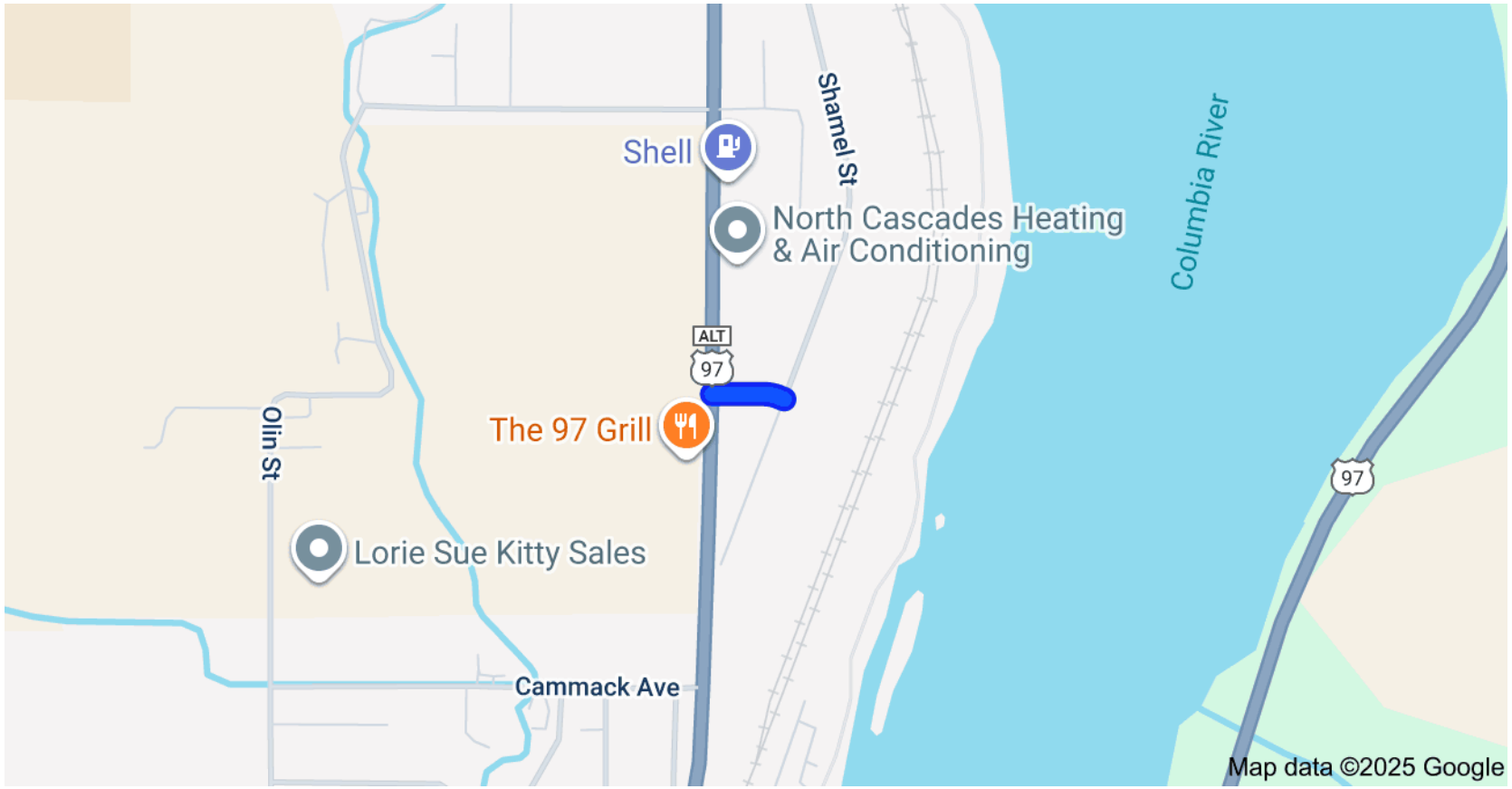
Sterility Assurance & Quality Risk Management Conference

