YOUR CONTRACT MANUFACTURER RECEIVED A WARNING LETTER. WHAT NOW?

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FDA regulates Contract Manufacturer

- 21 CFR 807.20 – Contract manufacturers must register and list. [Federal Register 45940, Aug 2, 2012]
- 21 CFR 820 – contract manufacturer need only comply with those requirements applicable to the operations in which it is engaged.
- FDA routinely inspects contract manufacturers of Class 2 and 3 devices (risk based workplan).
- If serious violations found during the inspections, FDA will follow-up at Original Equipment Manufacturer (OEM)

FDA regulates Manufacturer

21 CFR 820.50 Purchasing Controls

- Each manufacturer shall establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements.
  - *Evaluation of suppliers, contractors, and consultants.*
  - *Purchasing data.* Each manufacturer shall establish and maintain data that clearly describe or reference the specified requirements, including quality requirements, for purchased or otherwise received product and services.

Case Studies

Two case studies will be presented, simulated from real warning letters presented to contract manufacturers.

- Case study 1 – *in-vitro* diagnostic reagent contract manufacturer
- Case study 2 – orthopedic implant contract manufacturer

Case Study 1 - Background

FDA conducted an inspection of a contract manufacturer of in-vitro diagnostic reagents that are part of Class II and III in-vitro diagnostic kits.

The inspection results in the issuance of a Warning Letter to the contract manufacturer.

See Warning Letter handout for details.

Case Study 1 – Response to FDA

In light of these findings discuss the following questions and consider the role of the contract manufacturer and the manufacturer (OEM) as you would prepare to formulate your response to the FDA

Case Study 1 - Questions
Warning Letter items #1 and #2

1. What Quality System Requirements (21 CFR 820) were not met by the contract manufacturer? The manufacturer (OEM)?

2. Who should take responsibility for the identified requirements the contract manufacturer and/or the manufacturer?

Case Study 1
Warning Letter items #1 and #2

#1 - Failure to adequately validate a process whose results cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a).

#2 - Failure to establish and maintain procedures to ensure that sampling methods are adequate for their intended use and to ensure that when changes occur the sampling plans are reviewed, as required by 21 CFR 820.250(b).

Case Study 1- Questions
Warning Letter items #1 and #2

3. What systems should be reviewed at the manufacturer (OEM)?

4. List the systemic corrective actions that should be taken in these systems based on the information you were given in the Warning Letter for these 2 items?

Case Study 1 - Questions
Warning Letter items #3 and #4

1. What Quality System Requirements (21 CFR 820) were not met by the contract manufacturer? The manufacturer (OEM)?

2. Who should take responsibility for the identified requirements the contract manufacturer and/or the manufacturer?

Case Study 1
Warning Letter items #3 and #4

#3 - Failure to establish and maintain procedures for analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems, as required by 21 CFR 820.100(a)(1).

#4 – Failure to establish and maintain procedures to control product that does not conform to specified requirements, as required by 21 CFR 820.90(a).

Case Study 1 - Questions
Warning Letter items #3 and #4

3. What systems should be reviewed at the manufacturer (OEM)?

4. List the systemic corrective actions that should be taken in these systems based on the information you were given in the Warning Letter for these 2 items?

Case Study 1
Warning Letter items #5

#5 - Failure to define the type and extent of control to be exercised over the product, services, suppliers, contractors, and consultants, based on the evaluation results, as required by 21 CFR 820.50(a)(2).

