What Scares Us About Risk?

How Risk Tolerance Impacts our Thinking about Aseptic Processes

James Vesper, PhD, MPH
Director, Learning Solutions
ValSource, LLC

jvesper@valsource.com

Goals

- Examine what influences how we think about risk and make risk-based decisions
- Discuss how this can affect how we evaluate risks related to making sterile products

Seat belt usage, 1

- How many people routinely use seatbelts when driving or being a front-seat passenger?

Seat belt usage, 2

- How many people routinely use seatbelts when being a back-seat passenger (e.g., in a taxi, Uber)?

CDC data

- National (US) results: 86% front seat vs 75% rear seat (observed, 2012)
- Front seat safer than rear seat due to supplemental restraint systems (for people >15 years old)

Source: Bhat et al, Journal of Safety Research, Mar 2015

Why the difference in our risk decisions and resulting behaviors?

- Risk perceptions
- Risk tolerance
- Risk appetite

Risk appetite defined

- Risk appetite is the amount of risk, on a broad level an organization is willing to accept in pursuit of value [or goals].

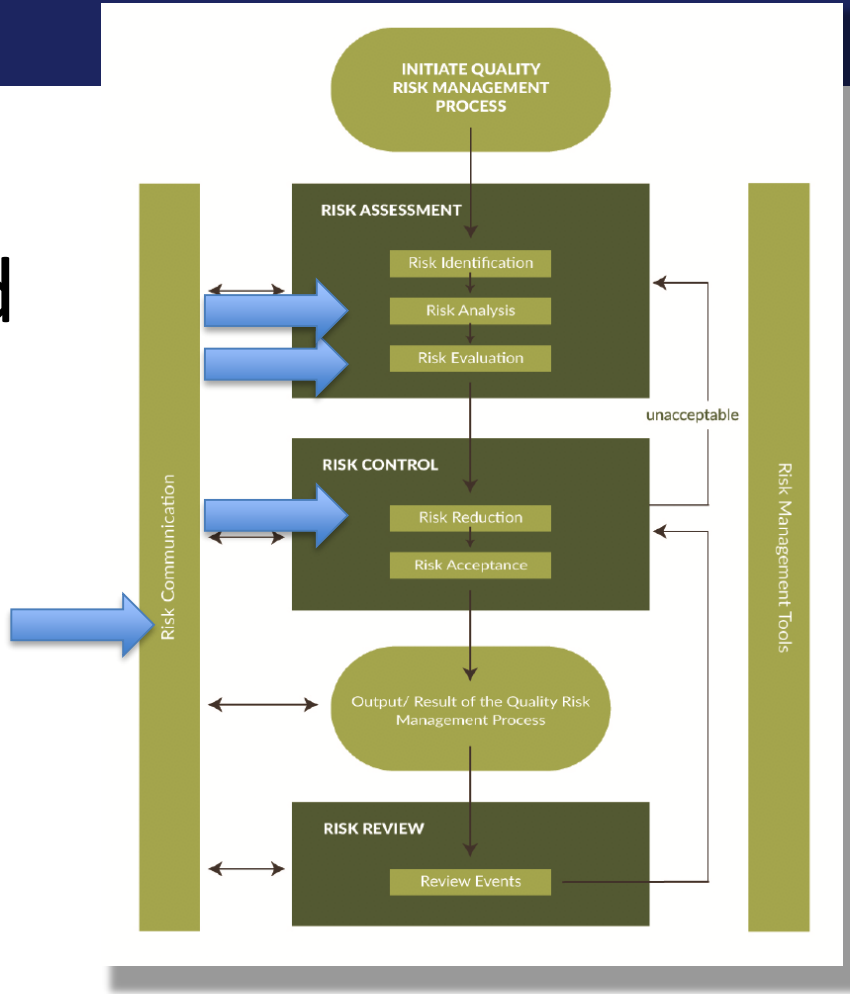
Source: Enterprise Risk Management — Understanding and Communicating Risk Appetite. COSO, 2012

Risk tolerance defined

- The acceptable level of variation relative to achievement of a specific objective, and often is best measured in the same units as those used to measure the related objective.

