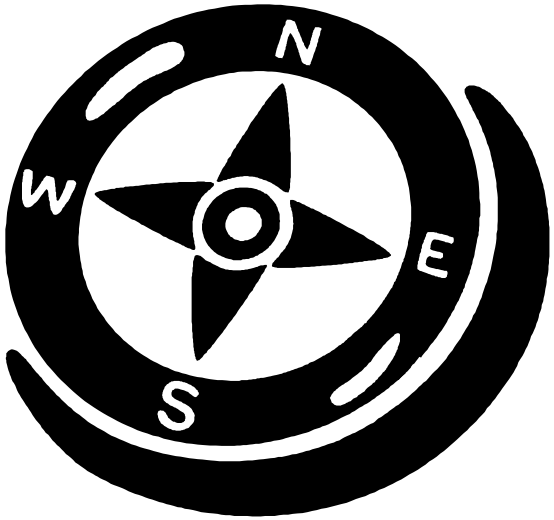


Direction for Leachables/Extractables

Helen N. Winkle
Director, Office of Pharmaceutical Science
Center for Drug Evaluation and Research
Food and Drug Administration
December 5-6, 2005

Map for Discussion

- FDA Direction
- PQRI Role
- Leachables and Extractables
- Desired Results

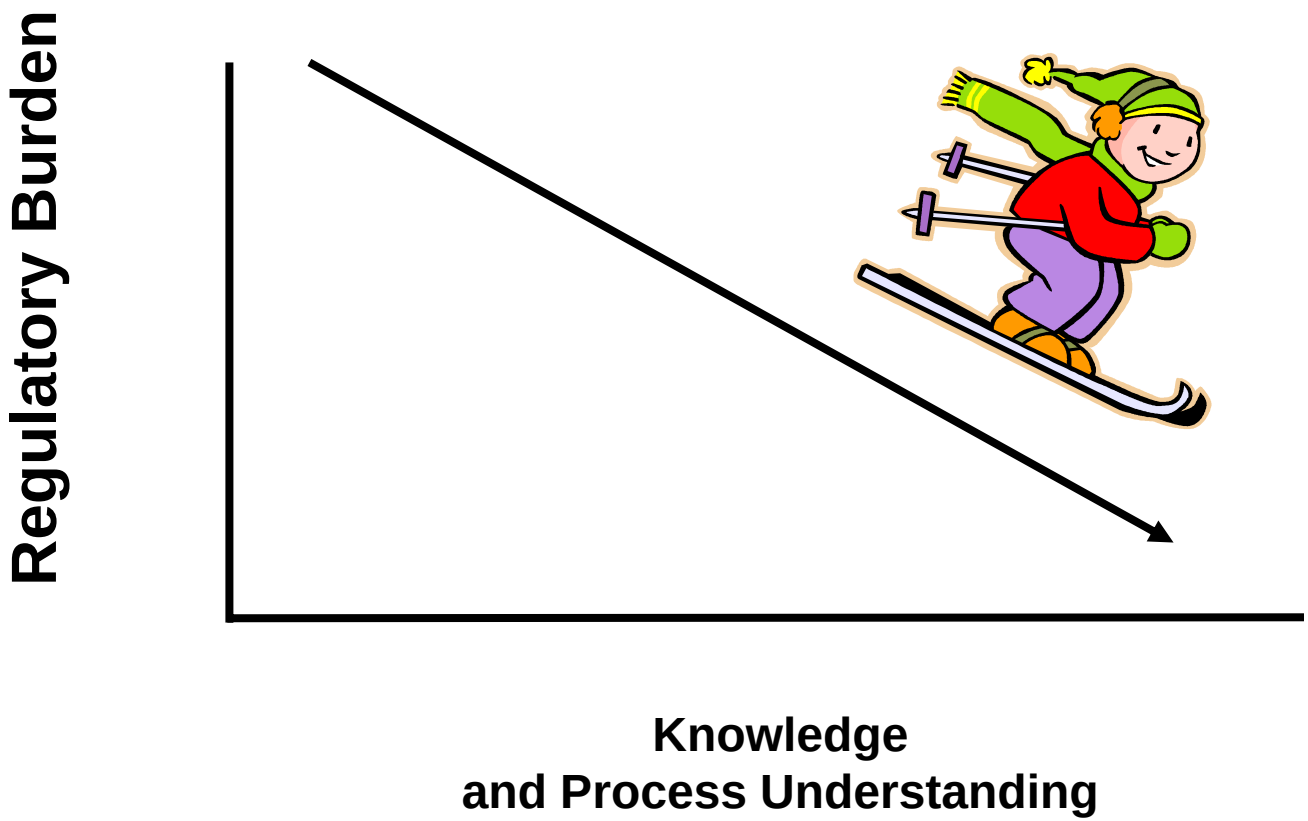
FDA Direction

- Risk-Based Approaches
  - cGMP for 21st Century Initiative
  - FDA oversight based on:
    - Understanding of Product and Process
    - Quality System Robustness
    - Impact on Public Health
    - Success History of Manufacturer

FDA Direction

- Science-Based Regulation
  - Implementation of new technologies
  - Facilitate continuous manufacturing improvements
  - Reducing variability
  - Science and engineering enhanced decisions
  - Science based policies and standards

