AI SUMMIT

COLUMBUS, OH • OCTOBER 25–27, 2022

Predetermined Change Control Plan: Best Practices aka "What do we need to change about how we manage change??"

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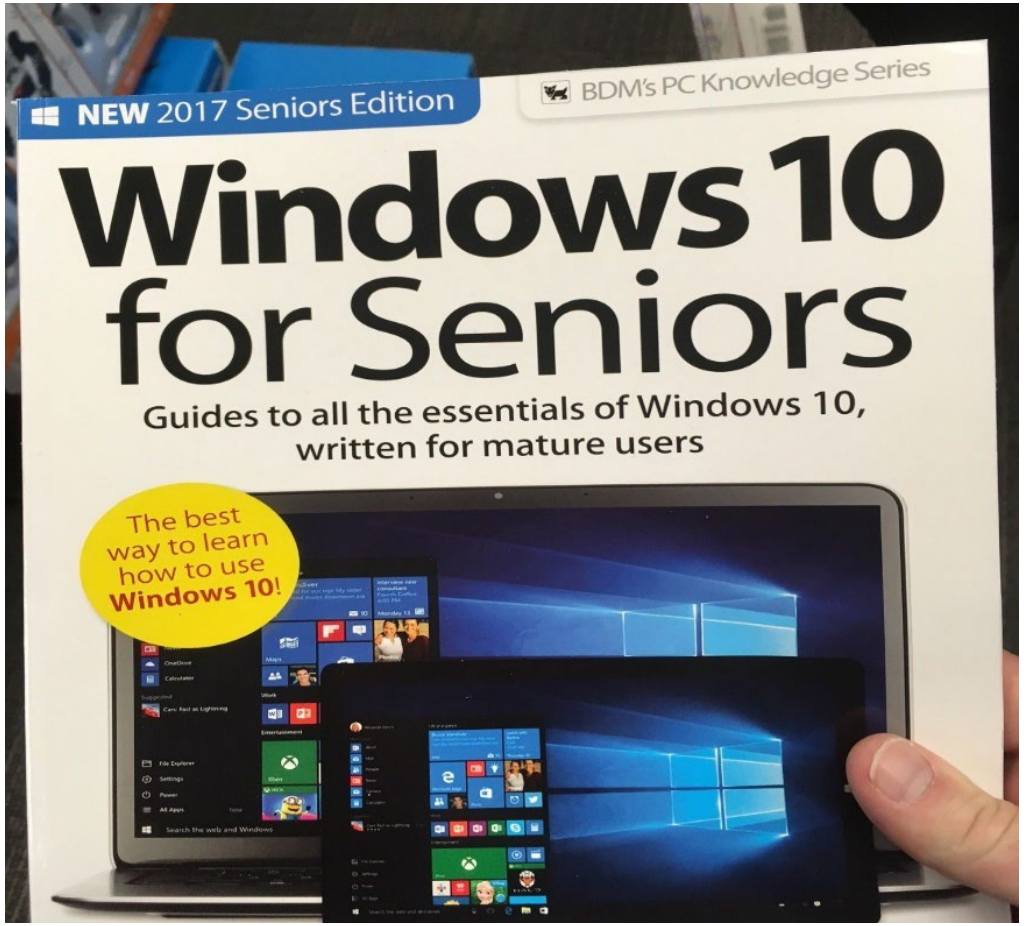
Observations from CES

- No longer the Internet of Things, it's the Internet of Everything (IoE)
  - Garage door openers
  - Door locks
  - Baby monitors
  - Activity tracker for dogs
- Analytics everywhere for everything
  - Litter box
- New applications have new risks
  - NIST Wearables Security Assessment Project

Impedance Mismatch

- While the promise of things to come (and things that are already here) is excellent, the future cannot easily plug into existing legacy processes, legacy regulations, and legacy business models.
- Neither viewpoint is incorrect; things simply aren't compatible – including things that we take for granted.



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Where did current regulations and approaches come from?

In 1996:
- Regulations: CGMP updated part 820
- Technology: IBM's Deep Blue beats Kasparov
- Movie: Happy Gilmore

In 1978:
- Regulations: CGMP published
- Technology: Microsoft Cobol-80
- Movie: Grease

In 1976:
- Regulations: Medical Device Regulation Act passed
- Technology: Apple I launched.
- Movie: Logan's Run

Managing Changes

Many well-known disasters can be traced back to design changes.

