Compounding Quality Center of Excellence Annual Conference

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Outsourcing Facilities: The Importance Of A Quality Culture – Points To Consider

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OBJECTIVES

- Background
- FDA presentation: “No Margin For Error”
- Cost of quality versus cost of lack of quality
- Responsibilities of Senior Management
- Legal considerations

The objectives for this presentation are to:

- Describe the surveillance activities of the compounding incidents team.
- Explain the adverse event reporting requirements for outsourcing facilities.
- Understand the overall process of investigating compounding incidents.
- Explain the intention of compounding risk alerts and provide examples.
- Discuss example compounding incidents investigated by the FDA.

FD&C – Section 501 – Adulterated Drugs and Devices

- "A drug or device shall be deemed to be adulterated…"
  - Section 501(a)(2)(B): "if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess."

Drug Quality Assurance

- Drug quality cannot be tested into the product.
  - Vast majority of all drug analytical tests are destructive.
  - Quality of non-tested units is inferred by test results, but not confirmed.
  - Out-of-specification results are more informative than passing results
- Drug quality must be intentional, predictable, consistent, and uniform.
- Drug quality is built into the drug by paying attention to and integrating facility and equipment design and maintenance, drug components, personnel behavior, and production processes with appropriate controls in places at each point.
  - These are the basic principles of current good manufacturing practices (CGMP).

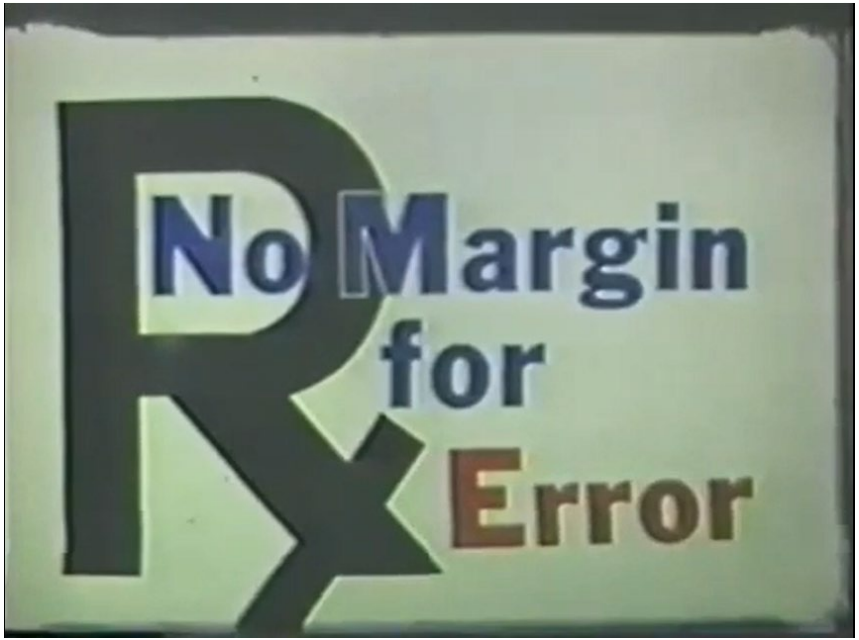
Definitions

- Quality Culture
  - From Parenteral Drug Association (PDA): "…Harvard Business Review defines "true culture of quality" as an environment in which employees not only follow quality guidelines but also consistently see others taking quality-focused actions, hear others talking about quality, and feel quality all around them."
  - See: www.pda.org/scientific-and-regulatory-affairs/quality-culture
- Senior Management
  - From FDA's Guidance for Industry (GUI) - *Q10 Pharmaceutical – Quality System*: "Person(s) who direct and control a company or site at the highest levels with the authority and responsibility to mobilize resources within the company or site."
  - See: www.fda.gov/regulatory-information/search-fda-guidance-documents/q10-pharmaceutical-quality-system

No Margin For Error

- Published by FDA in 1967 on CGMPs
  - Statutory CGMPs were established in 1962 as part of the Kefauver-Harris Drug Amendments
  - www.google.com/search?q=no+margin+for+error+fda+video#fpstate=ive&vld=cid:cd82bbcc,vid:FmOxDcimrBc