PDA®
Parenteral Drug Association
Midwest Chapter

A Random Walk Down Risk Street

Q: Where is Risk Street? A: Entiat, WA 98822



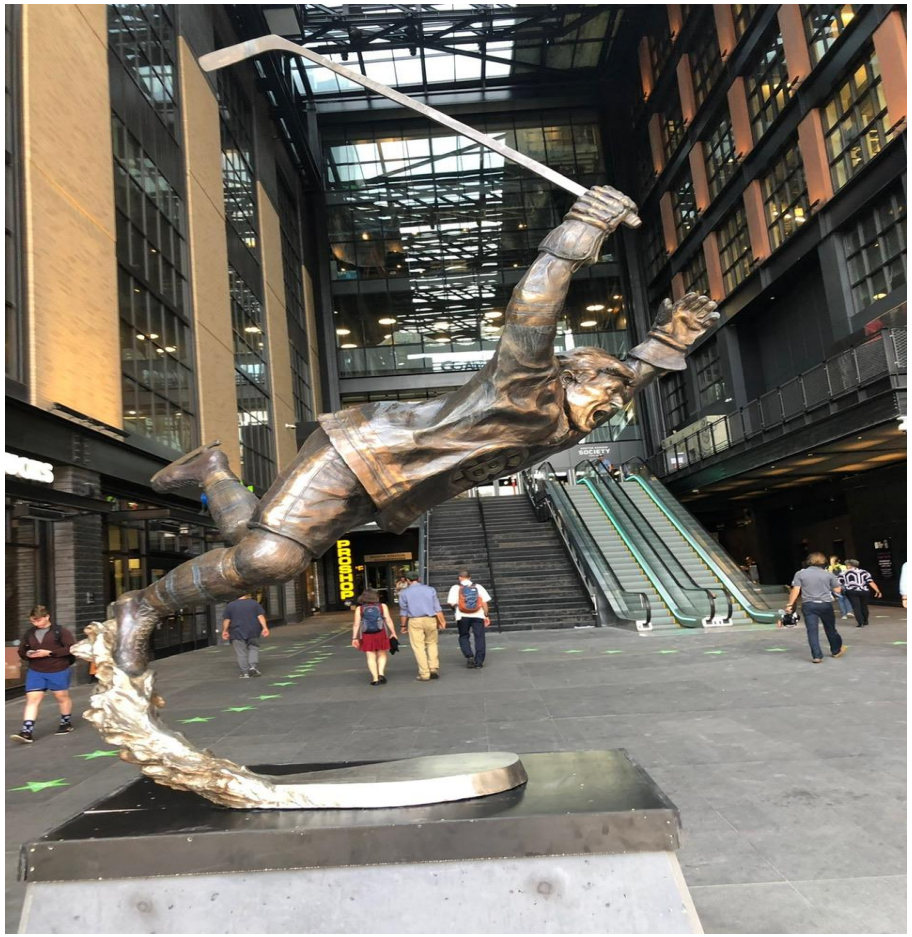
Disclaimer

The information within this presentation is based on the presenter's expertise and experience and represents the views of the presenter for the purposes of this conference.

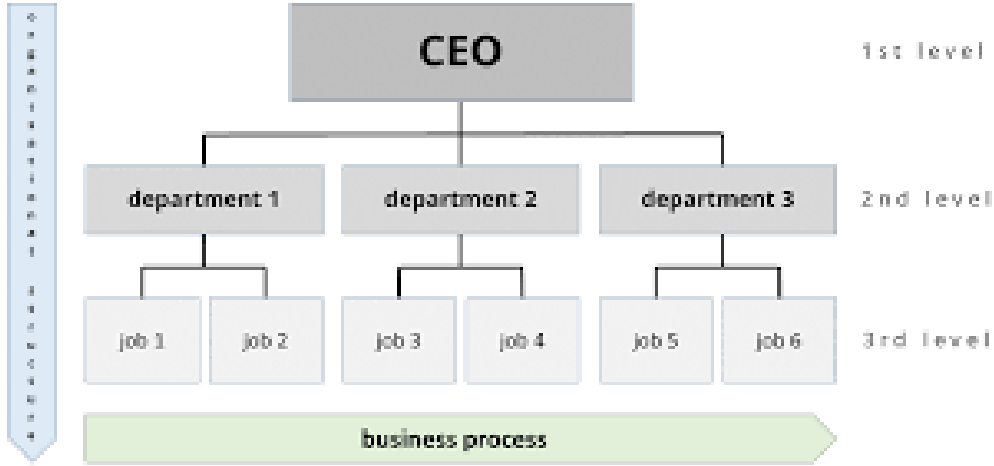
What aspects of risk are we going to talk about?