Although the Hindenburg tragedy is from another industry in another era, it provides a good lesson in change control.

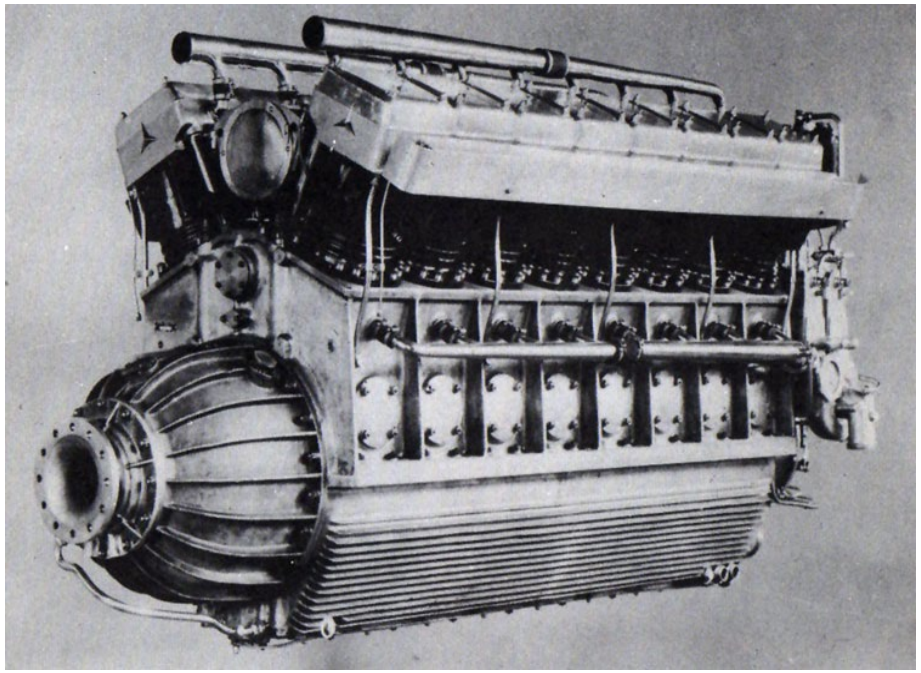
Recap: After crossing the Atlantic, the Hindenburg attempted to land in Lakehurst New Jersey.

Trivia: This flight was a partnership with American Airlines.

During the landing procedure, a fire started on the aircraft.

The aircraft was destroyed in 30 seconds.

Hindenburg, contd.



The Hindenburg design contained performance and safety improvements over the previous best-in-class airships from both Germany and the UK. **Even "better" can fail catastrophically.**

The designers originally specified Rolls-Royce gasoline engines, but the manufacturer refused to buy from a UK supplier.

So they used Benz diesels, with a lower power-to-weight ratio.

As a result, the designers had to quickly lighten the airship. They chose to remove the flame-retardant coating on the original skin. **Last-minute changes are risky (plan for change!)**

