Top Ten Deficiencies for Liquid Drug Products

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Disclaimer

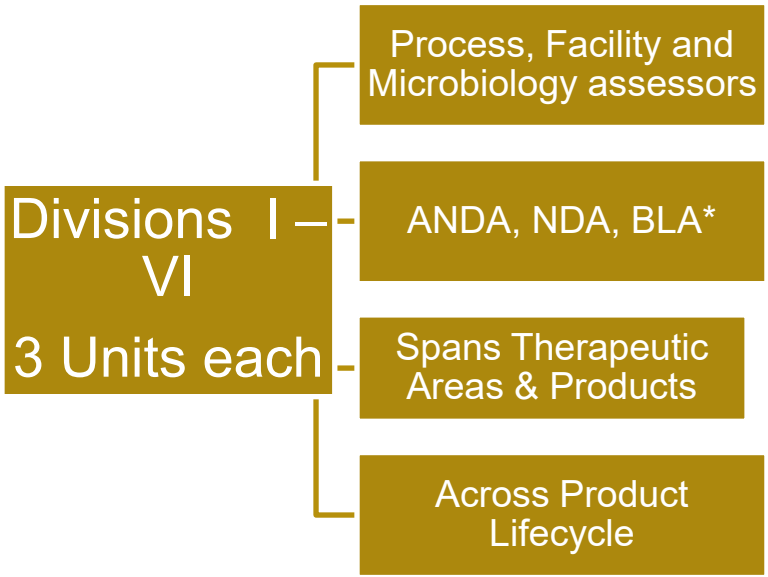
This presentation reflects the views of the speaker and should not be construed to represent FDA's views or policies


Everyone deserves
confidence in their *next* dose
of medicine.
Pharmaceutical quality
assures the
availability,
safety,
and efficacy
of *every* dose.

Office of Pharmaceutical Manufacturing Assessment

- Mission: Quality pharmaceuticals are consistently manufactured over product lifecycle
- Vision: To be the premier global regulatory organization for holistic assessment

Office of Pharmaceutical Manufacturing Assessment, cont'd



One Quality Voice through Integrated Quality Assessment teams

Learning Objectives

- FDA efforts to expedite drug approvals
- Analyze common manufacturing deficiency trends
- Review top ten deficiencies
- Identify documents to help applicants with submissions

FDA Enhancements

- Sending information requests (IRs) and discipline letters (DRLs) late in the assessment cycle (GDUFA III)
- Four Part Harmony (PDUFA VII) for IRs

Four Part Harmony

- Acknowledge information provided
- Identify the issue
- Identify information required to make a regulatory decision
- Provide specific reference or information to support request

Liquid Drug Products

- Injectables
- Oral dosage forms
- Topicals
- Insufflates

Poll Question

Which unit operation do you think has the number one deficiency?