- Perspectives from some recent meetings
- Case Study Warning Letter –

Perspectives Matter

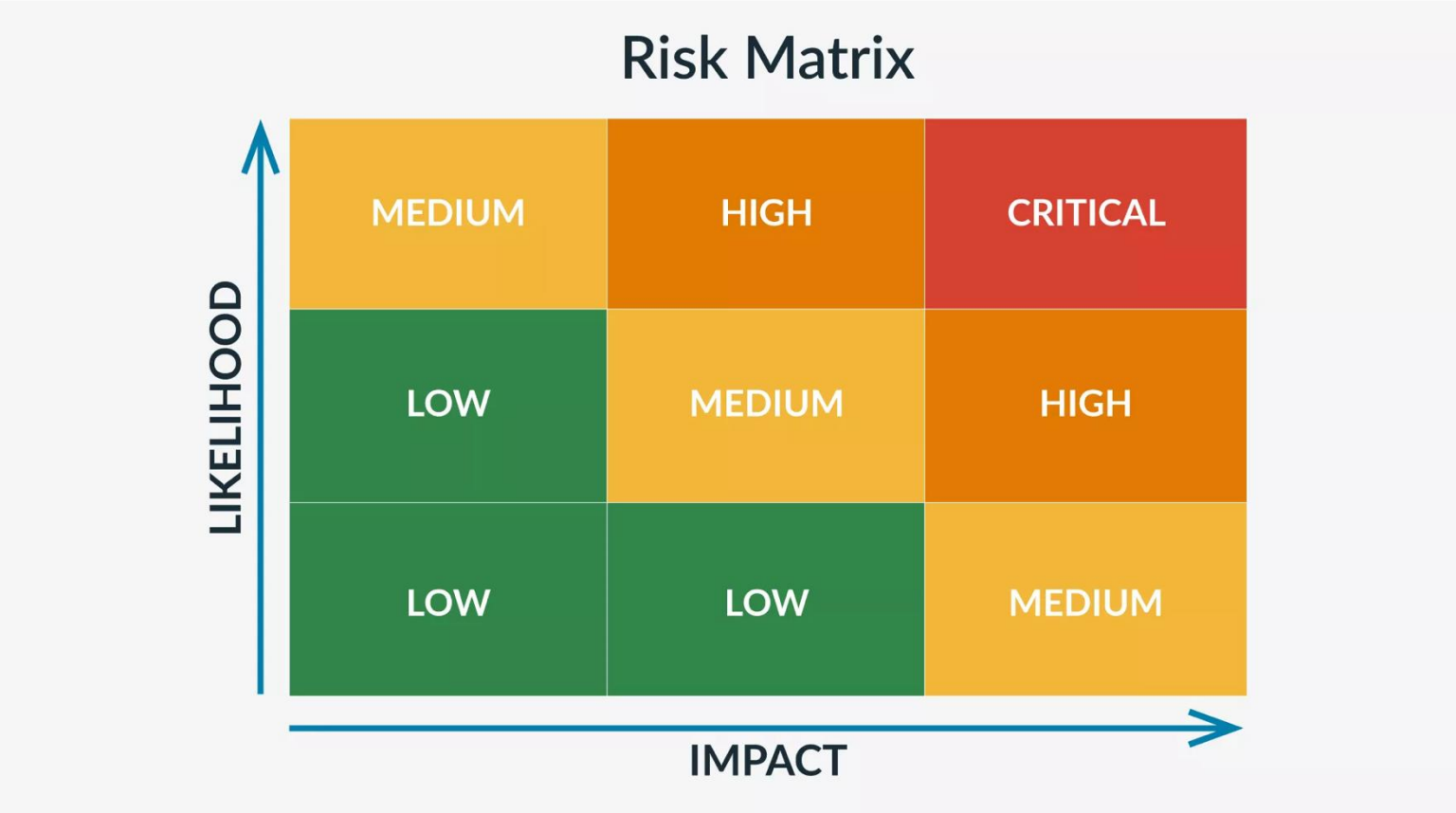


System vs. People



Sterility Assurance & Quality Risk Management Conference

October
8th & 9th


Risk Matrix
MEDIUM
HIGH
CRITICAL
LOW
MEDIUM
HIGH
LOW
LOW
MEDIUM
LIKELIHOOD
IMPACT

CASE STUDY

Background

Context

The problem statement

Where this went

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The Good...

- Paperless and Continuous Manufacturing
- Showcased to the FDA
- ISPE Factory of the Future Winner in XXXX
- ISPE Overall Factory of the Year Winner in XXXX

The Bad...

- 20% Rejection Rate for Contamination
- Constrained investigation 10 batches to get X
- Downsized and lost technical talent

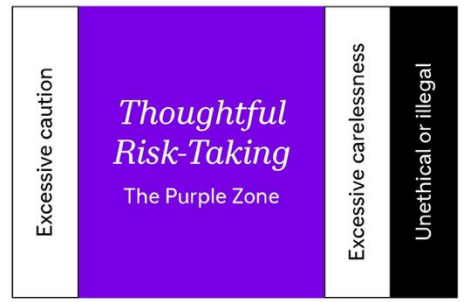
The Ugly...

- 28 Day FDA inspection
- 6 item 483
- Inadequate Response
- Warning Letter

Robust pipeline (83 Projects)

But how to finance?

- Optimizes its operational budget by channeling resources to advance R&D
- Embraced digital transformation to streamline operations and reduce costs
- Introduced programs to take risk "TRT" rolled out to all levels of the organization.



ppSchema of the Thoughtful Risk-Taking and the Purple Zone

What is Thoughtful Risk-Taking?

Thoughtful Risk-Taking is about making the right decisions by *maximizing opportunities* while *mastering risks* in the so-called *"The Purple Zone"*.

ppSchema of the Thoughtful Risk-Taking Catalyst

Setting the scene| **Before we go further…**

- This is a Drug substance
- All batches released met specifications

But FDA said "because your methods facilities or controls…do not conform to CGMP, **your APIs are adulterated**…"

This warning letter summarizes significant deviations from Current Good Manufacturing Practice (CGMP) for active pharmaceutical ingredients (APIs).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your APIs are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