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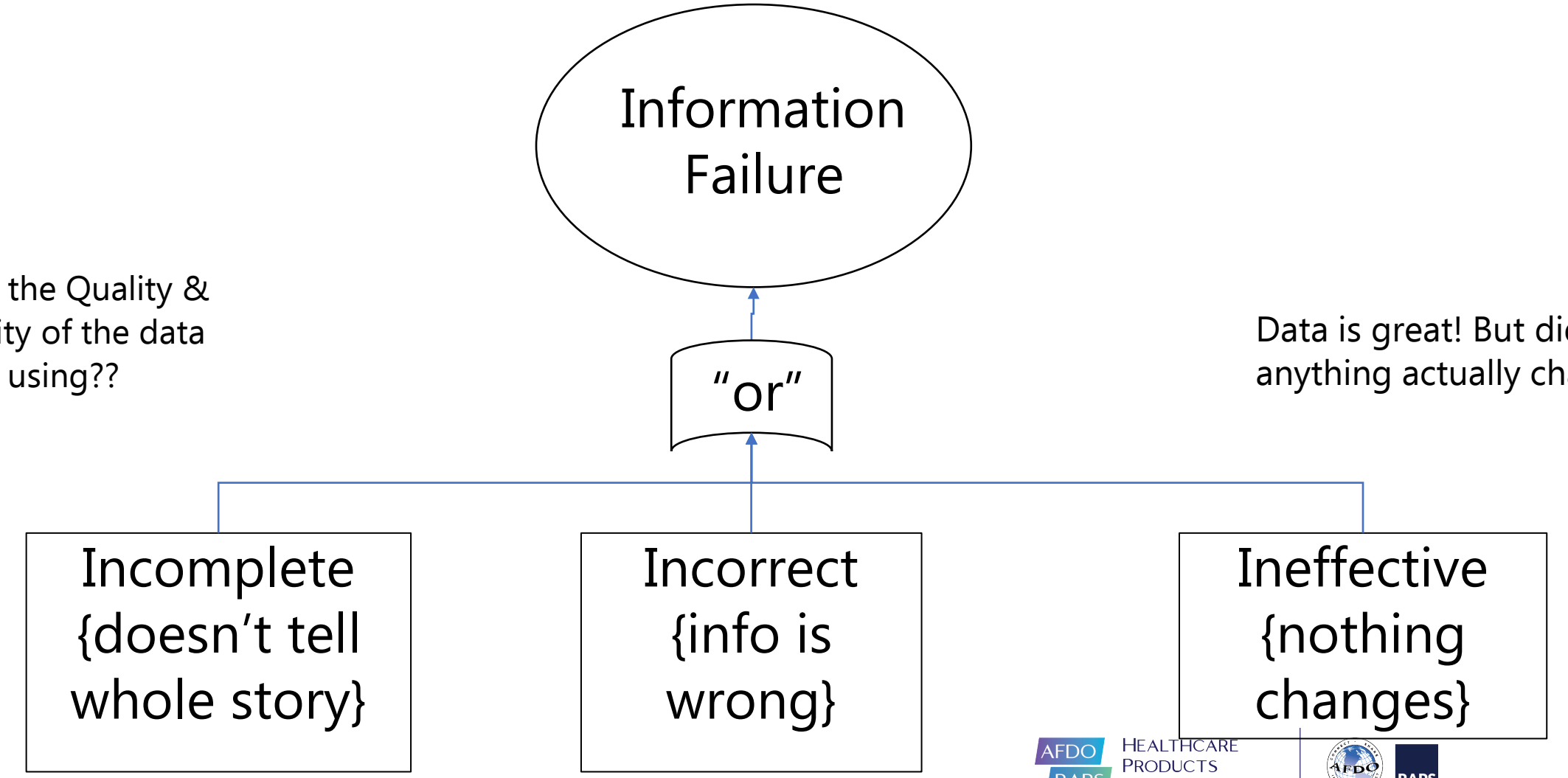
Simple Fault Tree for Information Failures

What is the Quality & Reliability of the data you are using??



Data is great! But did anything actually change??

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Failure: Incomplete Information

- Relevant information may be missing
- What happens if they didn't wear their wearable on Thursday? Can you still trend?
- Missing relevant context – examples:
  - Fast food chain - fish sandwich
  - Cycle donor season
  - Predicting early interventions

Failure: Incorrect Information

Sometimes the data being provided is wrong. This could be due to:

- Measurement error within tolerances
- Measurement error outside of tolerances
- Data entry errors
  - "Right data wrong field'
  - Not understanding a question
  - Transposition errors
- Information processing errors
  - Patient weight – pounds or kilos?
  - What if you are a teenager being transferred to an adult ward?
  - What if you are a German app developer working on a US release?

Failure: Ineffective / Failure To Act

- This information isn't useful if it never gets used.
- Does anyone believe what the software is saying? (Trust)
- Human behavior is difficult to change – how many treadmills are in basements being used as clothes racks?

Model Diversification – Refinement & Drift

- Many of us have a long history of working in an environment that is slow to change, and therefore we offer a generic solution to meet common healthcare problems.
- However, with Continuously Learning Systems, the system wants to change. It wants to be customized for a particular customer. A CLS system can learn about a local population and can optimize for that particular hospital.
- But the manufacturer is responsible for configuration management and change control. The manufacturer is responsible for root cause analysis when something goes wrong, and the application doesn't perform as it should.