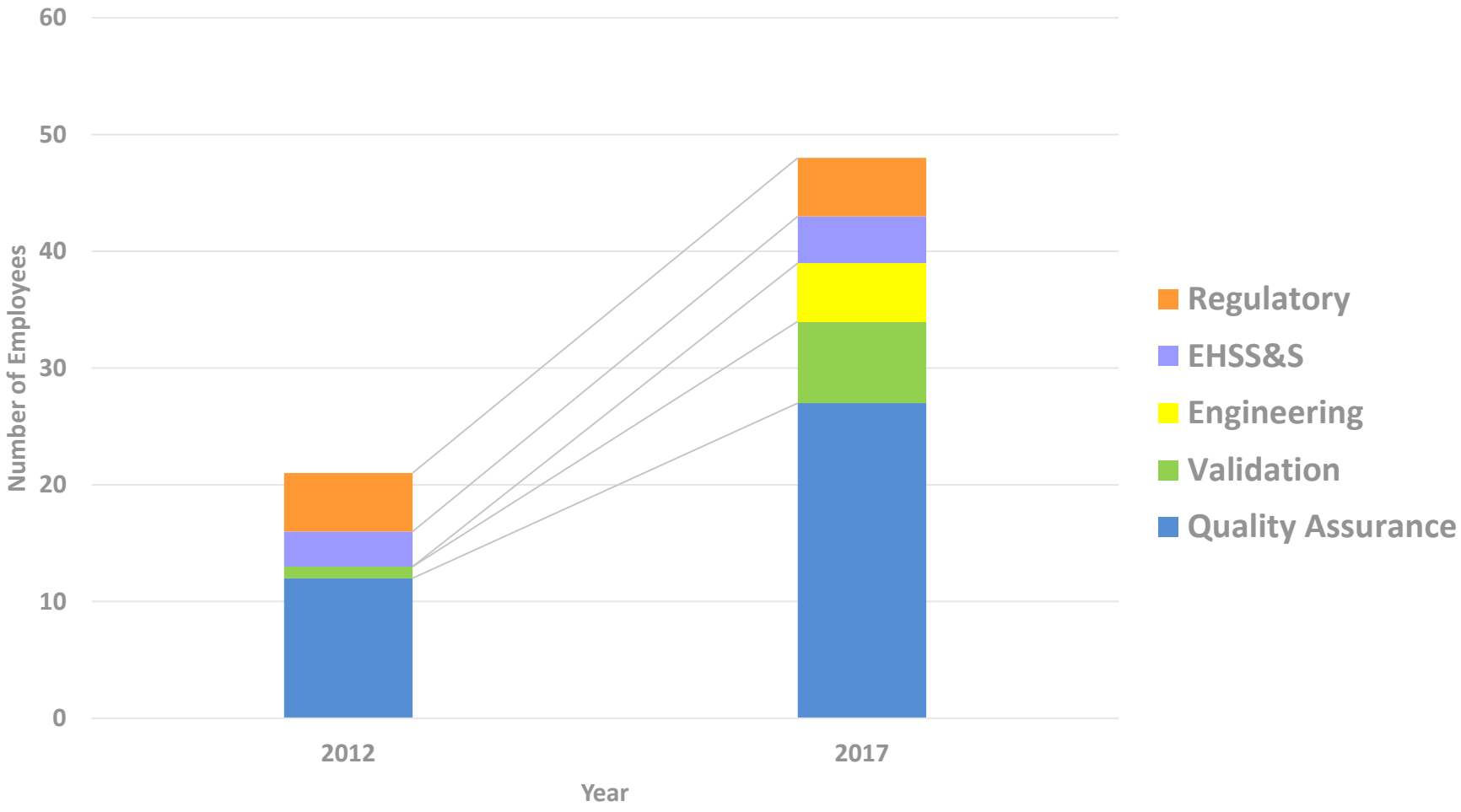
Case Study 1 Questions
Warning Letter items #5

Discuss the complexity of these arrangements regarding purchasing of components and supplier controls and how best to manage them.