Source: FDA website

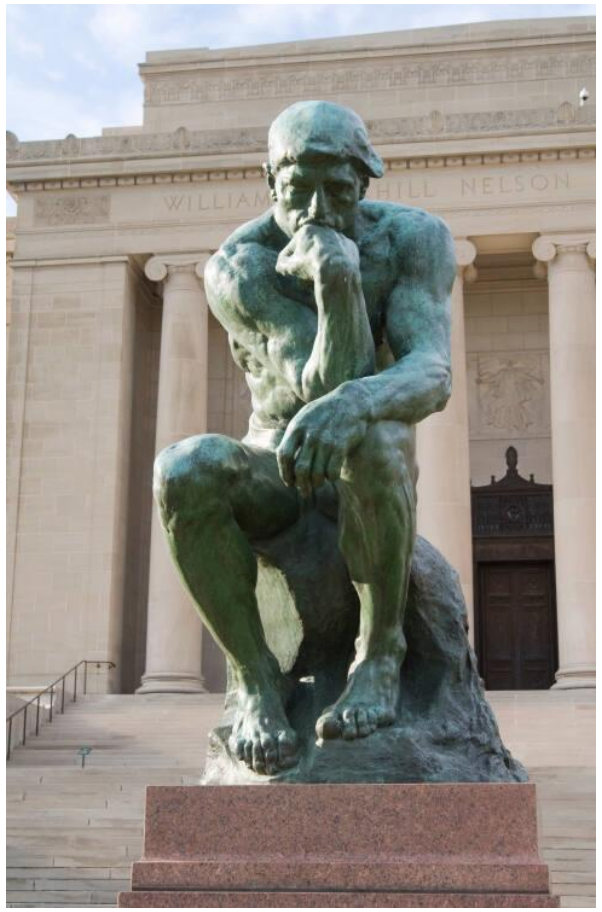
About the Warning Letter| Observations

The 483, failure to….

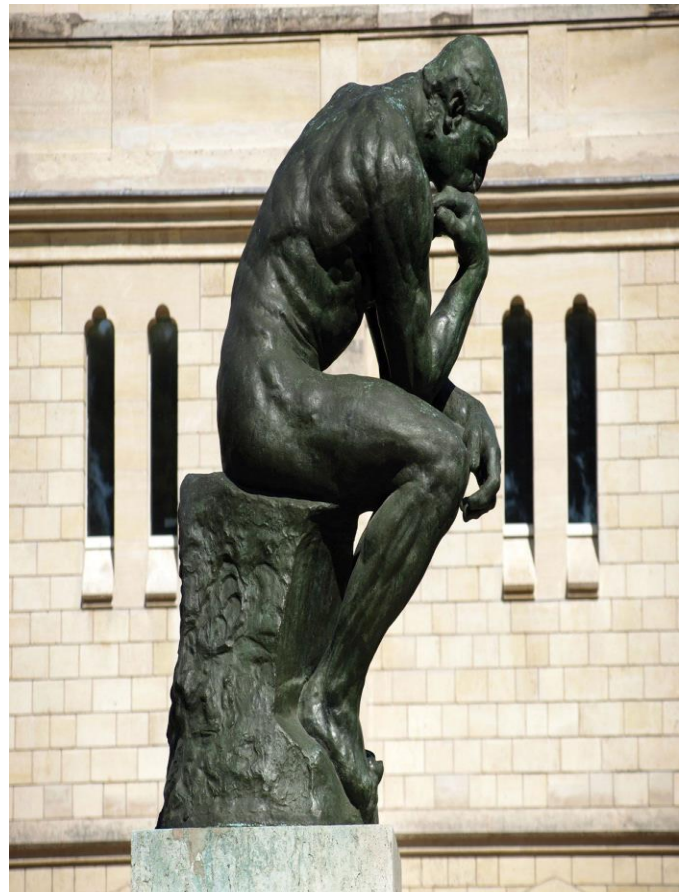
- Investigate (XX% rejection rate)
- Reproducibly manufacture (PPQ and Process Validation problems)
- Equipment design (operators have to get close to the floor)
- Quality Unit (not enough resources to do their job, past due deviations)
- Follow Procedure (Process lines on the floor, operators not sanitizing hands)
- Ensure facility and equipment are clean (residues, lack of instruction for cleaning and spill)

The Warning Letter addressed to CEO…

- It is essential for executive management to support…and ensure a continued state of control
- Improved systems for ongoing management review
- Describe how top management supports quality assurance and reliable operations
- Quality Unit is not able to fully exercise its authority and/or responsibilities
- You do not…assess your training or assess your oversight….
- Mentions Aseptic Operations…particle analysis….



Let's come back to perspectives…



What are the Perspectives of the 483 vs. WL

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Points to Consider

- Have more than one perspective (but also avoid "group think")
- Be deliberate about your choices and your decisions
- Exercise Accountability
- Personal Opinion is that People and Culture are the heart of our business