


The regulatory environment and the role of the statistician

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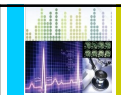
ICH




- ICH stands for International Conference on Harmonization of technical requirements for registration of pharmaceuticals for human use
- The ICH is an amalgamation of expertise from various agencies and organizations across the world, mainly from North America, Europe and Japan
- Founded in 1990
- ICS official website: www.ich.org

ICH
harmonisation for better health

ICH goals

- To maintain a forum for a constructive dialog between regulatory authorities and the pharmaceutical industry on differences in technical requirements for marketing approval in various countries
- To facilitate the adoption of new or improved technical research and development approaches that update or replace current practices
- To monitor and update harmonized technical requirements leading to a greater mutual acceptance of research and development data
- To contribute to the protection of public health from an international perspective
- To encourage the implementation and integration of common standards of documentation and submission of regulatory applications by disseminating harmonized guidelines

ICH process

- Expert Working Group consensus building
- Confirmation of Expert Working Group consensus by the Steering Committee
- Regulatory consultation and discussion
- Adoption of an ICH harmonized tripartite guideline
- Implementation

GXP

- GMP - Good Manufacturing Practice: quality standard covering the manufacture and testing of active pharmaceutical ingredients, diagnostics, foods, pharmaceutical products, and medical devices.
- GLP – Good Laboratory Practice: quality standard of management controls for laboratories and research organizations to ensure the consistency and reliability and reproducibility of results
- GCP - Good Clinical Practice: quality standard for clinical trials involving human subjects.

Development and approval process

- Nonclinical testing.
- Submission of an Investigational New Drug Application (IND)
- FDA review of the IND
- Preparation and submission of an New Drug Application (NDA) following clinical research
- FDA review and approval of the NDA

Both IND and NDA reviews include statistical review

Regulatory statistical review

- Pharmacokinetics and Pharmacodynamics.
- Bioavailability and bioequivalence
- Drug safety monitoring
- Demonstration of efficacy
- Chemical testing and product quality assessment and control

Kefauver-Harris Amendment

- This law, that was a response to the Thalidomide tragedy was signed by President Kennedy on October 10, 1962
- The amendment requires drug manufacturers to provide proof of the effectiveness and safety of their drugs before approval
- In particular, controlled clinical trials are required

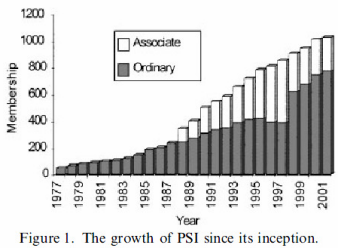


Figure 1. The growth of PSI since its inception.

How statisticians are seen by others?

- Compilers of data?
- Involved in all aspects of the design, analysis and the interpretation of experiments?
- Or, is there another view?

Pharmaceutical statistics vs. clinical statistics

- Statistical thinking, not just statistics, is important to any area in which data are collected
- collection of data in any field of activity is subject to variation
- Statisticians are the experts in
  - Designing experiments to investigate sources of variation
  - Analyzing and understanding sources of variability
  - Interpreting the consequences that come up from the analyses

Statisticians, not statistics, are important

Statistics does not:

- influence
- persuade
- design studies
- analyze data
- interpret findings
- Report results

Statisticians are the ones who make the discipline meaningful by doing all of the above!

The Status Quo

- "We've always done it this way in the past and it worked well, why change now?"
- "Everyone else does it this way, you can find a lot of examples in the literature."
- "We have to do it this way because the regulators want it."

However,

- The old methods are often not as efficient as more recent developments
- Regulatory authorities are open to discussion and persuasion concerning methodology

Statisticians need to

- Be more entrepreneurial
  - Suggest improvements without being asked to find them
- Be more communicative
  - Sell our profession, and ourselves
  - Show how our solutions will impact the bottom line
  - Collect positive examples of where statistics and statisticians have brought benefit to our organizations
- Be more persistent
  - stand up for what we believe in and have the courage of our convictions to argue our case

The proactive statistician

- Identifying the statistical and information requirements of the clients
- influencing clients to take on problems
- Developing solutions to problems
- Influencing clients to implement solutions
- Monitoring the long-term performance of the solutions