

M E M O R A N D U M

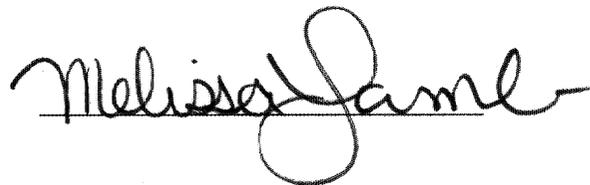
DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

5132 '01 NOV 30 P1:52

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 Opportunitites
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



Attachment

90S-0308

M723

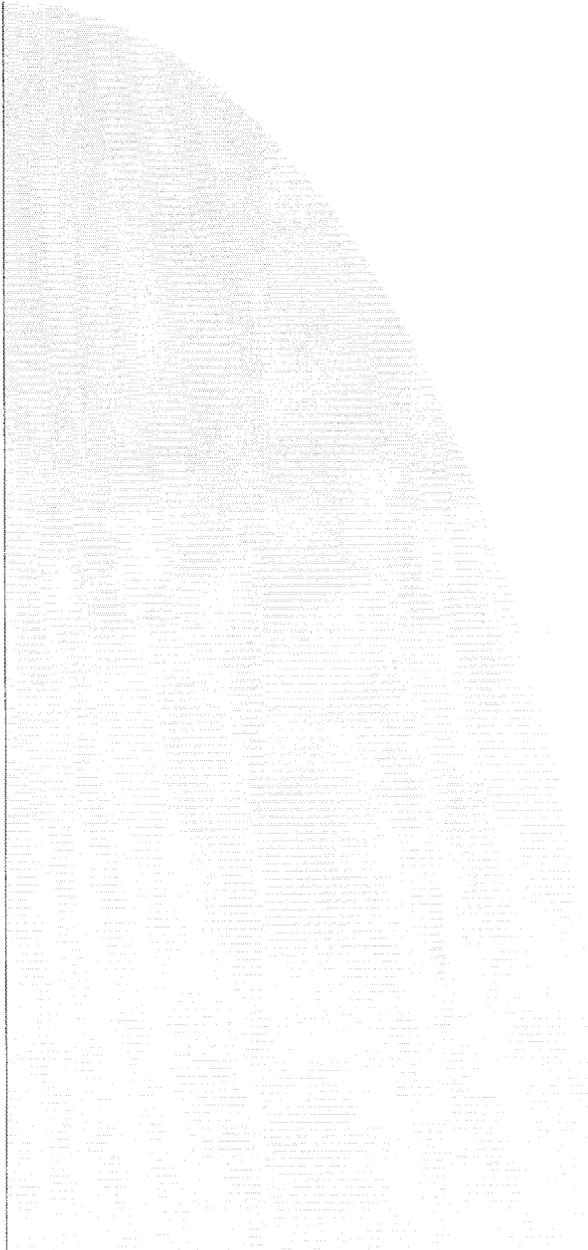
FDA/GPhA Fall Technical Workshop

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

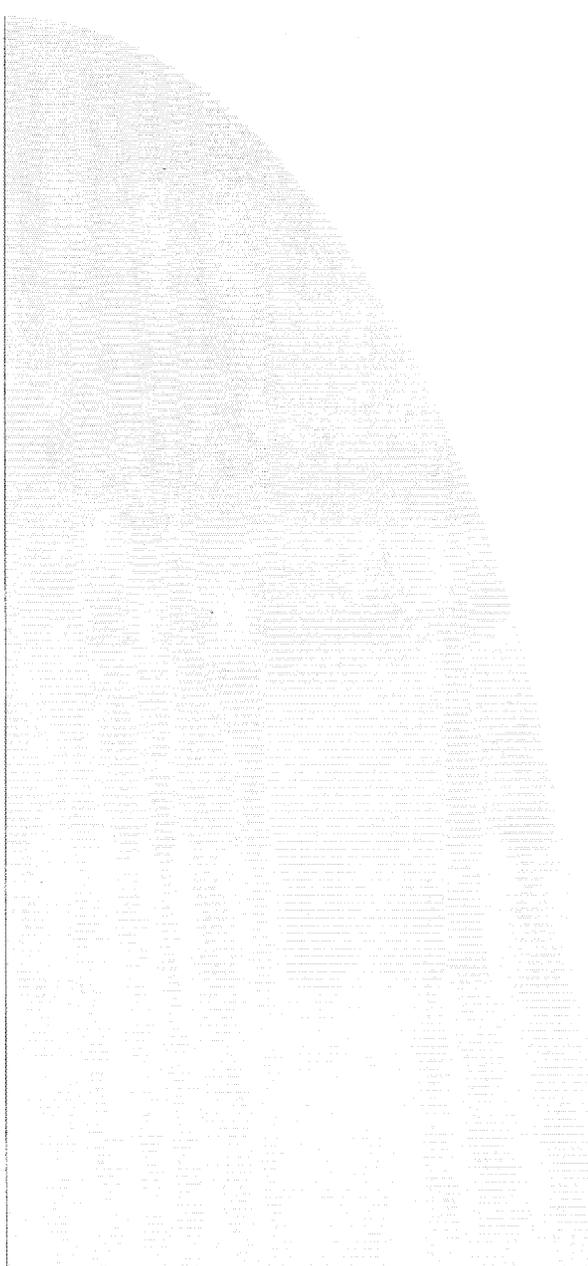
- Manufacture of a new batch for ANY reason
- New bioequivalence study is needed
- Overall poor quality of the application
- New analytical methods; full validation

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 can 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

Q₁ & Q₂ Inactive Ingredients

- Solutions, Suspensions - With or without PK systemic exposure data
- Qualitatively (Q₁) the same
- Quantitatively (Q₂) essentially the same---Cannot differ by more than $\pm 5\%$
- 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