Source: Enterprise Risk Management — Understanding and Communicating Risk Appetite. COSO, 2012

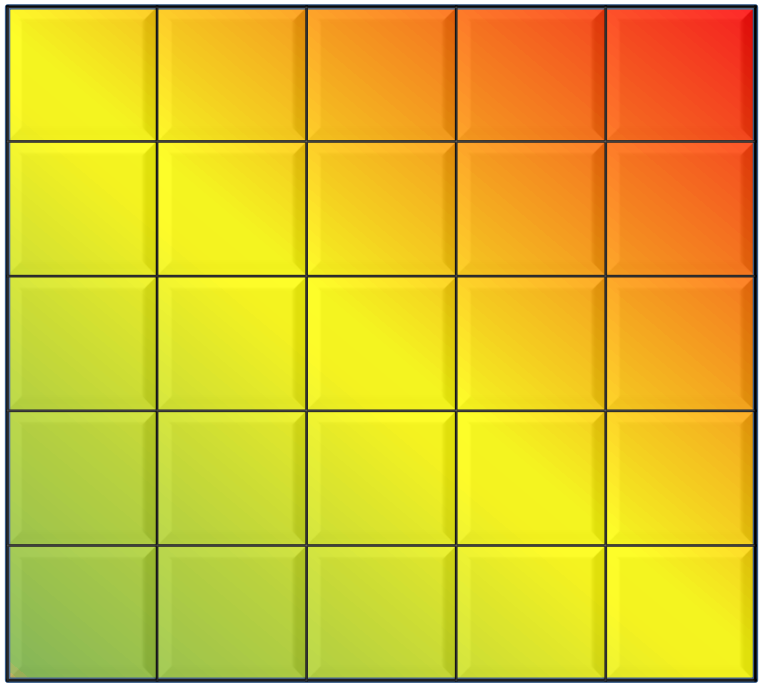
Where in QRM do we consider risk and its components?

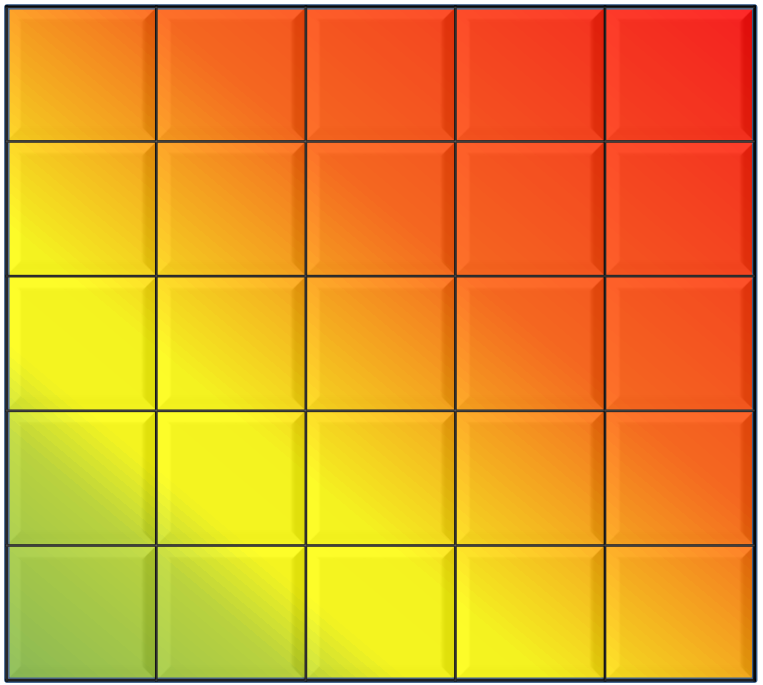


Scales – impact (severity)

Severity	Rank	Patient/User	Compliance	Process	Availability
Critical	5	Will cause permanent impairment or damage of a body structure or function. Could lead to patient death.	Product Seizure / Closure/ Consent Decree	Failure of the entire process - inherent or external problems so the product can no longer be made	Stock out of life saving single sourced product with no alternative.
Major	4	Could cause permanent impairment or damage to a body structure or function, but is not fatal or life threatening. Likely to impact product efficacy.	Recall / Warning Letter/Regulatory approval of all batches required	Multiple batch failures. Multiple CQAs within the same batch fail or there are multiple batches with the same CQA failure. No rework or reprocessing possible	Stock out of life saving product with alternatives, no safety stock available
Moderate	3	May cause significant temporary unintended impairment of a body function. May impact product efficacy.	Numerous/systemic HA Observations Requirement for Regulatory notification (ie. Field alerts) Major deviations to process. Confirmed stability failure. Internal critical observation	One or partial batch failure/rejection. CPP and CPA excursion. Significant lower yield or throughput outside historical performance Batch or partial requires rework	Stock of lifesaving product below safety stock minimum level. Stock out averted using emergency stock or stock out of non life threatening product single sourced
Minor	2	May cause transient, self-limiting, unintended, impact to a body function. May cause dissatisfaction to the patient and customer complaint.	HA recommendations. Other internal observation. Minor deviation with attribute impact, within spec	Elevated attribute level /robustness alert limit. Excursion to PP or PA. Lower yield or throughput but within historical performance. Batch or partial requires reprocessing	Stock out of non life threatening product with alternatives.
Negligible	1	No performance impact to patient. May have cosmetic defect which is unlikely to cause dissatisfaction to the patient.	Minor Deviation with no attribute impact	Minor cycle time / throughput /minimal yield impact	Stock of non life threatening product below minimum safety stock levels