A. Mixing

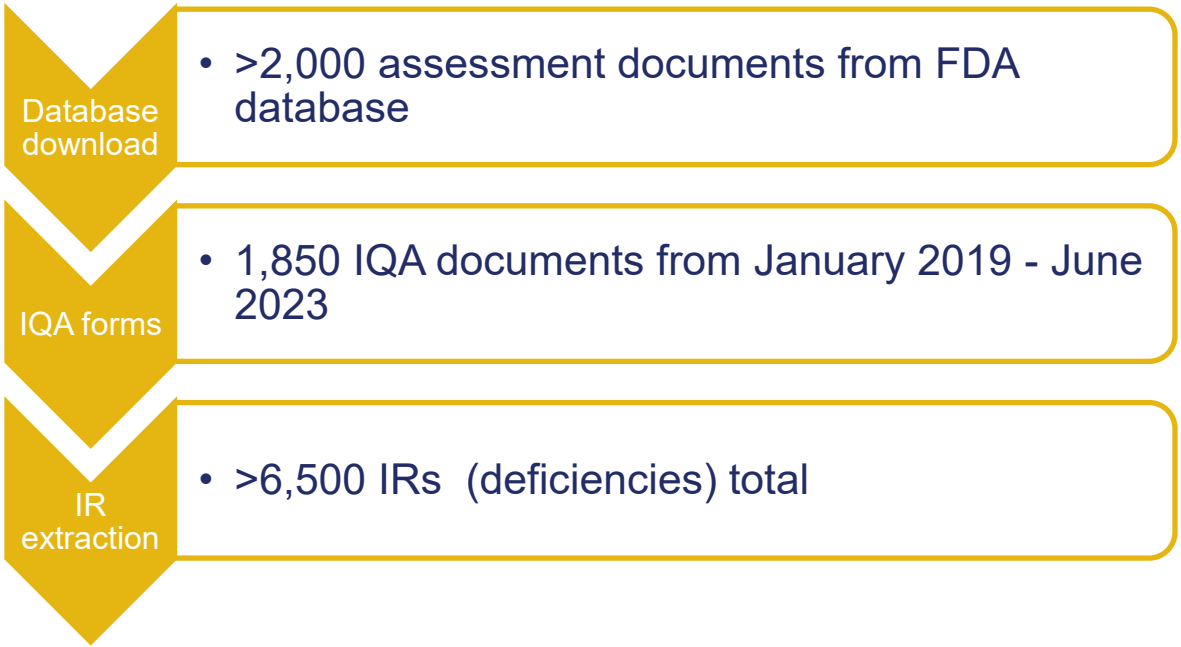
B. Filtration

C. Filling/Sealing

D. Packaging

Methods

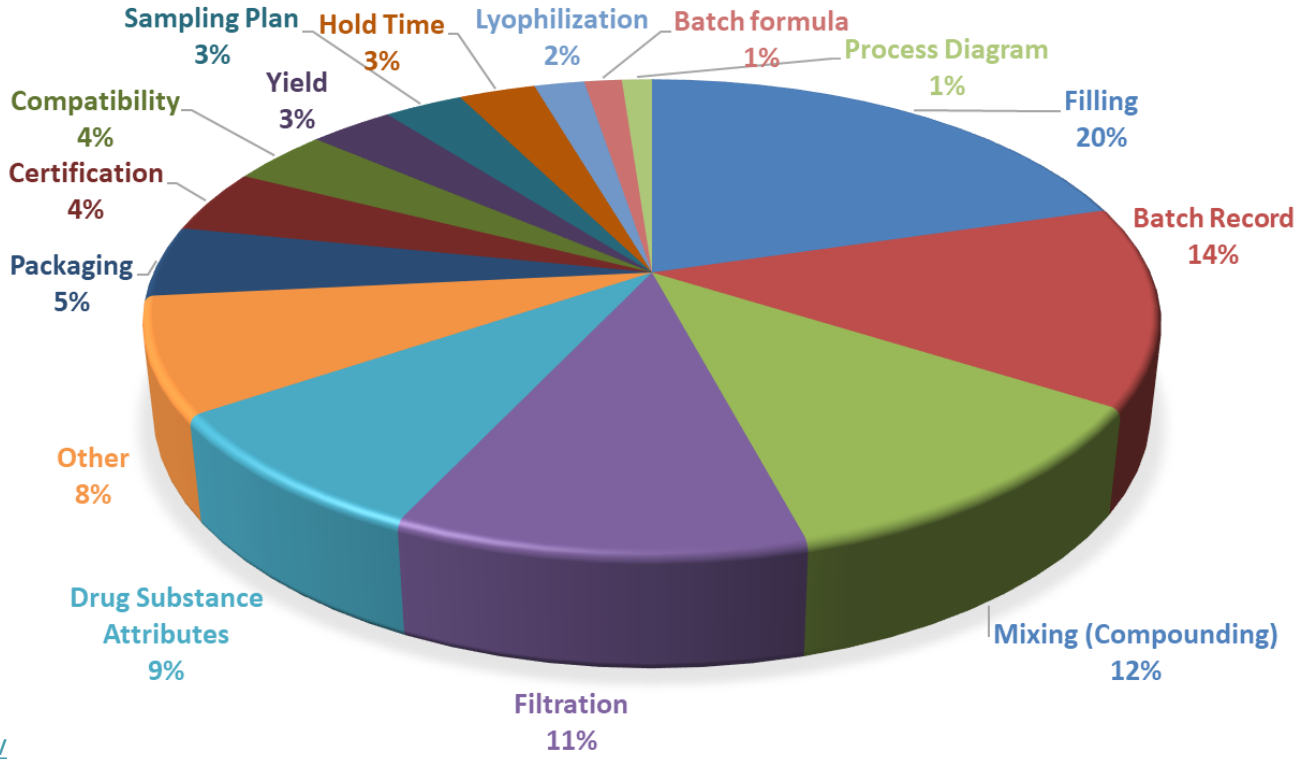
- Number of IQAs and IRs (Deficiencies)