No Margin for Error Video



Cost of Quality versus Cost of Lack of Quality

- For your consideration:
  - Preventing problems early costs considerably less than responding to, investigating, and fixing problems later.
    - It can mean the difference between continued business viability and bankruptcy.
    - More importantly, preventing problems early (especially before distribution) reduces the risk of serious, otherwise preventable adverse reactions, including death.
  - See:
    - Andy Barnett, 2017, NSF International/Pharma Biotech, *The cost of quality: can we really afford to ignore it*?
    - Jess Ahrendt, 2017, NSF International/Pharma Biotech, *What does poor quality cost*?
  - Question: Has your corporation estimated the cost of controlling for quality (e.g., prevention costs) comparing it to the cost of failing to control for quality [e.g., internal failures (detection of quality failures before distribution), external failures (notification of quality failures after distribution)]?
    - If yes, did this assessment include how much it cost to recall drug product and potential loss of future business?
    - If no, then why not?

Responsibility of Senior Management

- From FDA GUI, *Q10 Pharmaceutical – Quality System*
  - Senior management has the ultimate responsibility to ensure an effective pharmaceutical quality system is in place to achieve the quality objectives, and that roles, responsibilities, and authorities are defined, communicated, and implemented throughout the company.
  - Management should:
    - Participate in the design, implementation, monitoring, and maintenance of an effective pharmaceutical quality system
    - Demonstrate strong and visible support for the pharmaceutical quality system and ensure its implementation throughout their organization.
    - Define individual and collective roles, responsibilities, authorities, and interrelationships of all organizational units related to the pharmaceutical quality system. Ensure these interactions are communicated and understood at all levels of the organization. **An independent quality unit/structure with authority to fulfill certain pharmaceutical quality system responsibilities is required by … regulations**.
- See: www.fda.gov/regulatory-information/search-fda-guidance-documents/q10-pharmaceutical-quality-system

Legal Considerations – FDA's Regulatory Procedures Manual

- Chapter 4 – Advisory Actions
  - Examples: Untitled and Warning Letters
  - 4-1, *Warning Letters*
    - 4-1-1, *Warning Letter Procedures*:

      "**Responsible officials in positions of authority in regulated firms have a legal duty to implement whatever measures are necessary to ensure that their products, practices, processes, or other activities comply with the law**. Under the law such individuals are presumed to be fully aware of their responsibilities..."

Legal Considerations – FDA's Regulatory Procedures Manual (continued)

- FDA's Regulatory Procedures Manual, Chapter 6 – Judicial Actions
  - Seizures, Temporary Restraining Orders, Preliminary and Permanent Injunctions
  - 6-2-5, Adequate Notice Preceding Injunction Actions – A. *Identifying Individuals*

    "…**the individuals who have the authority and responsibility to correct or prevent the violations should be named as defendants**."

Legal Consideration – Park Doctrine

- *United States v. Park*, 421 U.S. 658
  - John R. Park, the president of a national food store chain, was convicted of a misdemeanor FD&C violation based on rodent contamination in the company's warehouses.
  - Mr. Park was not alleged to have had direct responsibility for sanitation but, as president, was indirectly responsible for overall operations.
- Sometimes referred to as the "Responsible Corporate Officer" Doctrine.

Pharmakon

"The former president of a drug compounding company was sentenced to prison for his convictions for conspiring to defraud the Food and Drug Administration (FDA) and for multiple counts of distributing adulterated drugs."

- See: www.justice.gov/opa/pr/former-ceo-sentenced-prison-defrauding-food-and-drug-administration-and-distributing

Ian's Suggested Readings

- W. Edwards Deming, *The New Economics for Industry, Government, Education, 2nd Edition*.
- W. Edwards Deming, *Out of the Crisis*.
- J.M. Duran, *Quality by Design – The New Steps for Planning Quality into Goods and Services.*
- ISPE's Pharmaceutical Engineering iSpeak Blog, 2016
  - How Leader Actions and Behaviors Influence Quality Culture, Part 1
  - How Leader Actions and Behaviors Influence Quality Culture, Part 2
- CDER's Quality Management Maturity (QMM) Program: Practice Areas and Prototype Assessment Protocol Development, August 2023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