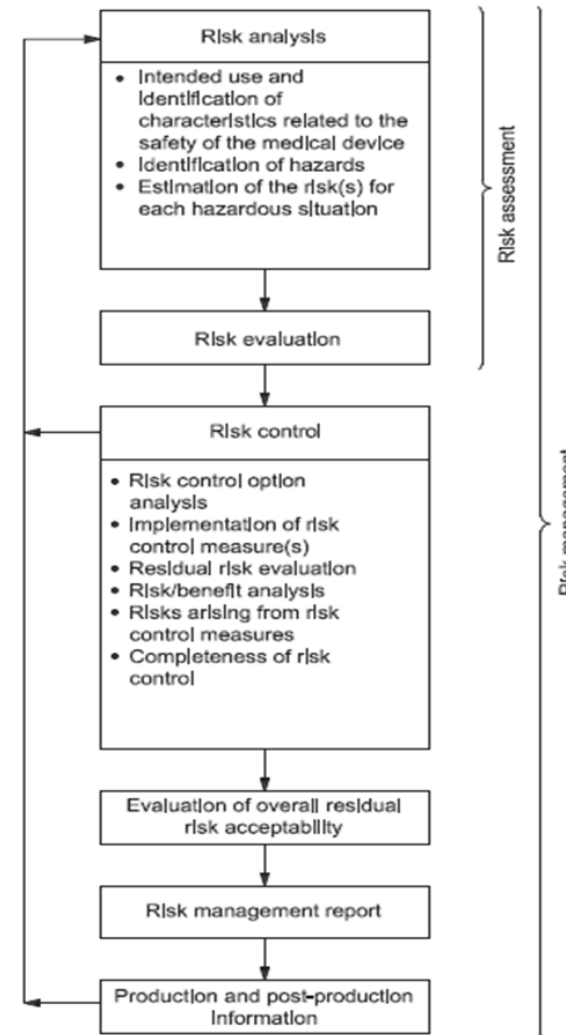


“Can I go to my friend’s house?”



- You’re the Mom.
- Yes or No, is it safe for her to go to her friend’s house?

What are the Risks? Are they acceptable?





Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



Hazards?

- Could injure feet walking.
- Could get lost walking journey.
- Could get wet in Rain/Snow Storm.
- Could get mugged/assaulted.
- Could get hit by traffic.
- Could arrive destination late.

Severity 3

Severity 4

Severity 2

Severity 5

Severity 5

Severity 1

ACCEPTABILITY CRITERIA – BECAUSE MOM SAYS SO!

MONITORING – Chris's parents will call Mom.

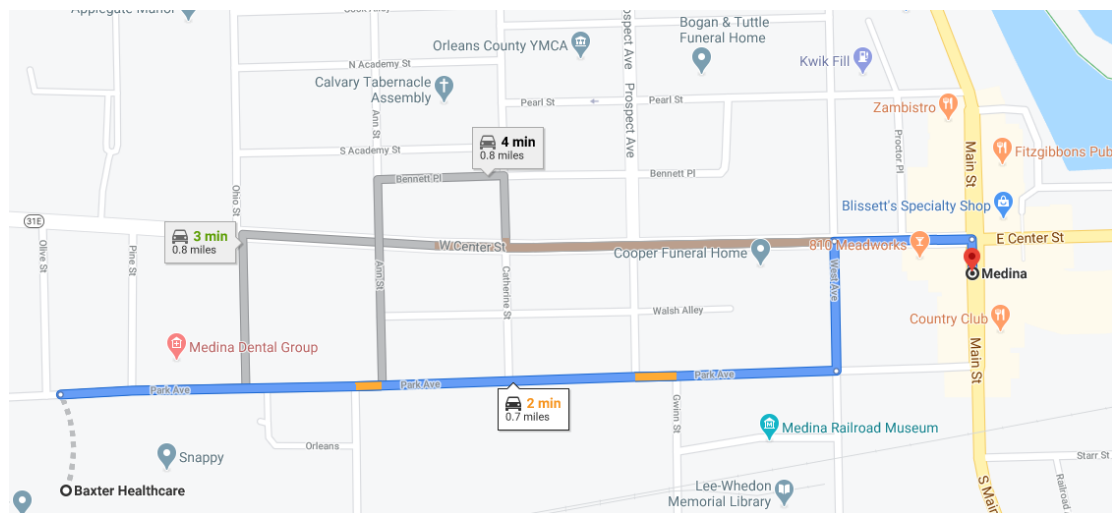


Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



“Can I go to my friend’s house?” Analysis?



Failure Modes & Causes And Effects:

Daughter takes wrong way

Daughter slips/trips/has problems walking

Daughter not able to cross the street properly

Acts of God (Weather)

Stranger Danger / Criminals

Construction sites

Leave too late (dark)



k25712761 fotosearch ©



Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



Risk Controls?

“I know the way, Ma!”

- ↑ Head east on Park Ave toward Pine St
0.1 mi
- ↶ Turn left onto Ohio St
0.1 mi
- ↷ Turn right onto W Center St
0.5 mi
- ↷ Turn right onto Main St
125 ft



“No crossing busy streets!” or “Wear a coat!”

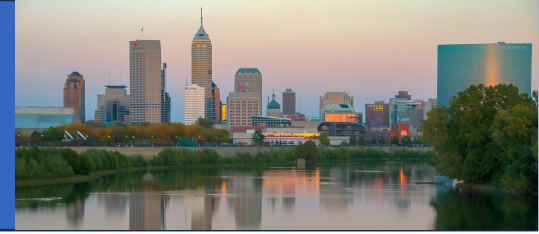
“Call or get a ride home if after dark”





Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



Unacceptable/Unneeded Risk Controls?

Risk of overheating, loss of peripheral vision,
loss of mobility



- A Christmas Story (1983) MGM

Stranger Danger / Criminals





Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



BENEFIT?

Clinical Risk Benefit Analysis

“Why should you be allowed to go to your friend’s house?”

- Good for child’s happiness, socialization and development
- Get some peace and quiet for Mom
- Mom doesn’t have to drive

“Fine you can go! Be back before dark.”



Follow On

Do Not Ignore Risk Management File when Writing Plans and Reports

Communicate! Work together...
Clinical design goals align with Risk



Do Standardize Hazardous Situations and their Harms

The Clinical focus on these



Severity of Harm modeling systems

ISO 14971:2019 Clause 5.5:

“The system used for...categorization of...*severity of harm*...shall be recorded in the *risk management file*.”