Evaluation table or risk block heat map





But what shapes how we think about risk?

Our view of “risk” is shaped by…

- **Structural factors**
- **Risk perceptions**
- **Trust in the source of information**
- Personal and societal values
- Organizational culture
- Biases
- Heuristics

Structural factors, 1

- FDA is responsible for *protecting* the public health… and advancing the public health…

- EMA *protects* public and animal health in 28 EU Member States, as well as the countries of the European Economic Area, by ensuring that all medicines available on the EU market are safe, effective and of high quality.

Structural factors, 2

- “We make medicines that help people live longer, healthier, more active lives.”
- [Our] “mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases.”
- “To discover, develop and provide innovative products and services that save and improve lives around the world.”

Other factors that affect how we perceive risk

- Uncertainty
- Surprise – unexpected events
- Understanding
- Dread
- Affect – if we see something favorably (a benefit/value) we associate it with less risk

Trust and risk perceptions

- Competence (ability, competence, expertise, knowledge)
- Motives (benevolence, integrity, honesty, fairness)

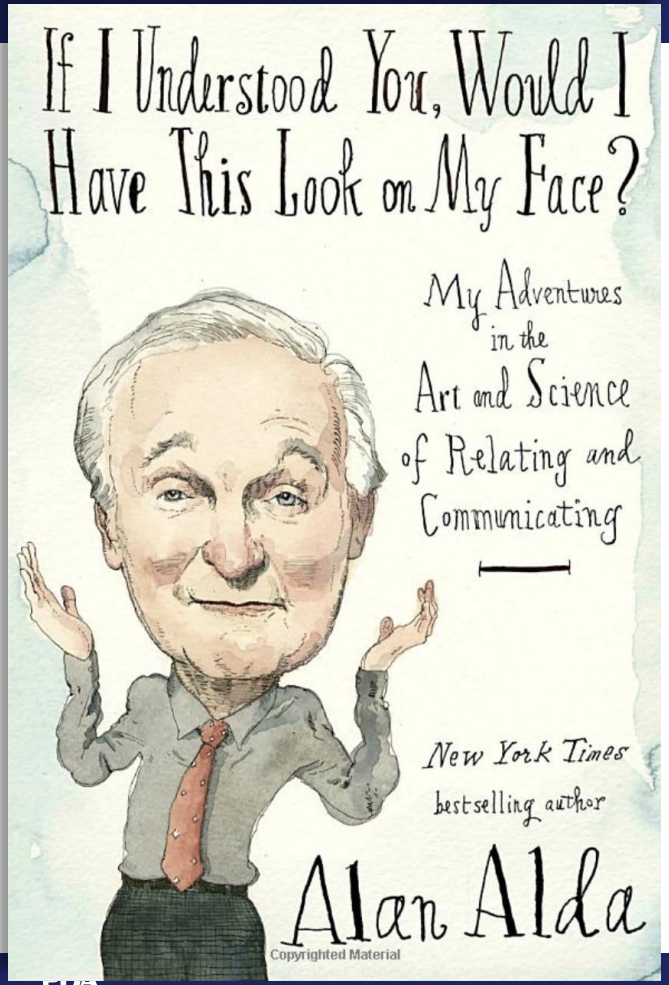
Source: Twyman, Harvey, and Harries (2008)

Summary point

How risk-based approaches have been used in sterile product production: examples

- Risk-based strategies for EM sampling (number and locations)
- New facility designs
- Interventions and simulations (media fills)

How can use use this knowledge as we talk about aseptic processing risks and ways to reduce them?



