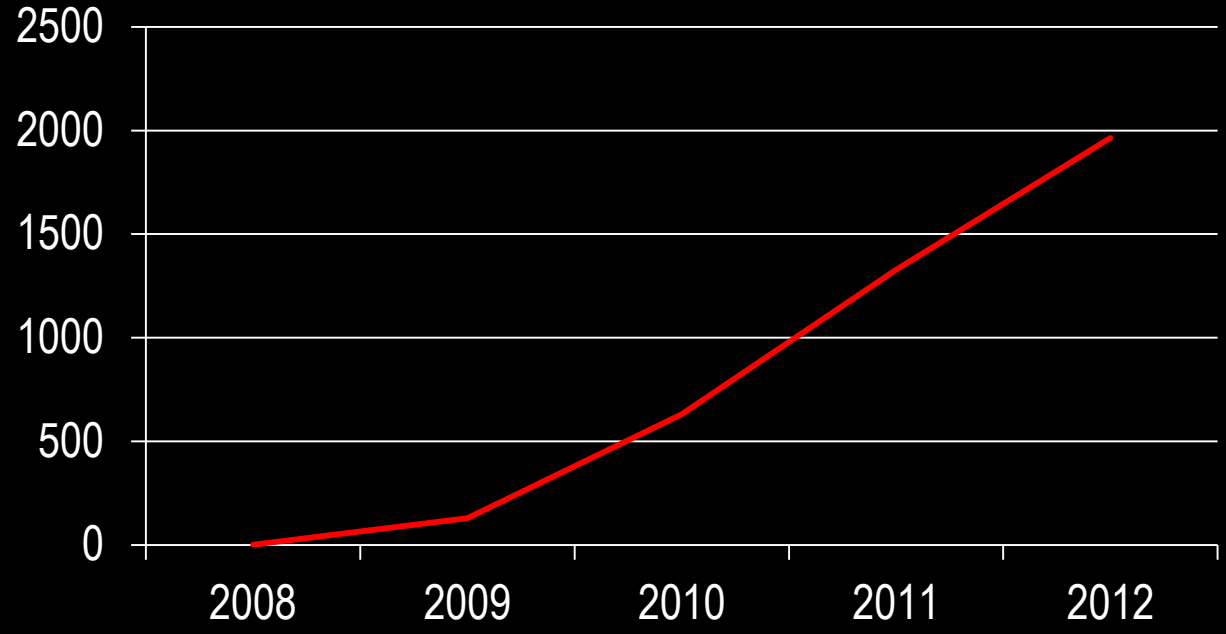
# PREVENT YOUR DIETARY SUPPLEMENT LABORATORY FROM BECOMING A COMPLIANCE RISK

Marian Boardley 2013

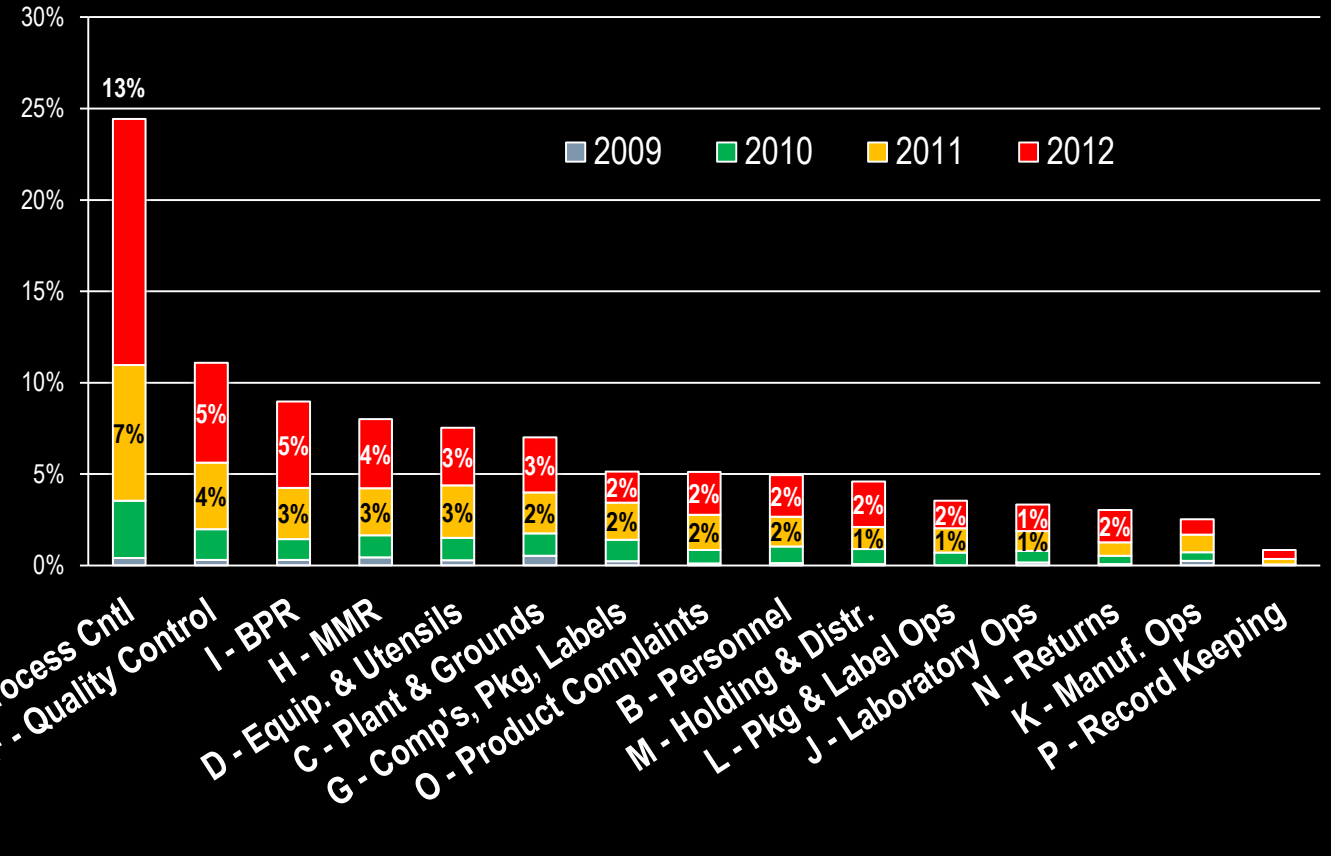
# APPLICABLE GMP'S: DIETARY SUPPLEMENT LABS

- Subparts for laboratory operations and testing, 21 CFR 111
  - D – Equipment & Utensils (calibration of instruments)
  - E – Requirements for specifications and testing to determine whether specifications are met (components, DI's, in-process, products) [111.70, 111.75]
  - F – Quality Control for laboratory operations [111.110]
  - J – Laboratory Operations
  - P – Recordkeeping
- 21 CFR Part 11 Electronic records & signatures