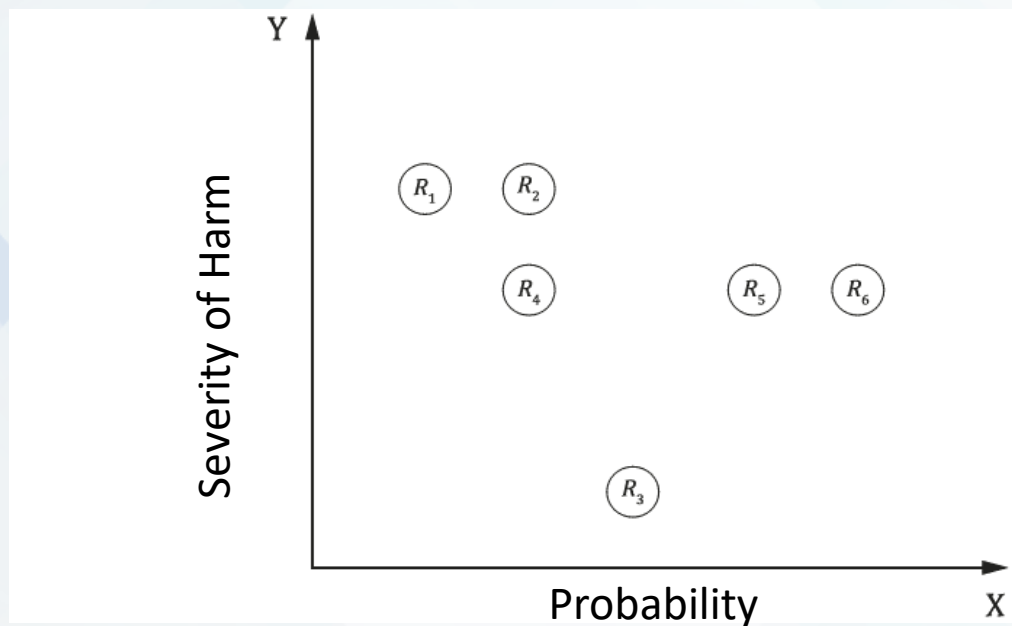
- **Manufacturers are responsible for identification of any system of their choice*** (*that works best for them)
 - Needs to function within their company
 - Needs to allow manufacturers to make wise decisions
 - Needs to allow manufacturers to innovate and adapt
 - Needs to help manufacturers to make safe products
- The system chosen **shall categorize the harms**
 - Categories by ‘level’ or ‘range’ enable consistent analysis
- The system **shall be recorded**
 - This enables communication to internal company functions that all use the risk model
 - The system is communicated to regulatory authorities in documents



TR 24971 Medical devices – Guidance on the application of ISO 14971

Informative Technical Report

Example



Plotting Severity of Harm on Y axis implies a continuous value, but placement of risk points implies discrete values. “Severity is, in reality, a continuum; however, in practice, the use of a discrete number of *severity* levels simplifies the analysis.”



TR 24971 examples

Table 2 — Example of three qualitative *severity* levels

Common terms	Possible description
Significant	Death or loss of function or structure
Moderate	Reversible or minor injury
Negligible	No injury or slight injury

Table 4 — Example of five qualitative *severity* levels

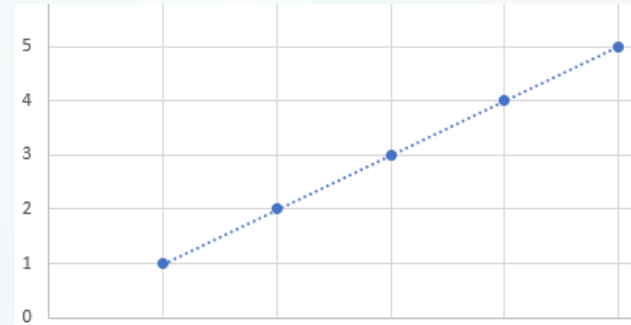
Common terms	Possible description	
Catastrophic / Fatal	Results in death	5
Critical	Results in permanent impairment or irreversible injury	4
Serious / Major	Results in injury or impairment requiring medical or surgical intervention	3
Minor	Results in temporary injury or impairment not requiring medical or surgical intervention	2
Negligible	Results in inconvenience or temporary discomfort	1

Definitions and levels are common, simple numbers can be used for levels



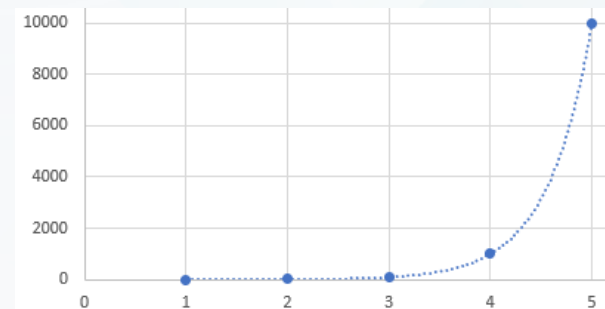
Limits with Simple numbers in Risk model

Linear?



No! Clearly five harms of level 1 severity are not the same as one 5+

Exponential?



Level 1 and Level 2 harms irrelevant, 3 pales in comparison to 4, 5

Mathematical operations on these categories are model abstractions that may not be meaningful or appropriate.



Problems with Simple numbers in Risk model

Can one number represent the result for a Hazardous Situation appropriately?

Example:

10 million units in field. 1000 complaints of event of Hazardous Situation
'Sharp Point at X' occurring to patient in the field.

Careful Study of the events of the same exposure of Hazardous Situation find:

- 887 patients had no injury observable, but reported the exposure to the H.S.
- 100 lacerations occurred to patients' limbs, needing only adhesive bandage
- 10 lacerations occurred to patients' limbs, needed reapproximation (surgical closure of wound) and sutures to prevent scarring
- 1 patient had arterial bleeding and needed blood transfusion and surgery
- 1 patient died, possibly of heart attack

What Number / Level represents the proper Severity of Harm to use in a Risk Model for Hazardous Situation 'Sharp Point at X' in this Case?

More Detailed Models of Severity of Harm may be More Useful in this case.



Not Every Exposure to a Hazardous Situation has the same result

Many people may be 'exposed to' a toy on the steps,
Few people will suffer the harm of fall and injury of broken bones



Hazardous Situation

The circumstance in which people are exposed to hazards

Harm

The injury or damage to people, property, or the environment



An Implementation: Three Ranks of Harms

Severity Rating	Harm Severity Description
Critical	Death, permanent impairment of function...etc.
Moderate	Temporary or non-life-threatening impairment...etc.
Minor	Results in no harm, or a temporary impairment that does not require additional medical interventions ...etc



Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



An Implementation of Seven Ranks of P2

Each Level of Harm has a P2 Probability Rating Term established, which also represents a mathematical range

Probability Rating Term	Qualitative Definition	Percentage Range
Expected	This is the outcome that will occur the majority of time	> 50% - 100%
Likely	This a frequent outcome	> 24% to < = 50%
Often	This outcome is expected to occur regularly	> 10% to < = 24%
Periodic	This outcome it expected to occur intermittently	> 1% to < =10%
Occasional	This outcome may occur	> 0.01% to <= 1%
Rare	This outcome is unlikely	> 0.0001% to <= 0.01%
Exceptional	This outcome is extraordinary	> 0 to <= 0.0001%



Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



Result

Table for each medical therapy, identifying the hazards, list of hazardous situations and classification of severity of harms to be considered for risk evaluation

Example Hazard, Hazardous Situation list with scored Harms:

Risk Identification (Therapy Level)		Risk Analysis (Therapy Level) (P2)		
Hazard	Hazardous Situation	Critical	Moderate	Minor
A	A1	Exceptional	Rare	Expected
A	A2	Rare	Expected	Often
A	A3	Expected	Likely	Often
B	B1	Exceptional	Likely	Expected
B	B2	Exceptional	Occasional	Expected
C	C1	Exceptional	Periodic	Expected
D	D1	Occasional	Likely	Expected
D	D2	Likely	Expected	Often



Follow On

Do Not
Overclassify the Severity of Harms for
Hazardous Situations

Overly conservative scoring does not lead to a safer product



Follow On

Do not define your Hazardous Situation Ranges down to Zero

At some level (band) there is no hazard

The background consists of a complex pattern of overlapping triangles in various shades of blue, ranging from light sky blue to deep navy blue. In the top right corner, there is a small, semi-transparent inset image of a city skyline, likely New York City, with the Empire State Building prominent, reflected in a body of water.

Tales of Weal and Woe



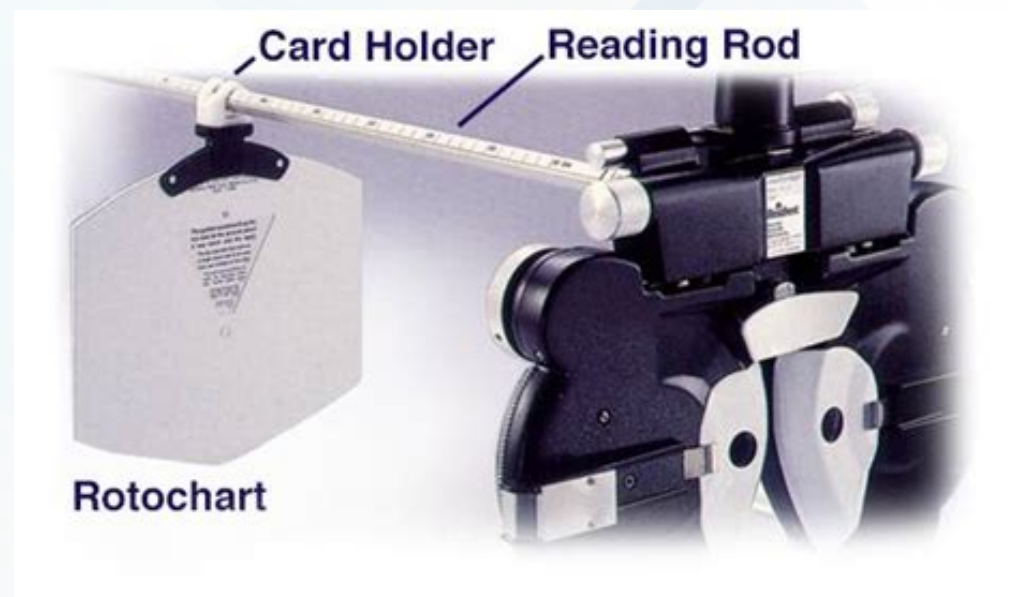
Do use the FDA Recall database to look at similar / competitive products

Learn from other's mistakes



The Tale of Heal Thyself Eye Doctor

- New Product Planned
- Performed Risk Analysis
- Identified Competitor Recall for issue
- Added foreseen risk in Risk Analysis
- Two mitigations
 - Fortify the mechanism
 - Improve the tip
- Successful product launch with no delays



Do learn from others
Do capture as foreseen risk
Do mitigate



Do Not Over Mitigate

Excessive Risk Controls can introduce risks



The Tale of Mitigating the Mitigating

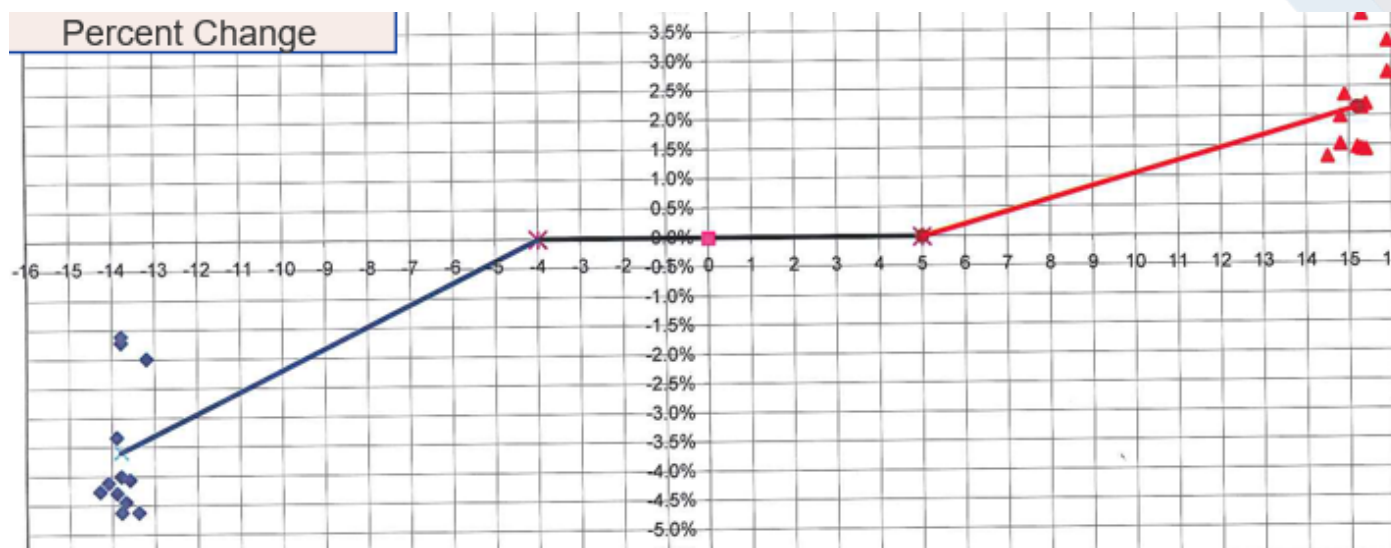
- Legacy fluid pumping device
- Had complaints related to an alarm code
- Alarm code to detect (mitigate) if two temperature sensors disagreed



Complaints of Alarm Stopping Fluid Flow



Tale of Mitigating the Mitigating



- First Temperature Sensor Compensated (Mitigation) for Temperature Error
 - Data showed that ambient temperature can cause error in accuracy
- Second Temperature sensor monitored the first, as a Risk Mitigation to the failure of the first Mitigation
 - If the temperature monitor disagreed during monitoring, Alarm and Stop



Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



- **Basic Safety & Essential Performance**

- Life saving / Life Sustaining
- Risk if doing something; risk if doing nothing.