Methods, cont'd

- IRs categorized via keyword searches using VBA Script
- Categories included unit operations and other IQA sections
- Keyword examples included filling, packaging, and in-process controls (IPCs)

Deficiencies by Keyword Search



Results

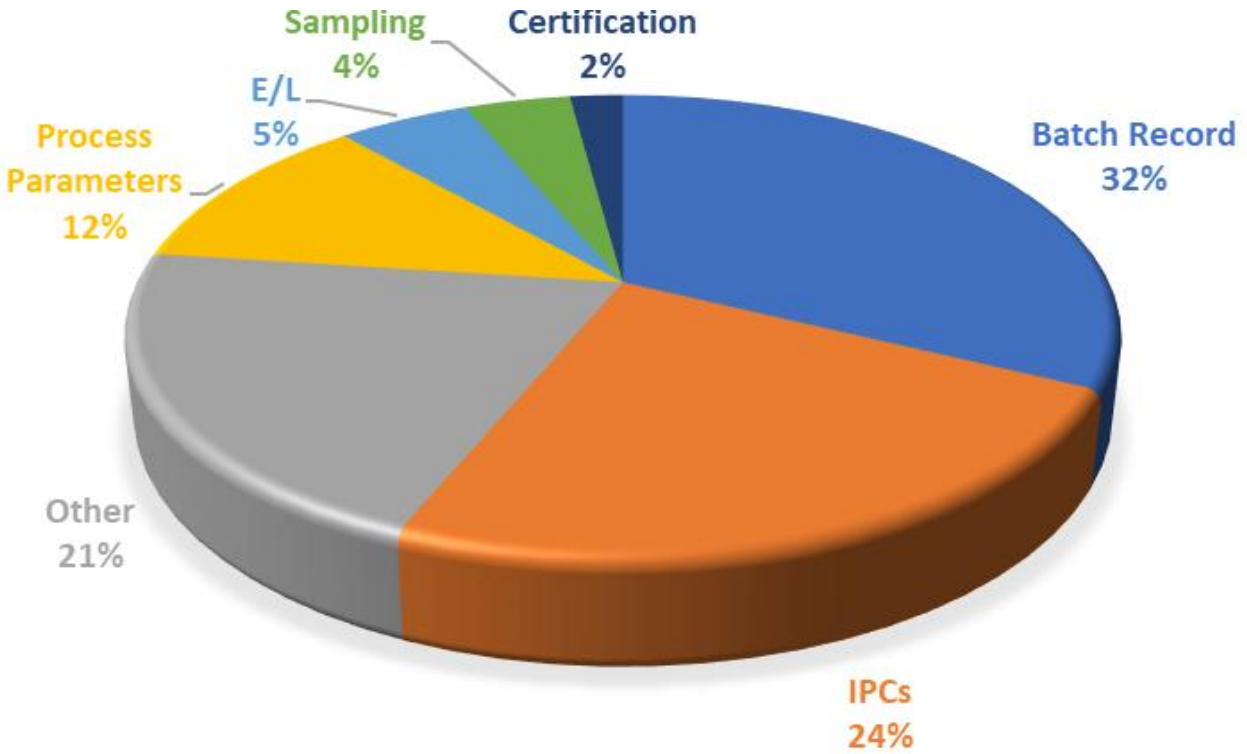
Unit Operations

- Mixing (compounding)
- Filtration
- Filling/sealing
- Lyophilization
- Packaging