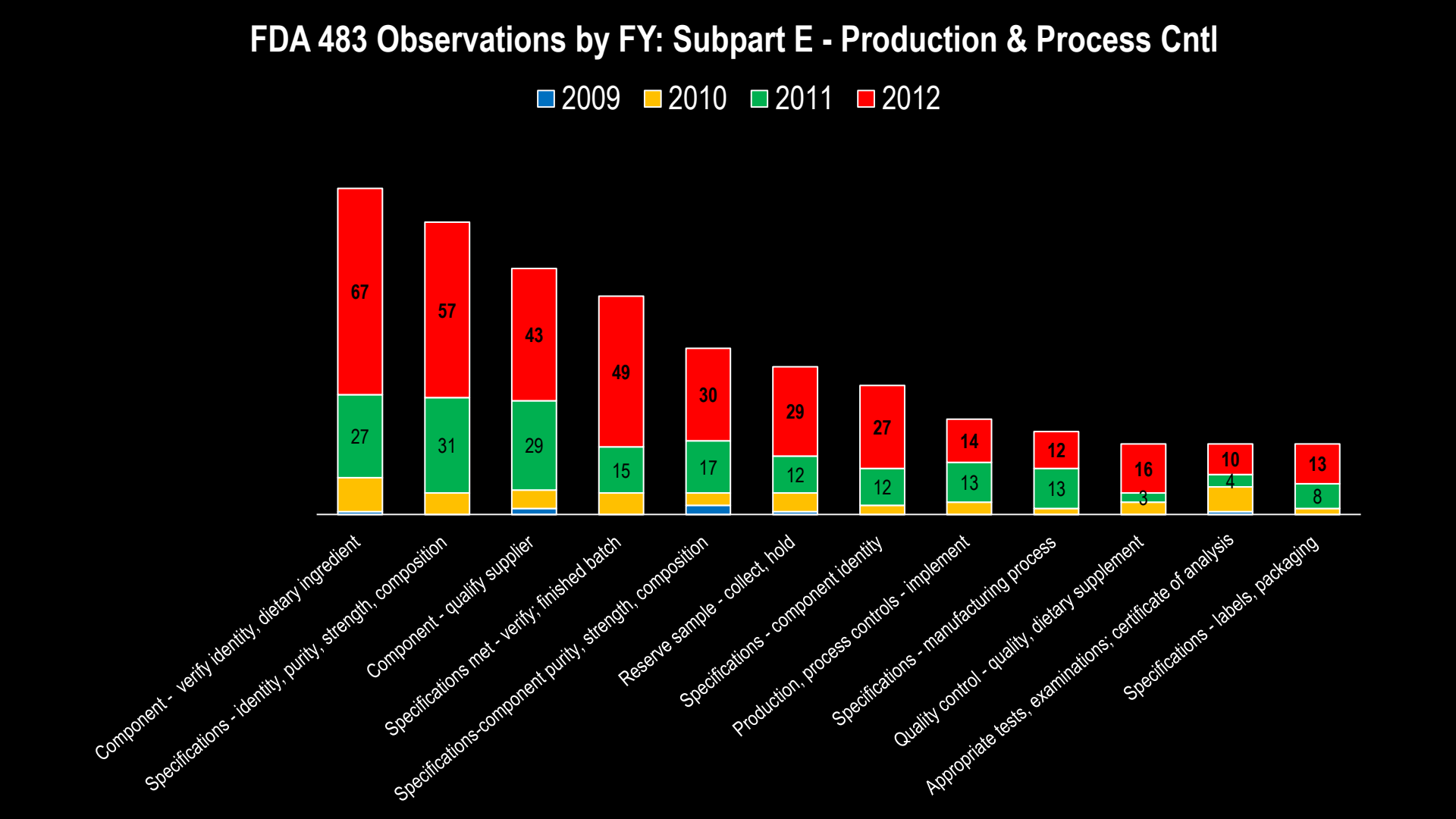
# 21 CFR 111 Dietary Supplement cGMP's Form 483 Observations by FDA Fiscal Year