You'll be "damned if you do, and
damned if you don't."

— *Eleanor Roosevelt* —

AZ QUOTES

"DO WHAT YOU FEEL IN
YOUR HEART TO BE RIGHT
- FOR YOU'LL BE
CRITICIZED ANYWAY.
YOU'LL BE DAMNED IF YOU
DO, AND DAMNED IF YOU
DON'T."

ELEANOR ROOSEVELT

NobleQuotes.com



The Tale of Mitigating the Mitigating

- Analysis showed LESS risk to NOT monitor the primary inaccuracy monitor with secondary monitor. Allow the primary monitor to function with other controls in place
- Primary monitor was reliable with self-tests; external monitor
- Result – Next gen product removed monitor of monitor from system
 - Lower Risk
 - Fewer complaints
 - Saved \$

**Do Not mitigate to excess, or incorrectly
Do assess mitigations for new risks
Fewer mitigations decreased risk in this case**



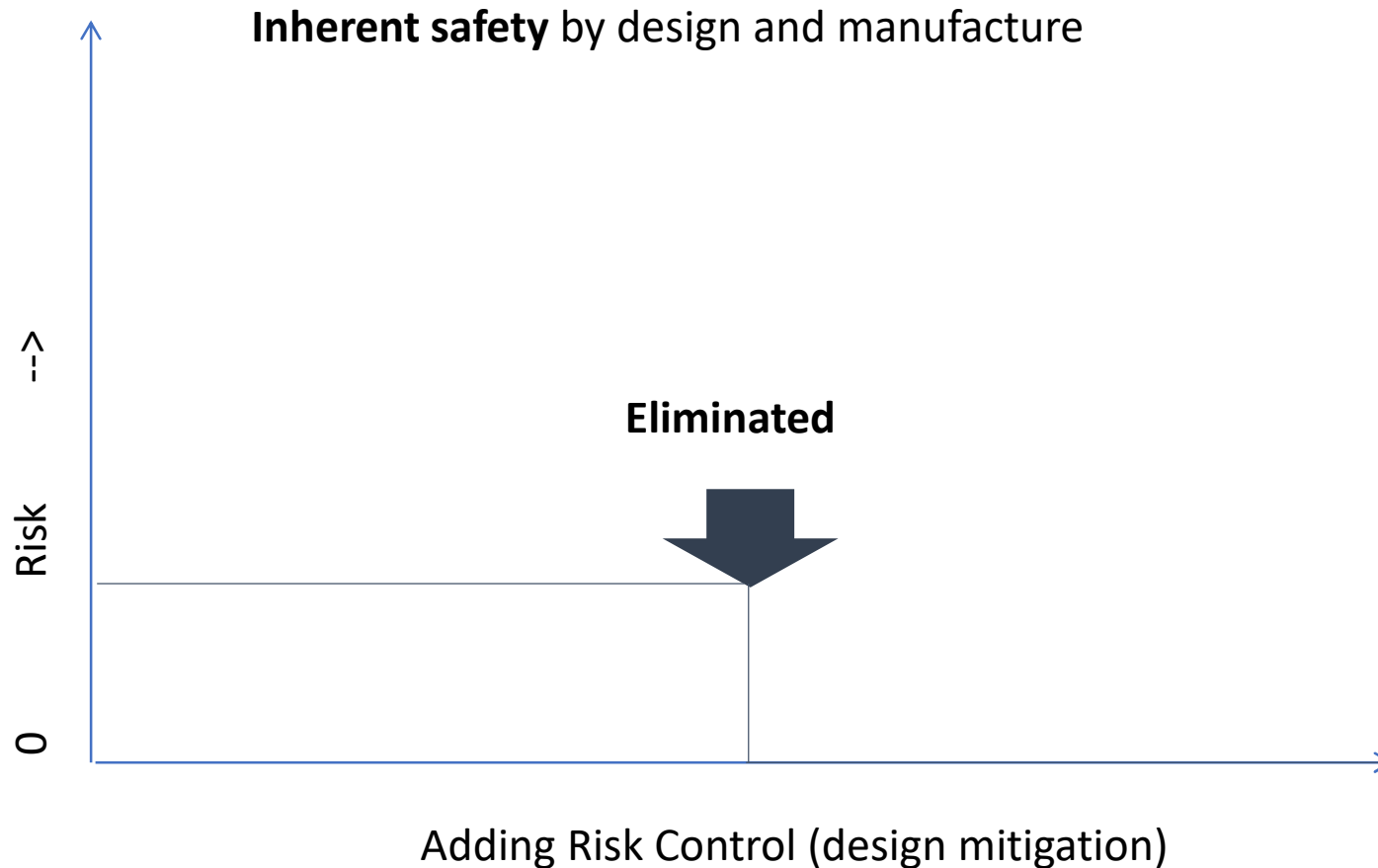
Follow On

Do Understand
how to mitigate As Far As Possible

What degree of controls is sufficient?

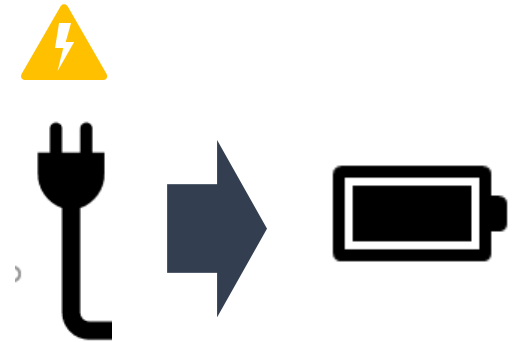


Risk Reduction Methods



Hazard is removed or cannot occur by design.