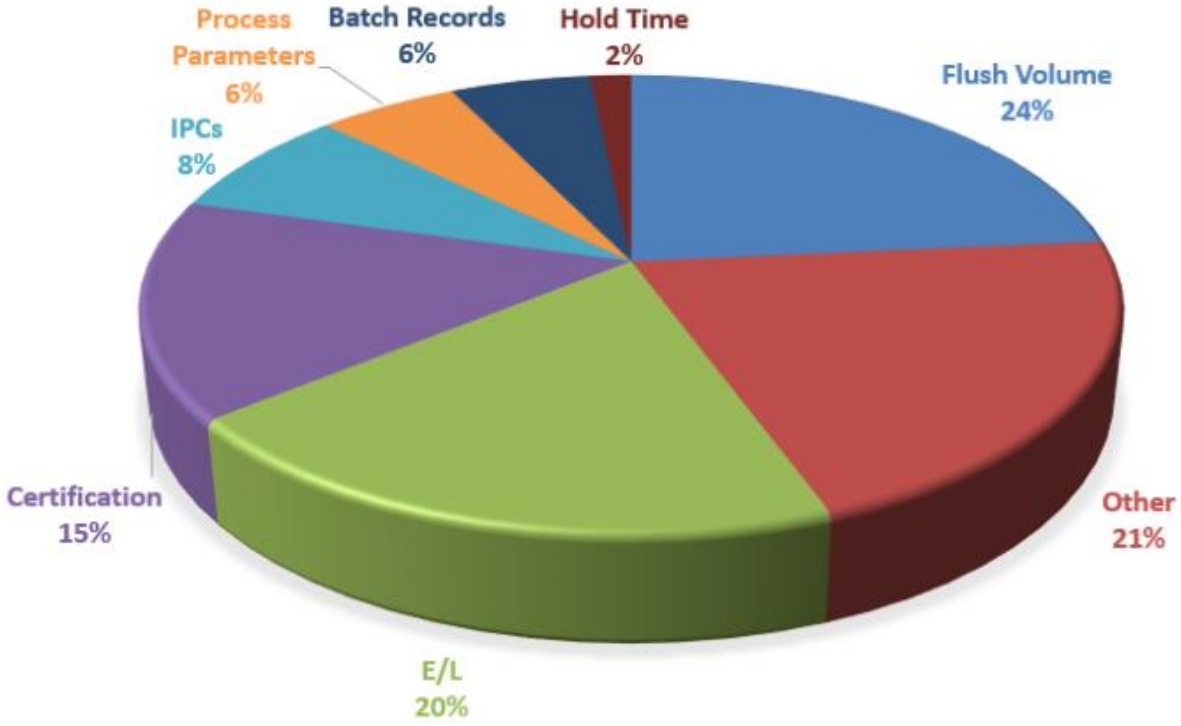
Other IQA Sections

- Drug substance attributes

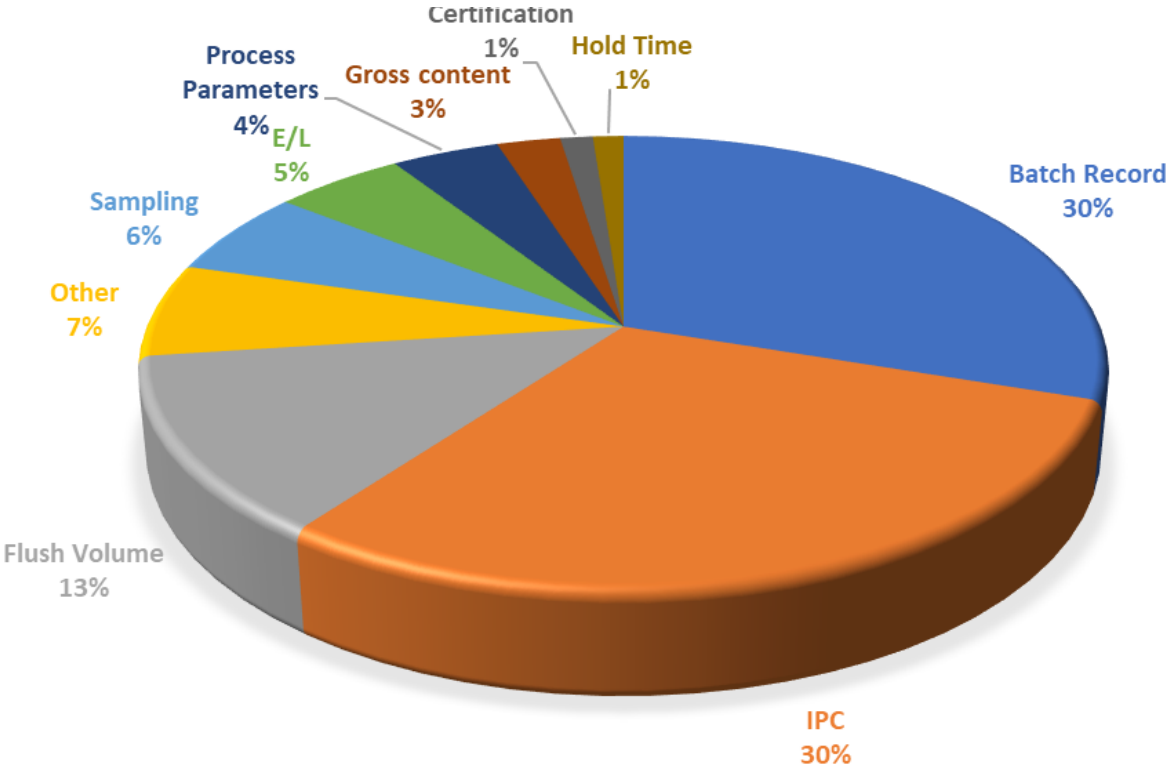
Mixing (Compounding)



