M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

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Date: November 27, 2001

To: Dockets Management Branch (HFA-305)

From: Melissa Lamb
Office of Generic Drugs

Subject: ANDA Amendments & Supplements

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: ANDA Amendments & Supplements
Issues and Opportunites

Presented for: FDA/GphA Fall Technical Workshop

Date Presented: October 29, 2001

Presented by: Gary J. Buehler, R.Ph.,
Director, Office of Generic Drugs

Number of Pages: 22

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Attachment

M723

90S-0308

FDA/GPhA Fall Technical Workshop

ANDA Amendments & Supplements

Issues and Opportunities

Gary J. Buehler, R.Ph.
Director, Office of Generic Drugs

October 29, 2001

Maintaining a Level Playing Field

- Amendment Designations
- Expedited Reviews
- Waivers
- Inactive Ingredients for Certain Products
- Supplement Types

Major Amendment Designation

- Manufacture of a new batch for ANY reason
- New bioequivalence study is needed
- Overall poor quality of the application
- New analytical methods; full validation

Minor Amendment Designation

- DMF Deficiencies
- GMP Issues
- Incomplete dissolution data
- Labeling

Telephone Amendment Designation

- Subset of minor amendments
- Response in 10 days possible
- Clarification of data
- Post approval commitment
- Final resolution of technical issues
- Office level review may generate

Benefits of Major Minor Designation Revision

- Decreases time to final action on applications
- Improve consistency of review results
- Increases efficiency of review process
- Decreases requests for reclassification

Disadvantages of Major Minor Designation Revision

- Decreased incentive for quality applications
- Minor reviews could take longer than 60 days
- Existing amendments will not be reclassified
- Period of adjustment upon implementation

Expedited Review of Supplements

- Can be a strain on limited resources
- If someone's application is expedited, someone else's will be delayed
- Limited - Based on clearly stated reason by applicant because of fairness

Valid Reasons to Expedite Review

- Public health need; NO alternative to product
- Hardship on applicant
  - Catastrophic events
  - Events not be reasonably foreseen
- Agency need
  - Government's drug purchase program

☛Yes, the decision <u>can</u> be appealed

Invalid Reasons for Expedited Review

- Economic
- Disagreements with suppliers
- Poor business decisions on the part of the applicant
- Perceived market demand; drug shortages

Bioequivalence Waivers for Additional Strengths

- Waiving Up
  - Exception in Guidance to be revised or changed per interim communication
  - Was an attempt to set limits
  - May still be done for safety reasons
- Reason for not waiving up
  - Potential safety concern over small bioavailability differences
  - Possible non-linearity

Q_1 & Q_2 Inactive Ingredients

- Solutions, Suspensions - With or without PK systemic exposure data
- Qualitatively (Q_1) the same
- Quantitatively (Q_2) essentially the same---Cannot differ by more than ±5%
- Confirmed with clinical division

Supplement Types

- The November 1999 guidance on *Changes to an Approved NDA or ANDA* represents FDA's current thinking on how it will apply the requirements of Section 506A of the Act for NDA and ANDA products
- Regulation in final clearance

FDAMA Section 116

- Reporting mechanisms are based on the ***potential*** for the change to adversely affect the identity, strength, quality, purity, or potency of a product as they may relate to the safety or effectiveness of the drug product

FDAMA Section 116: Reporting Mechanisms

- **Substantial** potential
  - Prior approval supplements
- **Moderate** potential
  - Changes being effected supplements (CBE-30)
  - Changes being effected supplement (CBE-0)
- **Minimal** potential
  - Annual Reports

FDAMA Section 116: Supplements--CBE-30

- Provides for:
  - FDA to determine if the change has been reported correctly as a CBE
  - Notification within 30 days if a prior approval supplement is recommended or if information is missing

FDAMA Section 116: Supplements--CBE-30

- Does NOT provide for:
  - FDA to specifically notify applicants that the change has been reported correctly and that the submission is complete
  - Reviews to be completed within 30 days or an action letter to be issued

FDAMA Section 116: Adverse Effect

- If a change is found to **adversely affect** the identity, strength, quality, purity and potency of the drug product, a **prior approval supplement** is recommended regardless of the reporting category given in this guidance

Continued

FDAMA Section 116: Adverse Effect

- Recommendation to consult with the chemistry or microbiology review staff for advice on whether an effect would be viewed as adverse

Questions can be sent to:

PAC314_70@cder.fda.gov

Guidances are available at

www.fda.gov/cder/guidance/index.htm

Chemistry

3. Changes to an Approved NDA or ANDA [HTML] or [PDF] (Issued 11/1999, Posted 11/19/1999)
4. Changes to an Approved NDA or ANDA: Questions and Answers [HTML] or [PDF] (Issued 1/2001, Posted 1/22/2001)

Summary

- Have to work within these limits to assure fair treatment of all
- Assures the outside world the ANDA review process is sound

Office of Generic Drugs