

An Introduction to the Draft Document: The Use of Bayesian Statistics in the Medical Device Clinical Trials

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Public Meeting on Draft Bayesian Guidance

Session 1

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Outline

- Focus of Today's Meeting on Draft Guidance
- History of experience with Bayesian statistics at CDRH
- Section 3 (What is Bayesian statistics, why use for medical device trials?)

FDA Guidance

- Draft Guidance for Industry and Food and Drug Administration Staff; Guidance for the Use of Bayesian Statistics in Medical Device
- <http://www.fda.gov/cdrh/osb/guidance/1601.html>
- Released May 23, 2006
- 90-day comment period ends August 21st.
- Docket No. 2006D-0191
- Dockets website
<http://www.fda.gov/ohrms/dockets/>

What FDA Guidance is

- It contains non-binding recommendations.
- When finalized, it will represent FDA's current thinking on this topic.
- It does not create or confer any rights for or on any person and does not bind FDA or the public.
- You can use an alternate approach if it satisfies the requirements of the applicable statutes and regulations. If you wish to discuss such an approach, contact FDA.

Draft Document

- This document is only a draft – not for implementation.
- It is out for public comment.
- The comment period ends August 21, 2006.
- Efforts will then be made to finalize the document.

Focus of Today's Meeting

- Focus is on the draft document: The Use of Bayesian Statistics in Medical Device Clinical Trials
- How do you provide comment to the draft?
- Submit your comments to the docket.

How to Provide Comments to the Docket

- Submit written comments to
 - Division of Dockets Management, HFA-305,
Food and Drug Administration, 5630 Fishers
Lane, Room 1601, Rockville MD 20852
- Submit electronic comments to
<http://www.fda.gov/dockets/ecomments>
using Docket No. 2006D-0191

Introduction

- Draft provides guidance on statistical aspects of the design and analysis of clinical trials for medical devices that use Bayesian statistical methods.
- It is not meant to describe the content of a submission to CDRH.
- The document is not all-inclusive; there are numerous books and papers on Bayesian theory and methods.

Least Burdensome Approach

- This document reflects FDA's careful review of what we believe are the issues related to the use of Bayesian statistics in medical device clinical trials and what we believe would be the least burdensome way of addressing them.
- If you have comments on whether there is a less burdensome approach, please submit your comments.

History of the Bayesian Initiative at FDA

- Begun in 1997.
- Support at the highest levels in CDRH: from the Center Director, the Office Directors, ODE Division Directors and branch chiefs
- Bayesian Medical Device Workshop in 1998, jointly sponsored with HIMA, drew 200 participants.

More General Bayesian Workshop in 2004

- “Can Bayesian Approaches to Studying New Treatments Improve Regulatory Decision-Making?”
- Jointly sponsored and planned by FDA and Johns Hopkins University
- Held May 20-21, 2004 at NIH

More General Bayesian Workshop in 2004

- Presentations by Janet Woodcock, Bob Temple, Steve Goodman, Tom Louis, Don Berry, Greg Campbell, 3 case studies and panel discussions.
- August, 2005, issue of the journal *Clinical Trials* is devoted to this workshop
- Available at
<http://webcasts.prous.com/bayesian2004/index.asp>

Bayesian Statistics: Submissions to CDRH

- At least 14 Original PMAs and PMA Supplements have been approved since 1999 with a Bayesian analysis as primary.
 - The Supplements include stent systems, a heart valve, and spinal cage systems.
- Many IDEs have also been approved.
- A number of reviews are in process.

3.1 What is Bayesian Statistics?

- Statistical theory and approach to data analysis that provides a coherent method from learning from evidence as it accumulates.
- It uses Bayes' theorem for combining prior information with current information on a quantity of interest.

Some Terminology

- Bayesian Statistics
- Frequentist Statistics
- Prior Distribution
- Posterior Distribution
- Likelihood

3.2 Why Bayesian Methods for Medical Devices?

- When there is good prior information, this approach may enable FDA to reach the same decision for a device submission with a smaller or shorter trial.
- If no prior is used, a Bayesian approach can provide flexible methods for interim analyses and other modifications. In addition, it can be used in complex modeling situations.

3.2 Why Bayesian Methods for Medical Devices?

- Often there is good prior information for a medical device. The mechanism of action is usually physical (not pharmacokinetic or pharmacodynamic) and local (not systemic).
- While the prior may be controversial if based mainly on personal opinion, it may be not be contentious if based on empirical evidence.

3.2 Why Bayesian Methods for Medical Device Studies?

- FDA Modernization Act of 1997 mandates FDA shall consider the least burdensome approach of demonstrating effectiveness or substantial equivalence
- A Bayesian approach when correctly employed may be less burdensome than a frequentist approach.

3.3 Why are Bayesian Methods More Commonly Used Now?

- Bayesian analyses can be computationally intense.
- But computing speeds have increased dramatically in the past few years and there have been breakthroughs in algorithms such as the crucial Bayesian tool called Markov Chain Monte Carlo (MCMC).

3.4 When Should FDA Participate in the Planning of a Bayesian Trial?

- Talk to CDRH before the study begins.
- If the study requires an Investigational Device Exemption, it is recommended you meet with FDA before you submit the IDE.