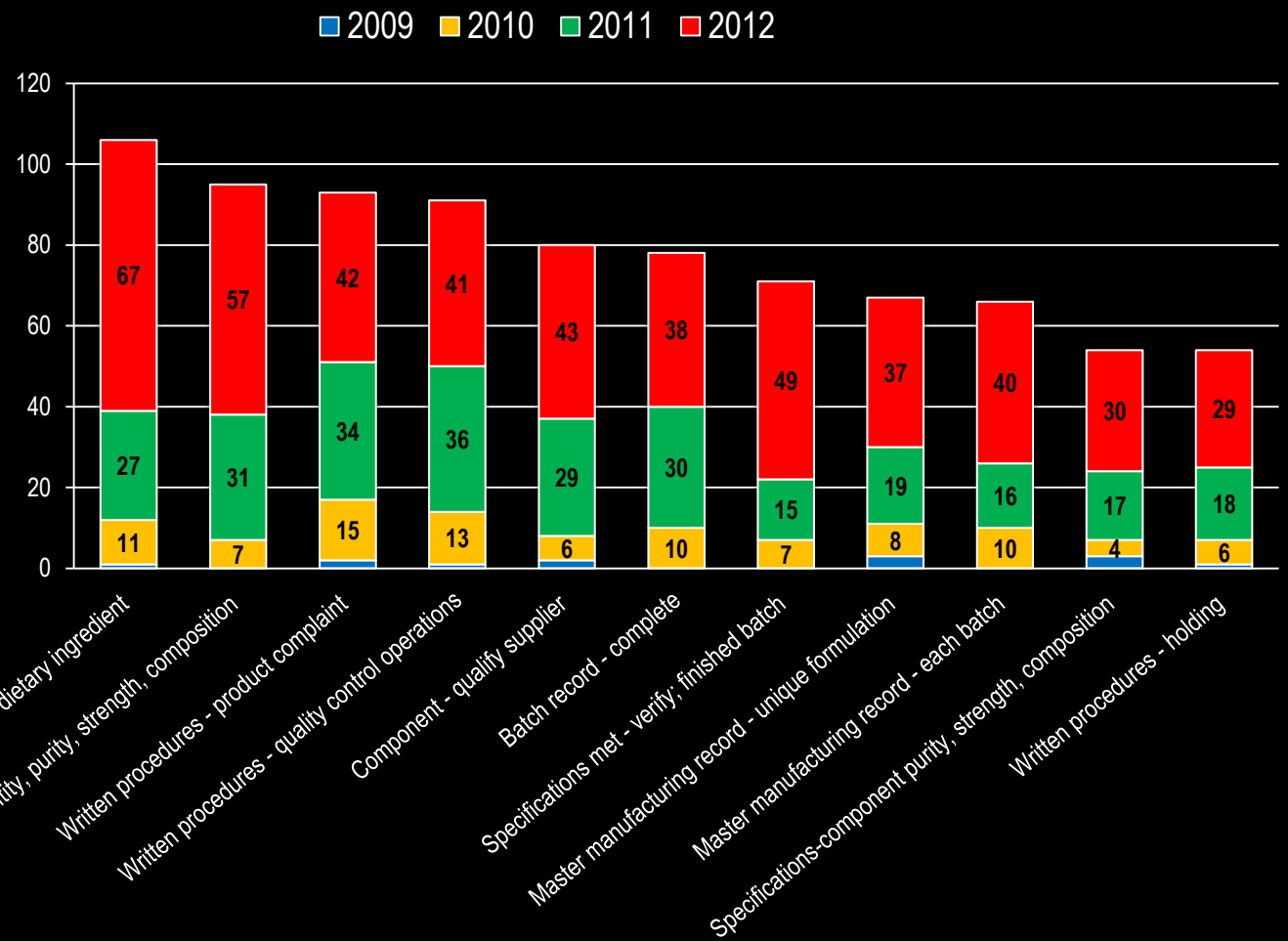
# 483 Observations By GMP Subpart