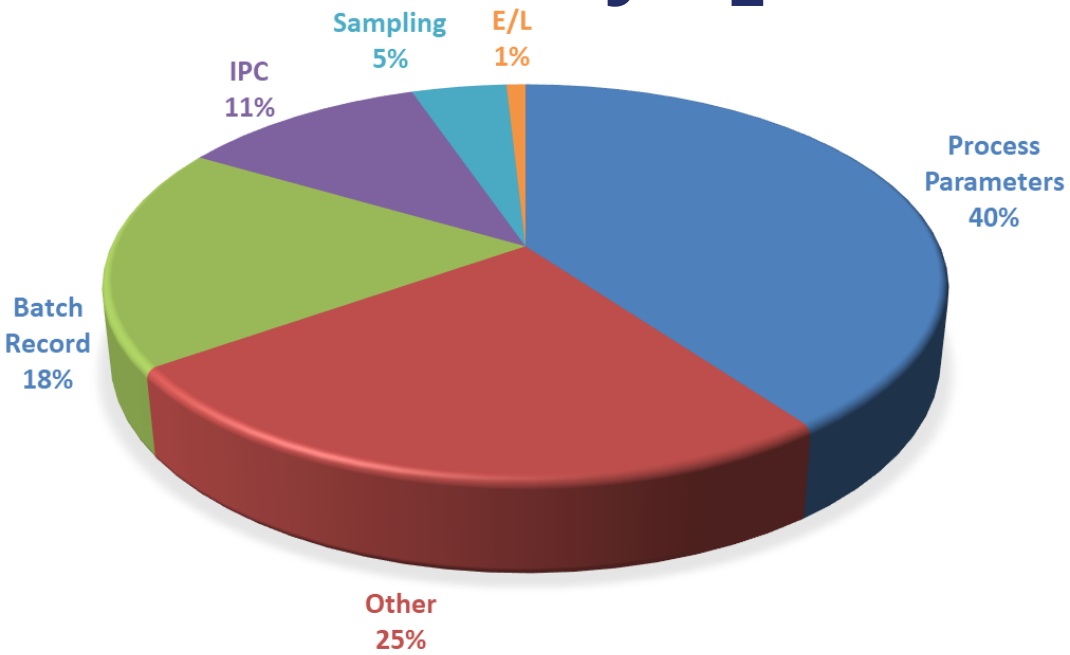
Filtration

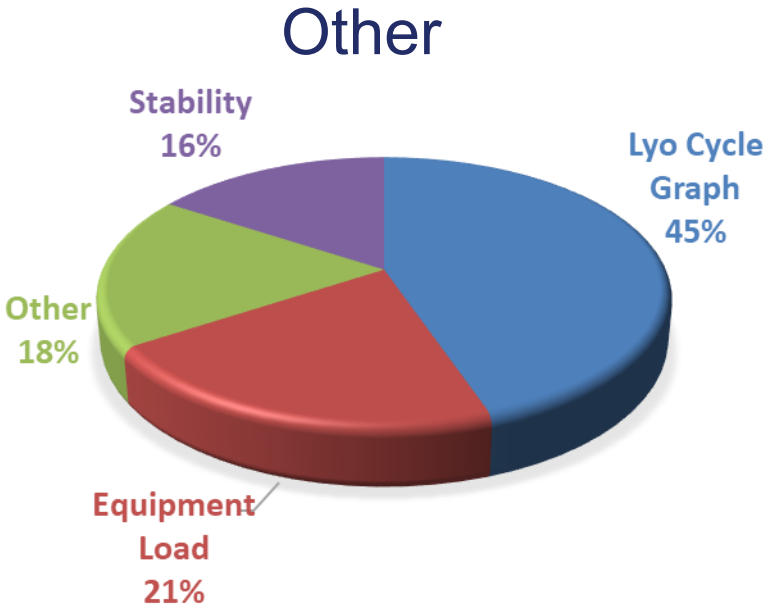

Process Parameters 6%
Batch Records 6%
Hold Time 2%
Flush Volume 24%
IPCs 8%
Certification 15%
Other 21%
E/L 20%