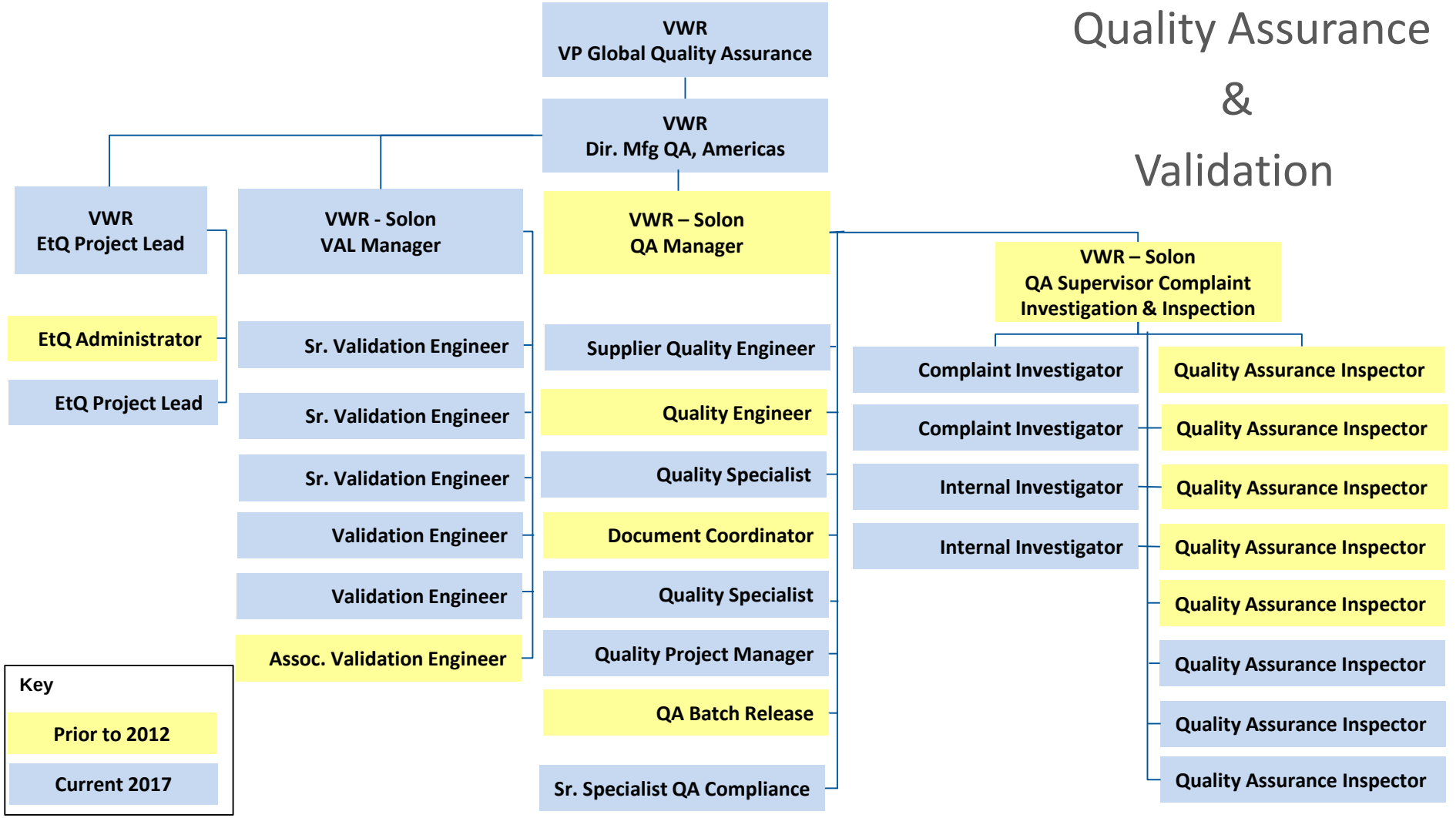
Contract Manufacturer perspective

How a contract manufacturer reacted to being given a warning letter – Michael Mascali

Investment of Quality & Compliance



Investment in Quality & Compliance



Quality Assurance & Validation

Investment of Quality & Compliance

Engineering

- VWR – VP Mfg & Engineering
  - VWR – Solon – Director Engineering
    - Sr. Process Engineer
    - Continuous Improvement Engineer
    - Process Engineer
    - Sr. Packaging Engineer

EHSS&S

- VWR – Director of EHSS&S, Americas
  - VWR – Solon – Manager, EHSS&S
    - Sr. Specialist – Environmental
    - Sr. Specialist – EHSS&S Mfg

Regulatory Affairs

- VWR - Interim Director of Regulatory Affairs, Americas
  - Specialist – Reg Affairs
  - Lead – Label Design
  - Label Designer
  - Label Designer

QC Validation

- VWR - Solon – Sr. Manager, Quality Control
  - VWR – Solon – Manager, Quality Control
    - Scientist – QC Validation
    - Scientist – QC Validation

Key

- Prior to 2012
- Current 2017

Summary

- Increase Headcount by 30 People
- Talent – Increased Technical Expertise
  - Dedicated Validation Team
  - Dedicated Engineering Team
  - Quality Associates with Regulated Industry Backgrounds
- Re-Alignment of Roles and Structure
- Global Compliance Governance
  - Regional & Local Expertise

OEM Manufacturer perspective

How an OEM prepares to work with a contract manufacturer. - Francis Blacha