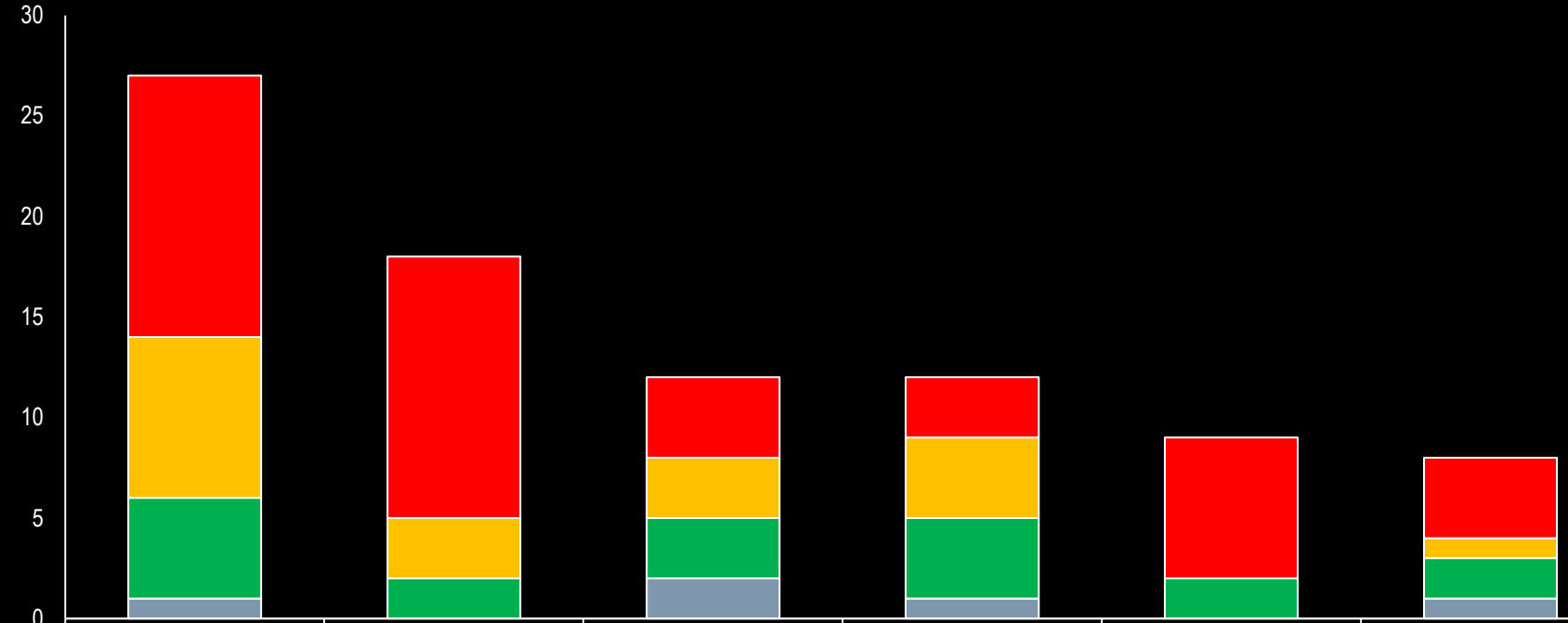
# FDA 483 Observations by FY: Subpart E - Production & Process Cntl