FDA Direction



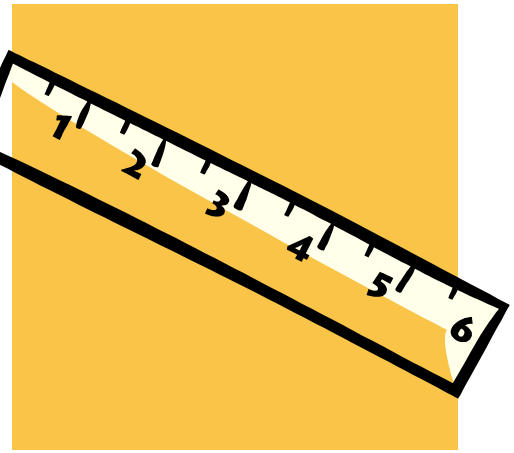
FDA Direction

- Internal use of quality system approach
  - Keep groups within the organizations going in the same direction
  - Find and apply best practices
  - Modernize our approach to setting standards
  - Maintain openness

FDA Direction

- Coordinated Approach to Regulating
  - Pharmaceutical Inspectorate
    - 5 Level III Investigators Certified 2005
    - 15 More During 2006
      - Awaiting Visitation Detail
    - 30 Additional Begin Training, March/April 2006
  - Teamwork Approach to Review and Inspection
    - Based on success of PAT Team
    - Training offerings to Investigators from OPS
    - Deciding when the reviewer should be at the facility
    - Improved communication

FDA Direction



- Standards Development
  - Adopt standards developed by non-government organizations (NGOs)
  - These are preferred to methods developed solely within FDA and its laboratories
  - FDA encouraged to participate with NGOs
    - But not to dominate

FDA Direction

- Authority for approach
  - NTTAA
    - National Technology Transfer and Advancement Act
    - Amended the Stevenson-Wydler Act of 1980
    - Signed by President Clinton on March 7, 1996
  - OMB CircularA-119
    - Defines terminology
    - Defines “Consensus Standard Organization” (CSO)
    - Authorizes government participation in CSOs
  - http://standards.gov/standards_gov/index.cfm

FDA Direction

- Consensus Standard Organization (CSO)
  - Benefits
    - Open
    - Balance of interest
    - Due process
    - Appeal process
    - Consensus
      - General agreement (not unanimity)
      - Process to resolve objections
      - Objector is advised of disposition of the objection

PQRI Role

- PQRI was created as a body to finance or coordinate laboratory or clinical research
- Additional role of PQRI
  - Conducts survey analysis, data mining, and workshops for balanced industry cross sections
  - Proposes results of these analyses to FDA to revise guidance
- Leachables and Extractables WG utilized bole roles
- Emerging role
  - Publication
  - Public Standards

PQRI Role

- PQRI is increasingly open
- PQRI has a balance of interest
- PQRI has due process
- “Consensus” organization

PQRI Role

- Areas for development
  - Dispositions of objections to positions
  - Appeal process
  - Revision process

PQRI Role

- PQRI Products (resemble standards)
  - Stratified Sampling (Blend Uniformity)
  - Aseptic Processing
  - Proposed Draft Leachables and Extractables Report to PQRI DPTC

Leachables and Extractables

- Systematic process for leachables safety assessment
- Exposure thresholds for qualification
- Best practices
  - Component selection
  - Controlled extraction studies
  - Leachables studies
  - Routine quality control methods

Leachables and Extractables – Lessons Learned from Working Group

- Consensus is achieved by hard work
- Learning process for everyone
- Make best use of available science
- Conduct further studies when needed
- Seek input from a wider audience
- Flexibility is important

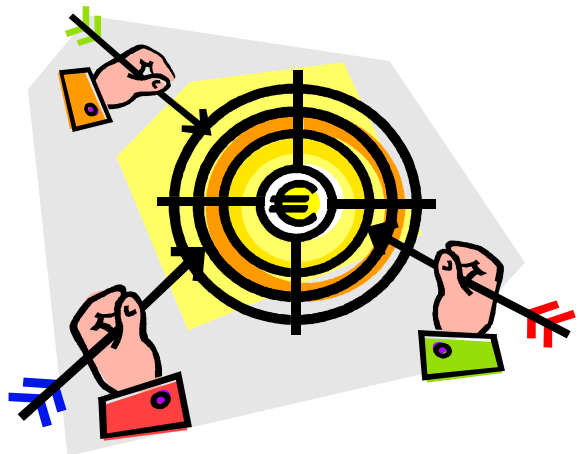
Desired Results of Working Group

- Recommendation to Agency
  - Written recommendations
  - Open and balanced consideration
  - Consider alternate points of view and document their disposition
  - Allow for future revision through an open appeal process

GOALS OF PQRI

- **Maintain high standards of product quality and the competitive edge of the US pharmaceutical industry**
  - ***improving efficiency of developing quality into products**

- **And ensure safe and effective products are available to the American public!!**



Thank You Working Group

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Thank You Supporters

- PQRI Member Companies
- Test Article Donations
- Laboratory Work Donations
- Document Reviewers
  - Threshold Justification
  - Best Practice Recommendations
- Workshop Functions
  - Organizers
  - Participants