



# Application of Failure Modes and Effects Analysis to Biological Manufacturing Processes

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# OUTLINE

Introduce risk assessment

Present “classical” FMEA

Adjustments to biological processes

Evaluation criteria

Severity rating scale

Review

References

# Purpose

**“Risk assessment is a systematic method of identifying and preventing product and process problems before they occur. It is focused on preventing defects, enhancing safety, and increasing customer satisfaction. Ideally it is conducted in the product design or process development stages.”**

**Ref. 1, P. 3**

# Purpose, continued

“It is a tool that provides a structure to thinking through and evaluating a production process, as well as a means of quantifying and documenting that thought process.”

Ref. 2

# TWO PRIMARY TECHNIQUES

## 1. Hazard Analysis and Critical Control Points (HACCP).

Qualitative.

Identifies critical control points associated with:

Biological (non-sterility)

Chemical (impurities)

Physical (deformities)

CCP monitoring requirements

Widely used in the food industry

# TWO PRIMARY TECHNIQUES

## 2. Failure Mode and Effect Analysis (FMEA)

**Quantitative (albeit with some subjectivity)**

**Addresses a wider range of failure modes**

**Prioritizes potential failure points**

**Widely used in manufacturing settings**

# HISTORY

**HACCP:** 1960s, Pillsbury, Astronaut food  
1973, canned food  
1997, sea food

**Guideline by FDA Dept. Agriculture**  
**21 CFR 820.30**

**1998, meat, medical devices**  
**FMEA:** Mid-1960s, chemical process  
industries

**Initially, aimed at safety issues,  
then failure prevention**

**Now, used in all areas of  
production**

# CLASSICAL FMEA

## Very detailed

I.D. all failure modes

Multiple effects for each failure mode

Multiple causes for each effect

Forces corrective action for every cause of failure

## Reiterative

Post-controls, re-do FMEA for every cause for new RPNs

# APPROACH for Process Transfers

1. Evaluate every parameter in the process: Which will definitely remain the same during the transfer, which will be changed? The ones that are not changing will not be subjected to FMEA.
2. The ones that will be changed, hopefully only a few, will be listed in the matrix and FMEA will be applied.

# APPROACH for Process Characterization

1. Evaluate every parameter in the process: The more classical FMEA will be performed.
2. The ones that are poorly understood or could cause serious processing problems will be applied to FMEA.

# Continued APPROACH for Both

- 3. Risk Priority Numbers will be assigned based on the 3 FMEA criteria of Severity, Occurrence and Detectability (SOD).**
- 4. The RPN will be adjusted upward if the S, O, and D cannot be assessed.**
- 5. The RPN will be adjusted upward if there is little or no data available to support the change.**

**6. A Pareto chart will be constructed to illustrate which parameters need further characterization before implementation.**

**7. The parameters that are scheduled to change will not necessarily be linked to the same acceptance criteria used for previous process validation(s).**

**8. A summary report will be written (as a Technical Assessment) and filed with Site Validation.**

# EVALUATION CRITERIA

Severity of failure

How severe is the result of the failure?

Occurrence

How likely is it to fail?

Detectability

Is the failure readily detectable?

Scale of 1-10 (no zeros allowed)

$S \times O \times D = \text{Risk Priority Number}$

# RISK CATEGORY DEFINITIONS

**Rath & Strong's Six Sigma Guide**

**Honeywell**

**Others?**

**Custom fit to your needs**

# NEXT STEPS

**Calculate RPNs**

**Plot on Pareto chart**

**Look for clustering**

**Finalization:**

**Evaluate high RPN parameters**

**Use RPN to classify variables into key/non-key**

**Document why some have low RPNs, and are therefore non-key**

**Write report**

# REVIEW

**FMEA and HACCP are 2 of several risk assessment tools.**

**FMEA is quantitative and most applicable to biological processes.**

**It is a structured means to thinking through a process Identifying potential points of failure.**

**Documents the (group) thought process.**

**It prioritizes risk areas in terms of S, O and D.**

**It supports classification of variables as non-key.**

**A Pareto chart is an effective visual way to determine cut-off.**

# REFERENCES

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3. [www.fmeainfocentre.com/index.htm](http://www.fmeainfocentre.com/index.htm)
4. P. Nobel, *Reduction of Risk and the Evaluation of Quality Assurance*, *J. Pharm. Sci. & Technol.*, 55, p.235-239 (2001).
5. CDRH, *HACCP; A study for Medical Device Manufacturing*, 01/11/2001.