# FDA 483 Observations by FY: Subpart (All)

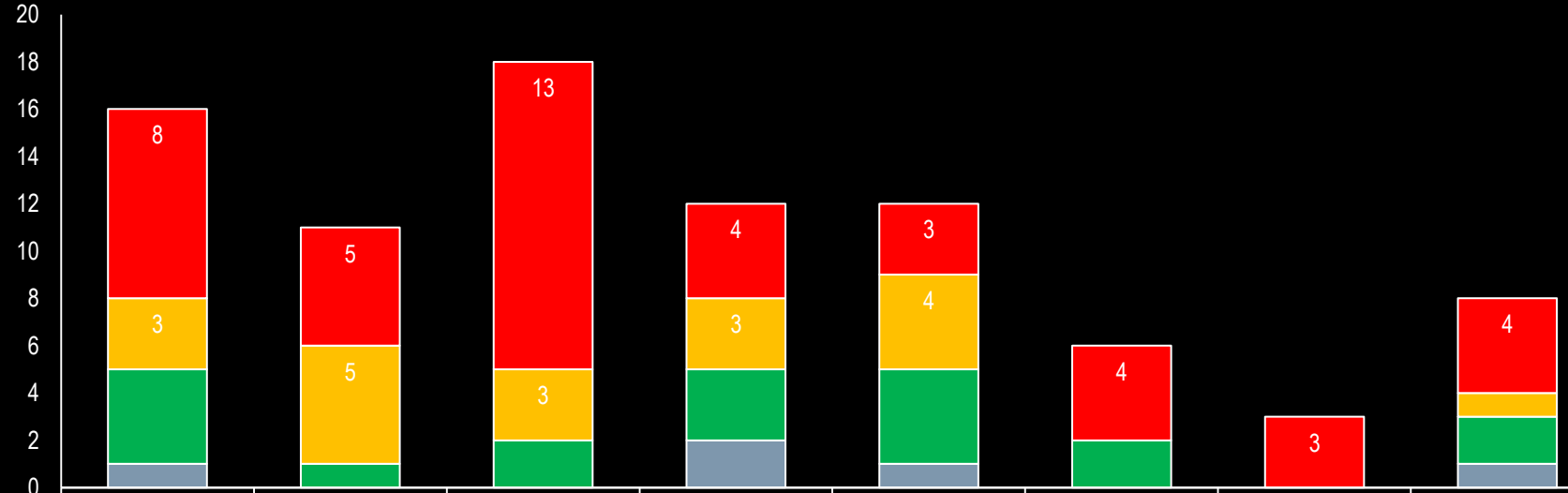


# FDA 483 Observations Subpart J - Laboratory Ops by Ref No




| | 21 CFR 111.303 | 21 CFR 111.320(b) | 21 CFR 111.315(b) | 21 CFR 111.320(a) | 21 CFR 111.325(a) | 21 CFR 111.325(b)(2)(ii) |
|---|---|---|---|---|---|---|
| 2012 | 13 | 13 | 4 | 3 | 7 | 4 |
| 2011 | 8 | 3 | 3 | 4 | | 1 |
| 2010 | 5 | 2 | 3 | 4 | 2 | 2 |
| 2009 | 1 | | 2 | 1 | | 1 |