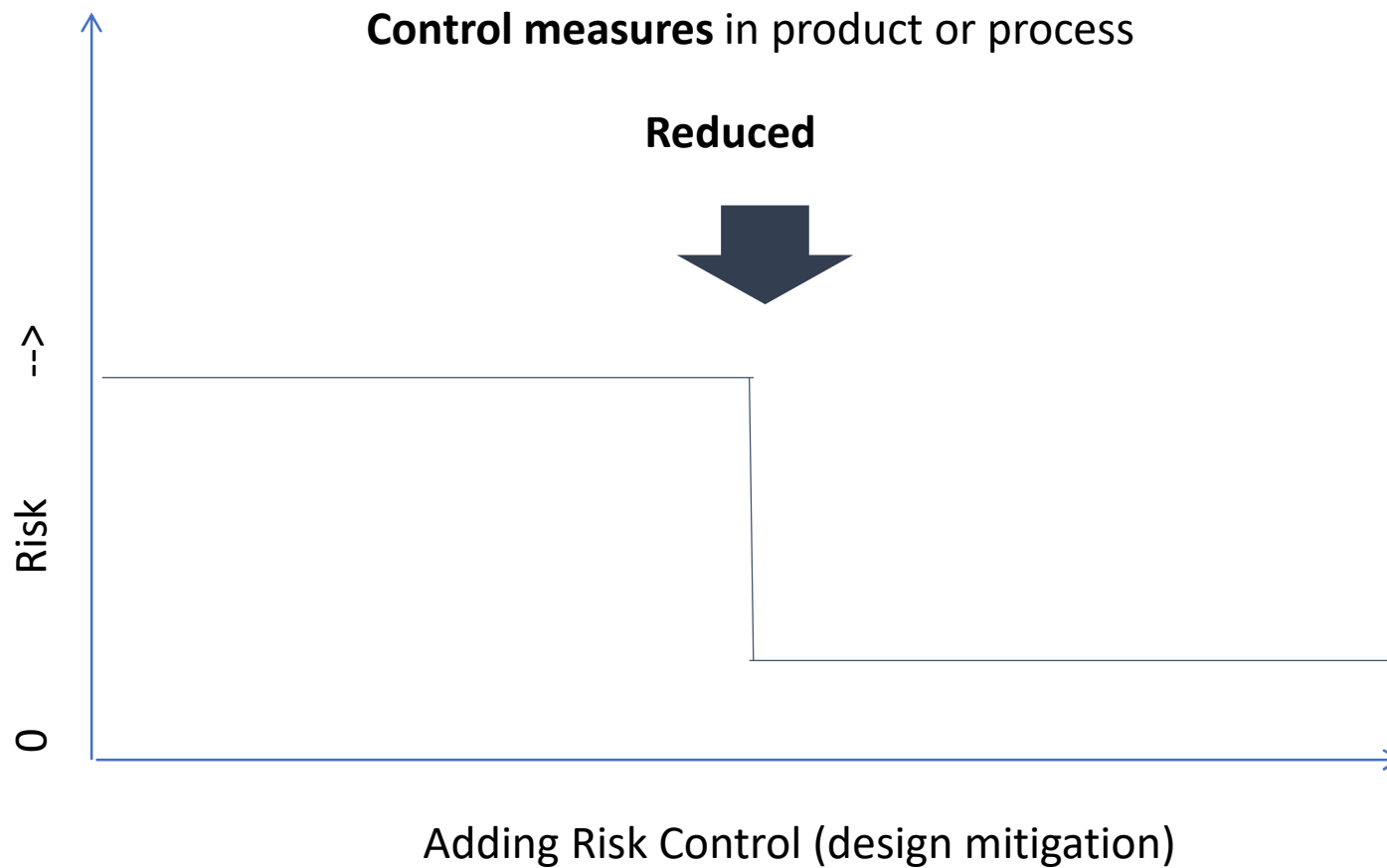
Applies when risk is no longer reasonably foreseeable by product's inherent properties



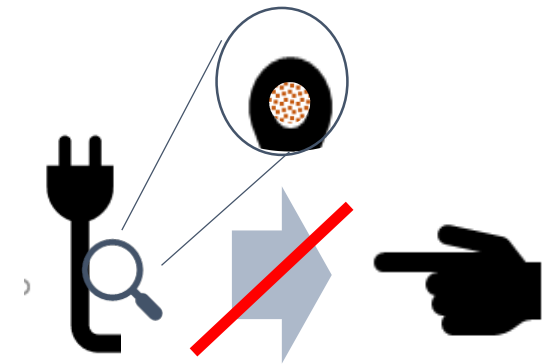
Example: Design with an alkaline battery power eliminates risk of electric shock from AC power.



Risk Reduction Methods



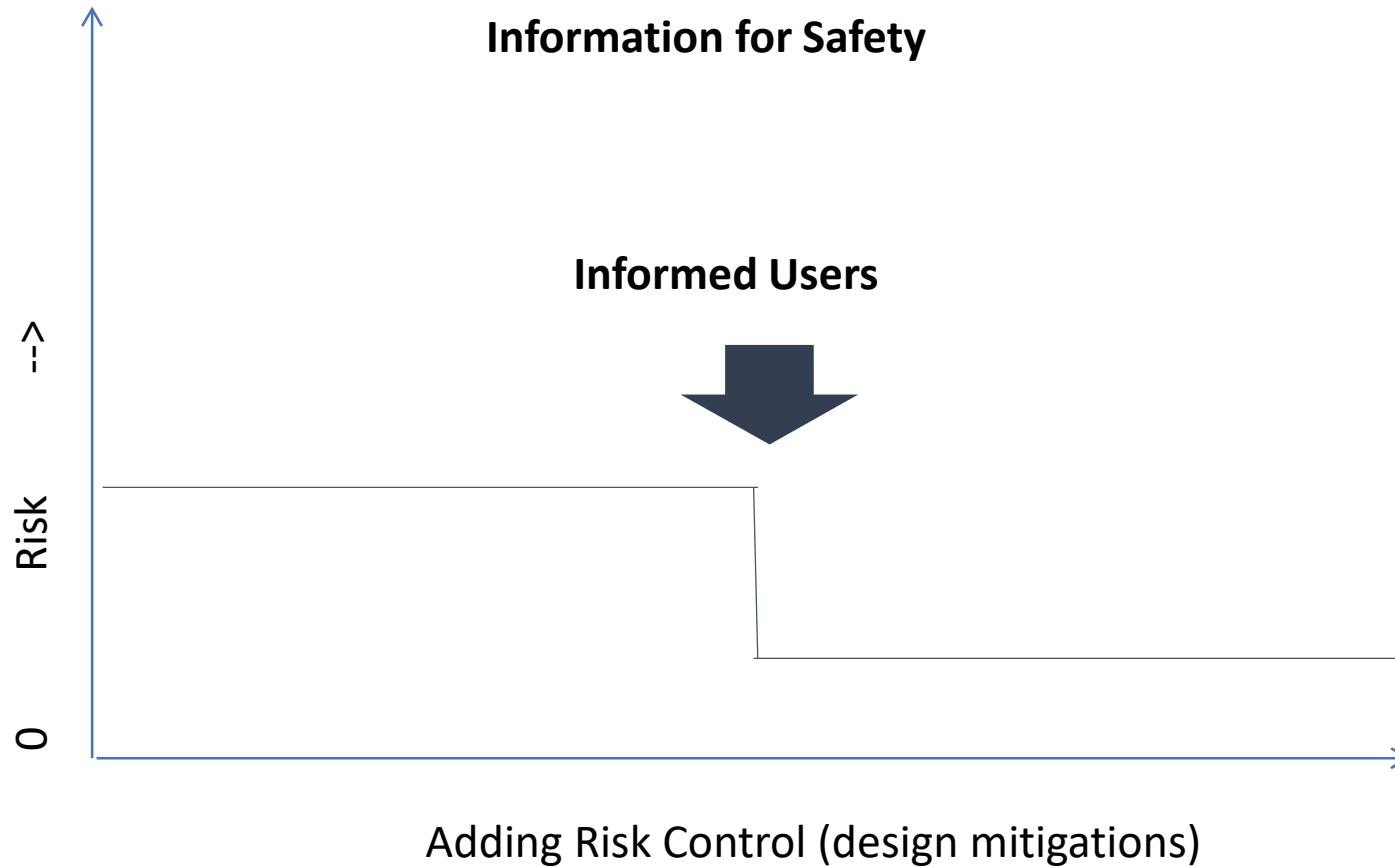
Most typically control measures are applied. Control measures can reduce the risk. Controls measures that apply to process can reduce risk of defects.