Model Diversification – Refinement & Drift

- If every hospital is different, how can you compare performance? How do you handle performance claims that change over time?
- DRIFT: Even if you lock a system and don't allow changes, patient populations DO change over time, and the performance you had 5 years ago might not be the level you are at today. Medical practice also changes over time and that may have an impact to performance.
- Therefore, having a completely locked system isn't necessarily the best idea either…

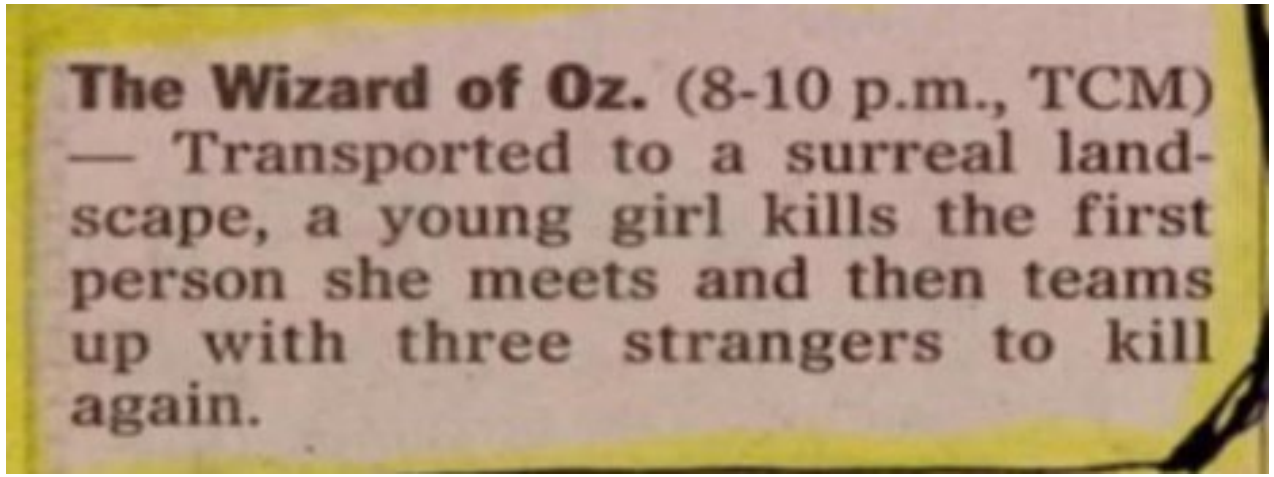
Current Approaches

Some challenges with current methodologies include:

They can get the job done, but do they still make sense in today's environment?

Are we using the existing techniques as intended?

As we asking too much of our current systems?



You made a change – do you need to revalidate?

In classic medical device design, we know that there is a difference between meeting a written requirement (“must stop speeding motorcycle”) and meeting a user need (“Aaaarrrggg!”)

One of the topics to consider when developing PCCP is the triggers for re-validation & how that will be executed.

Good Machine Learning Practice: Guiding Principles

Good Machine Learning Practice for Medical Device Development: Guiding Principles	
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices are Implemented
Clinical Study Participants and Data Sets are Representative of the Intended Population	Training Data Sets are Independent of Test Sets
Selected Reference Datasets are Based Upon Best Available Methods	Model Design is Tailored to the Available Data and Reflects the Intended Use of the Device
Focus is Placed on the Performance of the Human-AI Team	Testing Demonstrates Device Performance during Clinically Relevant Conditions
Users are Provided Clear, Essential Information	Deployed Models are Monitored for Performance and Re-training Risks are Managed

https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles

Predetermined Change Control Plan (PCCP)

Initial Premarket Assurance of Safety and Effectiveness:

- *This framework gives manufacturers the option to submit a "**predetermined change control plan**" for modifications during the initial premarket review of an AI/ML-based SaMD::*

Software Pre-Specifications (SPS): based on the retraining and model update strategy, and the associated methodology

Algorithm Change Protocol (ACP): being used to implement those changes in a controlled manner that manages risks to patients

Data Management	➢ For new training & test data: • Collection protocols • Quality assurance • Reference standard determination ➢ Auditing and sequestration of training and test sets
Re-training	➢ Re-training objectives ➢ Changes related to: • ML methods, including architecture and parameters • Data pre-processing ➢ Criteria to initiate performance evaluation
Performance Evaluation	➢ Assessment metrics ➢ Statistical analysis plans ➢ Frequency and triggers for evaluation ➢ Performance targets ➢ Methods for testing with "clinicians in the loop" when necessary
Update Procedures	➢ Software verification and validation ➢ When and how updates will be implemented ➢ Plans for global and local updates ➢ Communication and transparency to users