# FDA 483 Observations Subpart J - Laboratory Ops by Ref No

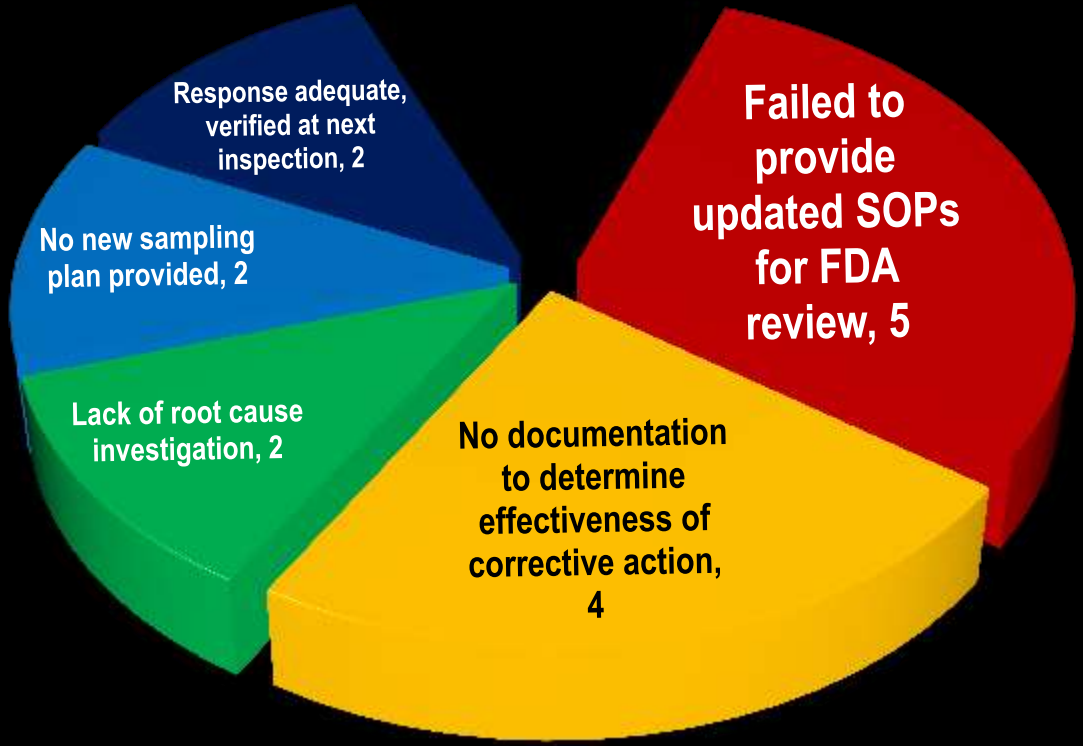



| | Written procedures - tests, examinations; specifications met | Written procedures - laboratory operations | Examination, testing; scientifically valid | Sampling plans; establish, follow | Examination, testing; appropriate | Written procedures, laboratory operations | Laboratory operations: electronic | Records - document; results |
|---|---|---|---|---|---|---|---|---|
| | 21 CFR 111.303 | | 21 CFR 111.320(b) | 21 CFR 111.315(b) | 21 CFR 111.320(a) | 21 CFR 111.325(a) | | 21 CFR 111.325(b)(2)(ii) |
| 2012 | 8 | 5 | 13 | 4 | 3 | 4 | 3 | 4 |
| 2011 | 3 | 5 | 3 | 3 | 4 | | | 1 |
| 2010 | 4 | 1 | 2 | 3 | 4 | 2 | | 2 |
| 2009 | 1 | | | 2 | 1 | | | 1 |

# LABORATORY GMP'S: 483 FINDINGS, SUMMARY

- Did not establish or follow written procedures for laboratory operations [21 CFR 111.303]
- Did not establish or follow sampling plans for obtaining representative samples [21 CFR 111.315(b)]
- Did not establish or follow laboratory control processes for use of criteria for selecting appropriate examination and testing methods [21 CFR 111.315(c)]
- Did not verify laboratory examination and testing methodologies appropriate for their intended use [21 CFR 111.320(a)]
- Did not identify and use an appropriate scientifically valid method for each established specification for which testing or examination is required [21 CFR 111.320(b)]

# Adequacy of Response to 483 items (from Warning Letters)



# WARNING LETTER: JULY 24, 2012 PHILADELPHIA DISTRICT

- Firm failed to calibrate instruments or controls used in manufacturing or testing a component or dietary supplement as required by 21 CFR 111.27(b)
- Failed to calibrate the infrared spectroscopy instrument used in finished product release
- Response Inadequate:
  - Stated that the instrument was calibrated as of 12/14/2011 and that all testing will restart with the newly calibrated instrument, but…
  - Failed to provide any documentation of these changes

# WARNING LETTER: FEBRUARY 20, 2013 LOS ANGELES DISTRICT

- Laboratory does not follow the USP Microbial Limits Method for Total Plate Count and Yeast and Molds **as referenced in batch records**
  - Total aerobic counts are not performed in duplicate in accordance with the USP
  - Sample volumes for total aerobic count 1mL, not 10mL as indicated in the USP
- "Response Inadequate"
  - Firm committed to following USP, but did not provide documentation to show amended protocols
  - Therefore FDA could not evaluate the adequacy of modified protocols

# WARNING LETTER: FEBRUARY 20, 2013 LOS ANGELES DISTRICT

- 21 CFR 111.315(d) – use of criteria for selecting standard reference materials used in performing tests and examinations
  - Firm used first shipment of raw materials received as the standard
  - Failed to identify the reference standard used for identity testing
  - No certification of accuracy of the reference standard
- "Response Inadequate"
  - Firm provided a completion date of August 30, 2012. However, they did not provide FDA with new protocols as of November 1, 2012