Example electrical insulation is a risk control to reduce the risk of electric shock.

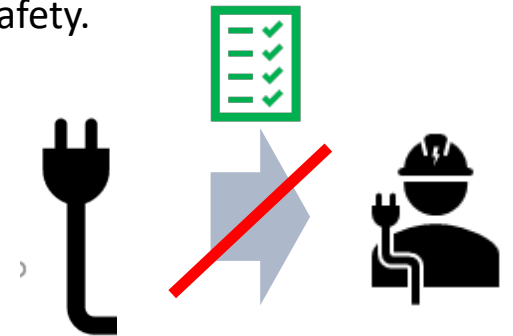


Risk Reduction Methods



Information for Safety (Labeling, Training) can instruct users on behaviors to be aware of residual risks.

Trained and educated users benefit from more complete information for safety.



Example: warnings, procedures, and training helps service personnel avoid the hazard of electric shock.



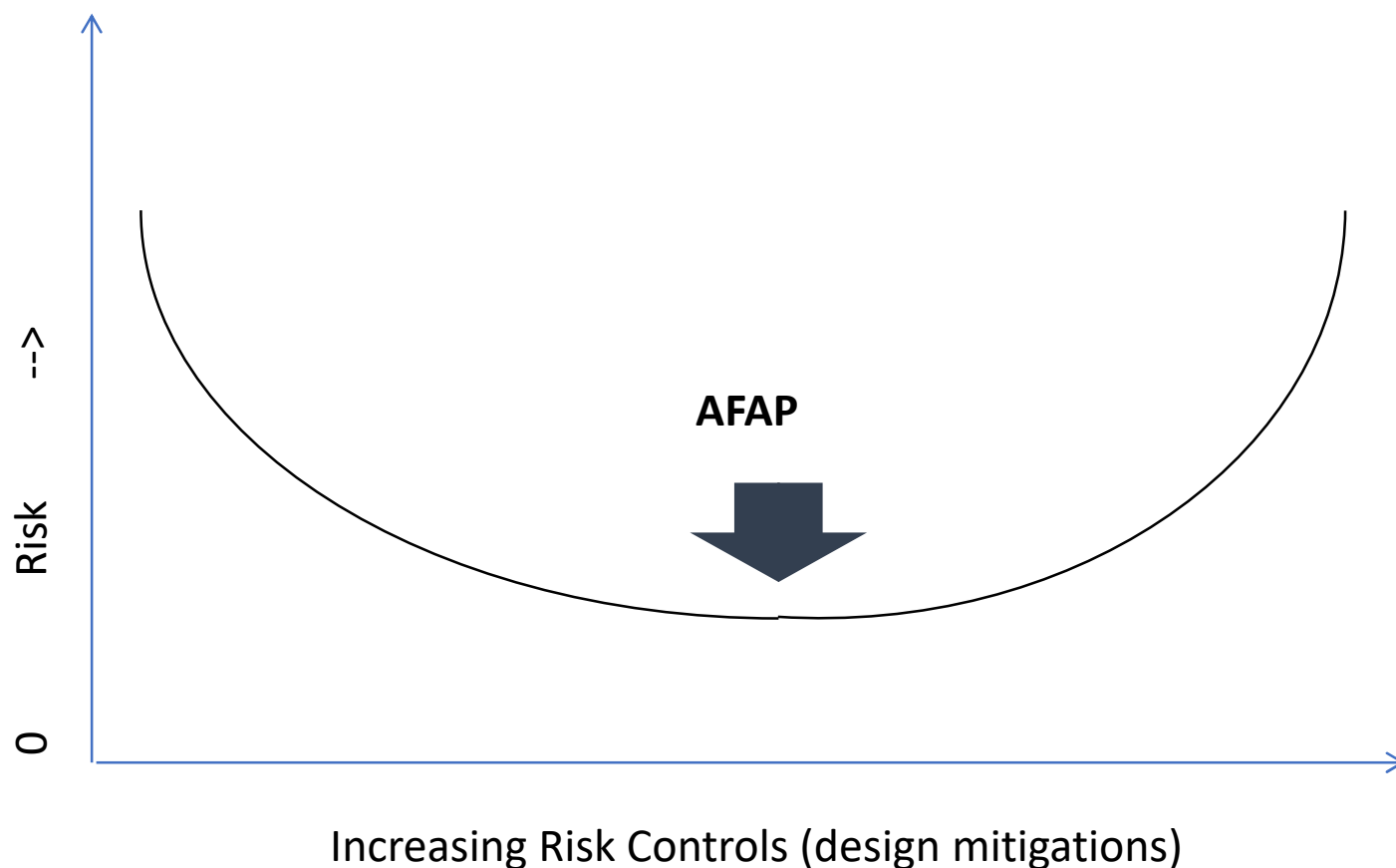
Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



Risk

Reduce risk “As Far As Possible” - AFAP



AFAP does not mean infinite risk mitigation, rather, the right amount of mitigation

Adding too many mitigations can increase risk

...from usability complexity, loss of reliability, more failure modes, deskilling, unexpected behavior




Follow On

Do not associate All Alarms with Malfunctions if not appropriate

Some Alarms are related to normal function

Do use Risk Management to manage Alarm prioritization



Do not 'Systems Engineer' the Risk Management File overmuch

Overdoing a risk file makes it hard for others to comprehend



Did a Survey for speaking topics

Topic	Votes:	1 (least)	2	3	4	5 (most)
A		0	0	4	2	0
B		1	1	4	0	0
C		0	0	4	2	0
D		1	0	2	1	2
E		1	2	0	2	1
F		1	0	3	1	1
G		0	2	1	1	1
H		0	0	4	1	1
I		2	1	2	1	0
J		1	1	3	1	0
K		1	0	1	2	2
L		2	1	1	0	2
M		1	1	0	1	3
N		1	0	2	2	1