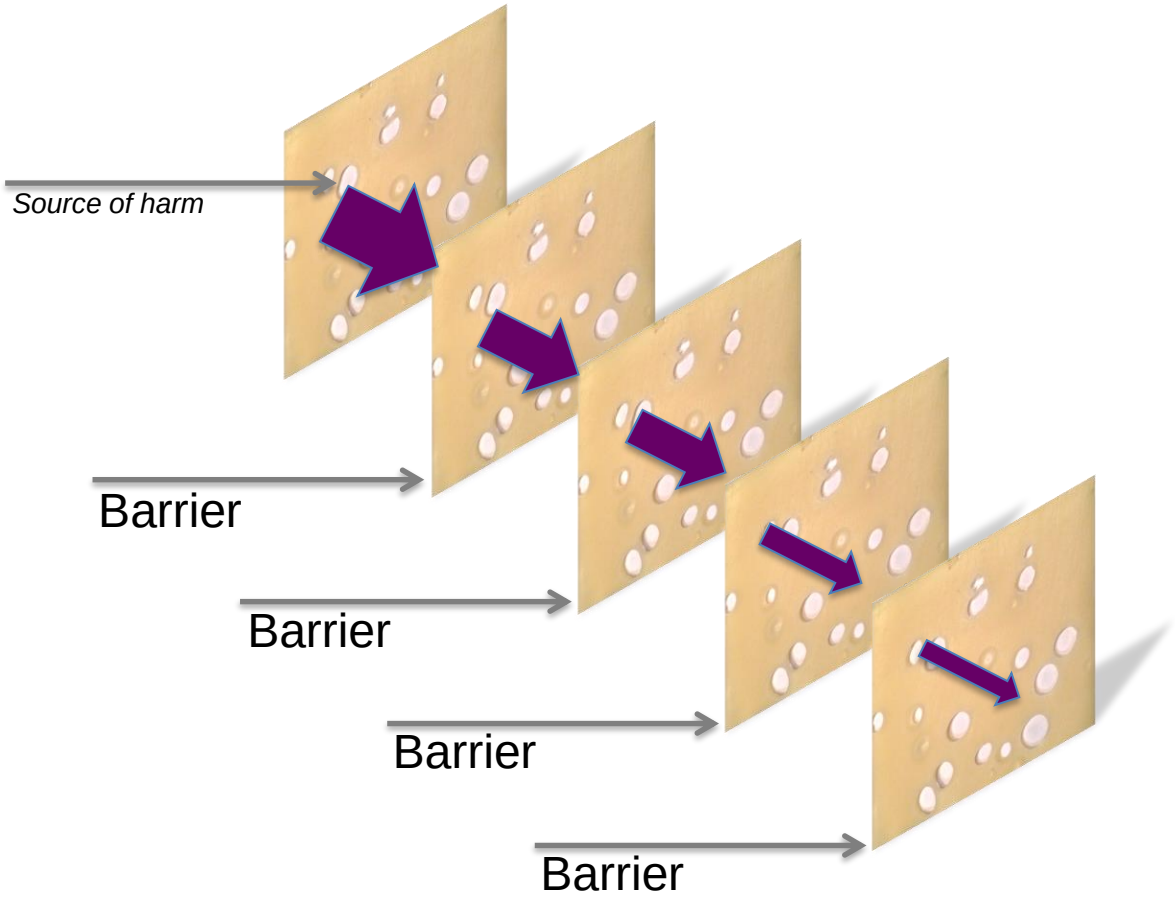
1. Be open to new possibilities

- **“True listening means there is the possibility of your being changed.”**

2. Be aware of biases and heuristics

- Confirmation bias
- Overconfidence bias
- Hammer bias (using the same assessment tool for everything)
- Authority bias
- Anchoring bias
- Optimism bias

3. Consider the layers of risk reduction available



Source: James Reason

Sources: James Reason, US NTSB, DOT, Insurance Institute for Highway Safety

4. Speak with data, not just intuition

- *Thinking Fast, Thinking Slow* (Kahneman)

Two approaches for making risk- based decisions

Experiential system ("System 1")	Rational system ("System 2")
Holistic	Analytic
Affective pleasure/pain oriented	Logical: reason oriented
Associative connections	Logical connections
Behavior mediated by "vibes" from experiences	Behavior mediated by conscious appraisal of events
Encodes reality in concrete images	Encodes reality into abstract systems
More rapid processing – immediate action	Slower processing -– delayed action
Self-evidently valid - "experiencing is believing"	Requires justification via logic and evidence

Source: Epstein (2004) in *Risk as Feelings*

5. Develop trust

- Confidence in competence
- Understanding and trust in motivation
- Mutual respect

So what now?

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