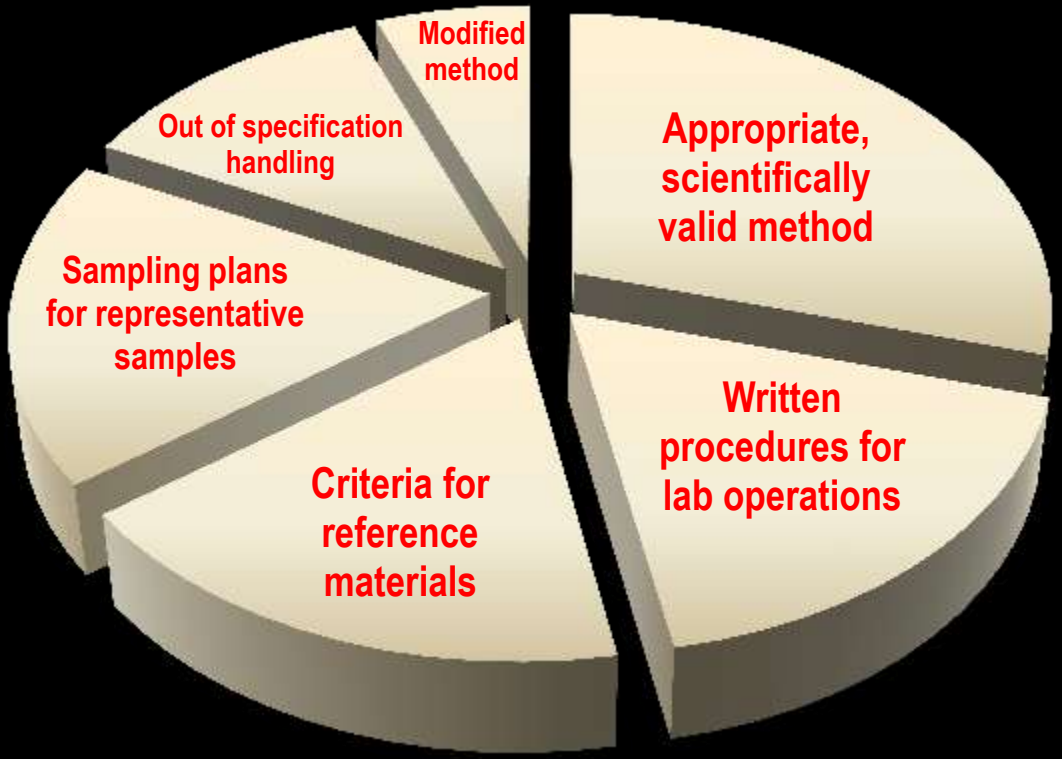
# WARNING LETTER: FEBRUARY 8, 2013 MINNEAPOLIS DISTRICT

- For approximately 80% or more of ingredients, did not confirm that reference materials were the biological material they purported to be prior to acceptance
- Firm's protocols require that subsequent lots of ingredients match the initially set standard
  - Different ingredients were shown to be capable of making such a match
  - Procedure allows analysts to select a different lot of received ingredient as a comparison when the incoming material does not match

# WARNING LETTER: FEBRUARY 8, 2013 MINNEAPOLIS DISTRICT

- "Response Inadequate"
  - Information was not provided to demonstrate that the reference material was confirmed to be the actual botanical ingredient
  - Additionally, firm did not provide a timeframe when correction would be completed

# Summary of Requirements for Laboratory Compliance



# REFERENCES

- 483 OBSERVATION DATA: http://www.fda.gov/iceci/EnforcementActions/ucm250720.htm

  (Food & Dietary Supplements, TurboEIR)

  *"These spreadsheets are not a comprehensive listing of all inspectional observations but represent the area of regulation and the number of times it was cited as an observation on an FDA Form 483 during inspections conducted by FDA and its representatives."*

- *WARNING LETTERS*
  - *http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm313468.htm*
  - *http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm340946.htm*
  - *http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm339823.htm*

# Questions?

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