Weighted the Results by Vote Preference

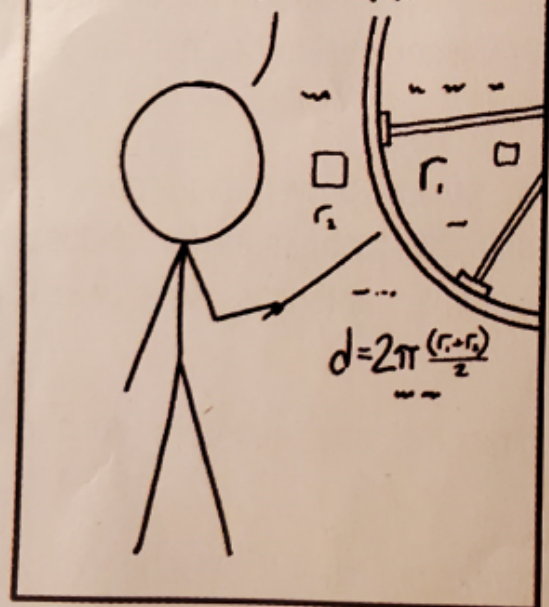
	1x(least)	2x	3x	4x	5x (most)	SUM	Rank
A	0	0	12	8	0	20	3
B	1	2	12	0	0	15	8
C	0	0	12	8	0	20	3
D	1	0	6	4	10	21	2
E	1	4	0	8	5	18	5
F	1	0	9	4	5	19	4
G	0	4	3	4	5	16	7
H	0	0	12	4	5	21	2
I	2	2	6	4	0	14	9
J	1	2	9	4	0	16	7
K	1	0	3	8	10	22	1
L	2	2	3	0	10	17	6
M	1	2	0	4	15	22	1
N	1	0	6	8	5	20	3

Isn't this Weighting just
like risk?
Are these 22's and 16's
really important?

RESOURCES_Q&A

PHYSICIST APPROXIMATIONS

WE'LL ASSUME THE
CURVE OF THIS RAIL
IS A CIRCULAR ARC
WITH RADIUS R .

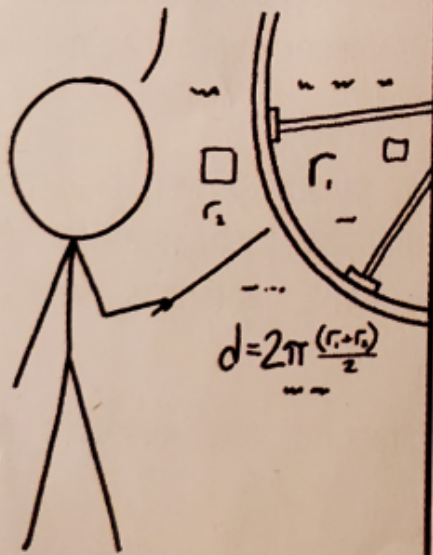


IEEE *Spectrum*
magazine, 2020

RESOURCES_Q&A

PHYSICIST APPROXIMATIONS

WE'LL ASSUME THE
CURVE OF THIS RAIL
IS A CIRCULAR ARC
WITH RADIUS R .



ENGINEER APPROXIMATIONS

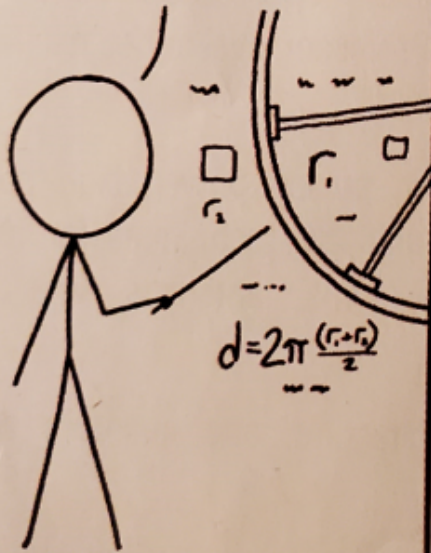
LET'S ASSUME THIS
CURVE DEVIATES FROM
A CIRCLE BY NO MORE
THAN 1 PART IN 1,000.



IEEE Spectrum
magazine, 2020

PHYSICIST APPROXIMATIONS

WE'LL ASSUME THE
CURVE OF THIS RAIL
IS A CIRCULAR ARC
WITH RADIUS R .



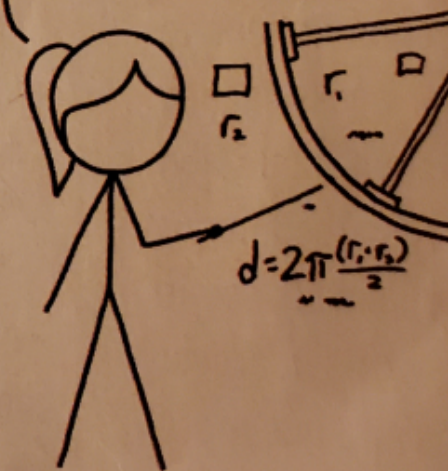
ENGINEER APPROXIMATIONS

LET'S ASSUME THIS
CURVE DEVIATES FROM
A CIRCLE BY NO MORE
THAN 1 PART IN 1,000.



RISK COSMOLOGIST APPROXIMATIONS

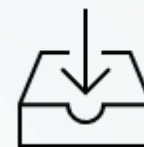
ASSUME π IS ONE.
PRETTY SURE IT'S
BIGGER THAN THAT.
OK, WE CAN MAKE
IT TEN. WHATEVER.





The Tale of Missing the Point

- Submission to Regulatory Body for approval
- Did not submit the list of hazards
- Did not submit the procedure for risk management
- Some parts of the risk management file absent
- Complex analysis submitted
- Receive Finding / non-acceptance
- Needed corrective action
- New procedure and training



Do Not forget that Risk Management communicates safety to the Regulator
Failure to be clear and to submit a complete risk file necessary for context can result in non-acceptance



Follow On

Do not use Numerical Probability of Occurrence Estimates in Human Factors or Software Risk Analysis

Do use Severity of Harm in such analyses;
Regulators do not accept veracity of estimates of occurrence



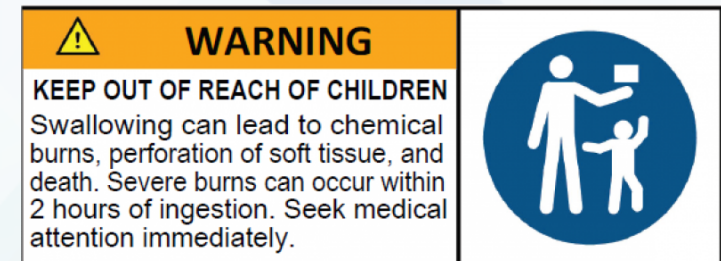
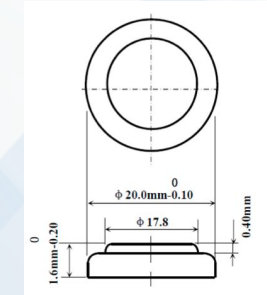
Do Focus on the New and Novel

Do Not assume what was good enough before
will be enough to prevent disaster



The Tale of Change for the Worse

- Battery company that made alkaline 1.5 V button-cells released a new lithium metal 3 V coin cell
- Did foresee ingestion from past alkaline knowledge
- Did have warnings against ingestion
- Did meet all standards at the time
- Yet incidents in home with battery like loose change
- 2-year-old children ingest a battery
- Suffered esophageal burns and severe harms
- Lawsuit
- Company could not show risk management had considered the new risk - of tissue necrosis from electrolysis
- New Regs, new warnings



April 2019: IEC 60086-4 – edition 5 - Primary batteries - Part 4: Safety of lithium batteries.