Filling/Sealing

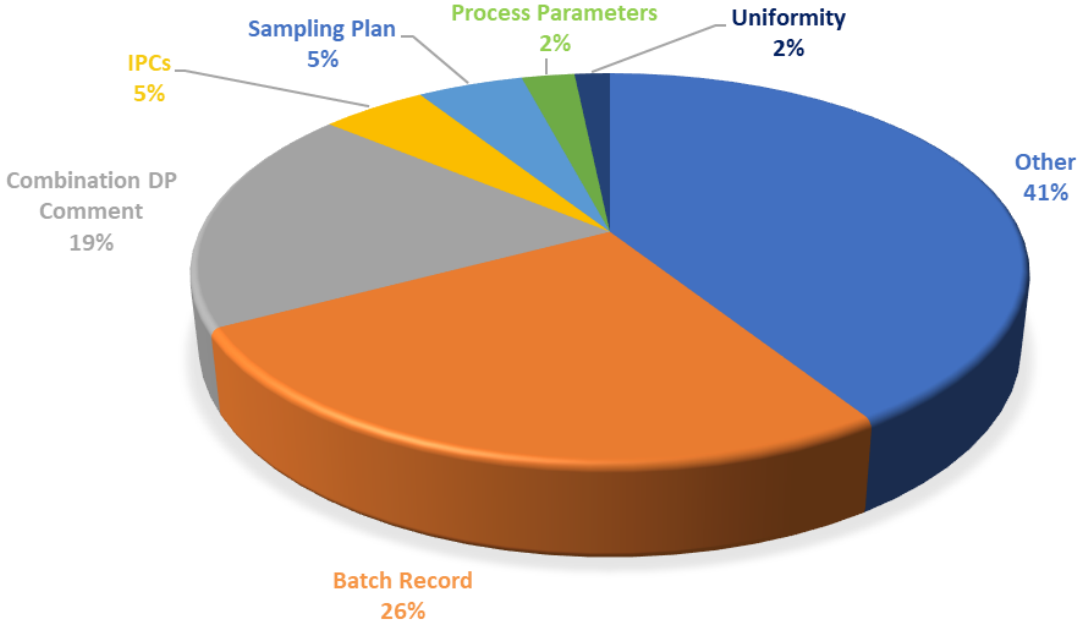


Lyophilization

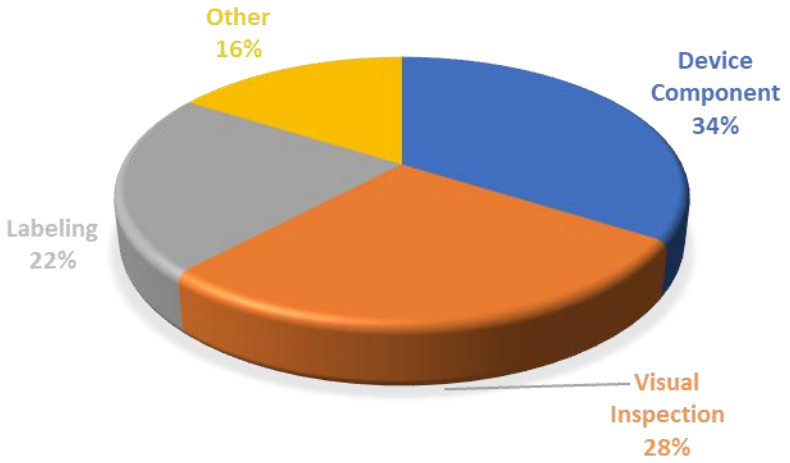




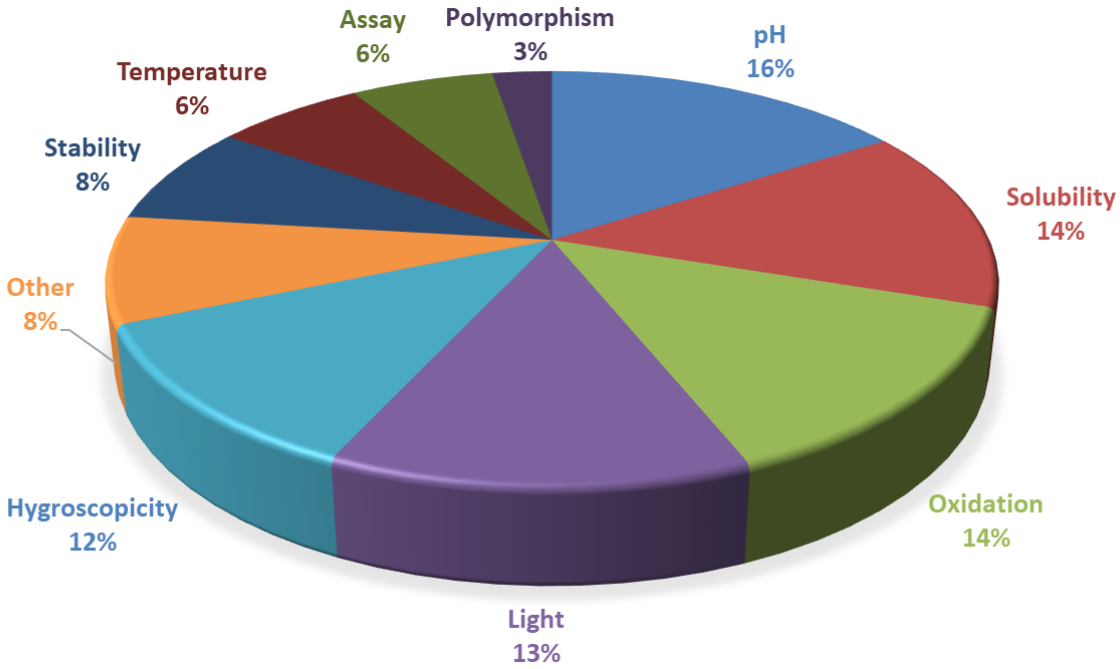
Packaging



Other



Drug Substance Attributes



Top Ten Deficiencies

10. Drug Substance Attributes-Solubility (n=55)

9. Drug Substance Attributes-pH (n=61)

8. Mixing-Process Parameters (n=62)

7. Filling/Sealing-E&L (n=64)

Top Ten Deficiencies, cont'd

6. Filling/Sealing-Sampling Plan (n=76)

5. Mixing-IPCs (n=125)

4. Filling/Sealing-Flush Volume (n=159)

3. Mixing-Batch Record (n=167)

Top Ten Deficiencies, cont'd

2. Filling/Sealing-IPCs (n=375)

1. Filling/Sealing Batch Record (n=376)

Reference Documents

- FDA Guidances
- 21 CFR 210 and 211
- United States Pharmacopeia (USP)

Take Home Message

- The goal is quicker approvals
- The filling unit operation had the most deficiencies
- Refer to FDA guidances, 21 CFR 210 and 211 and the USP

Acknowledgements

- David McChesney
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Challenge Question #1

What is one of the FDA enhancements to help with quicker approvals:

A. Complete response letters

B. Refusing to file applications

C. Sending IRS and DRLs late in the assessment cycle

D. Four Part Harmony for IRs

Challenge Question #2

Which of the following statements is NOT true?

A. The most common mixing operation deficiency was batch records.

B. The filling/sealing operation had the least number of deficiencies.

C. The most common drug substance attribute deficiency was pH.

D. Filtration deficiencies did not make the top ten.

U.S. FOOD & DRUG ADMINISTRATION

Questions?

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