Do look at what's new and novel in context of what's known

Do not limit thinking and fail to capture alternatives

Higher Voltage -> electrolytic current that hydrolyzed tissue fluids -> caustic hydroxide was unappreciated at time

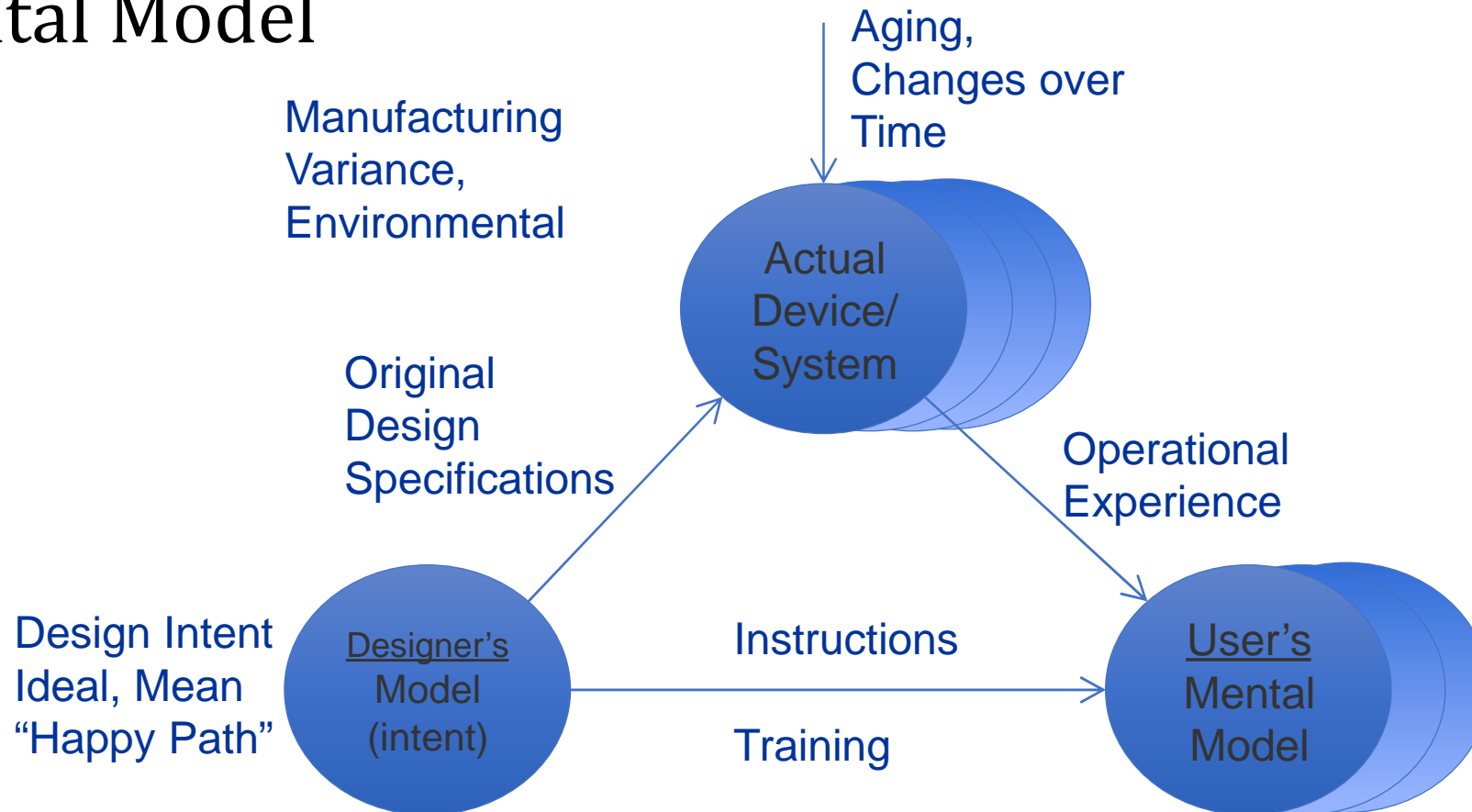


Do Consider complex systems, and man-machine interface

Human Responses are based on their
Mental Model of System Operation



Mental Model



Mental Model of Designer and User, differ from reality

Adapted from Fig 2.9 *Engineering a Safer World, Systems Thinking Applied to Safety*
Nancy G. Leveson, The MIT Press, © 2011 ISBN 978-0-262-01662-9



Sterility Assurance & Quality Risk Management Conference

October
25th & 26th



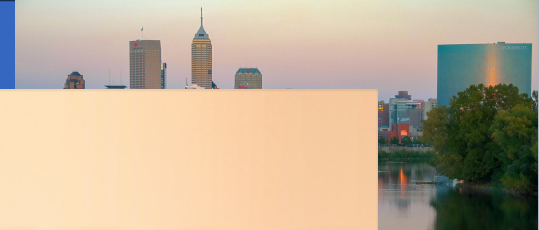
Tale of the Boeing 737 MAX 800

- New engines applied to old airframe body
- New engines more efficient – larger diameter
- Moved engines forward on wing to allow landing without ground-strike
- Airframe tendency to nose up at cruise with engines forward
- Software fix – “MCAS” maneuvering characteristics augmentation system to control pitch at cruise, to prevent nose up stall
- Software fix was assessed, accepted, documented as minor adjustment, low risk, based upon severity of control, and single actuation
- Second change adjusted MCAS severity, and made cumulative
- Boeing didn’t want simulator training of users, not documented in detail in user facing documents
- 2 crashes
 - Oct 29, 2018: Lion Air 610 prior day’s crew had problem, extra pilot identified, and turned off trim power; incomplete logs, incomplete fix overnight miscalibrated Angle of Attack sensor; airline didn’t notify next aircrew of that solution or ground the plane
 - Boeing issued operational manual guidance
 - Mar 10, 2019: Ethiopia Air 302, crew may have turned off, then turned on; tried to debug... Man-machine interface issues
- Angle of Attack sensor issues
- Culture that employees felt not empowered or comfortable to raise issues up
- Blamed schedule pressures, outsourcing, and distant HQ office from design activities
- Boeing initially thought FAA would give quick clearance of the fix
- Reorganized engineering oversight, to report to chief engineers rather business
- Added safety group, assuring work independent, reporting to the board
- New CEO
- \$20B+ cost, years until cleared to fly; no 2019 bonuses to employees



Conclusion





Manage Risk well and a Ship can go Anywhere

Perseverance Rover & Ingenuity Helicopter

“The Ingenuity Mars Helicopter project is a **high-risk, high-reward** technology demonstration” – NASA 2021





Discussion / Questions



Baxter

Thank You