ANDA Labeling
Overview & Updates

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Office of Generic Drugs

GPhA/FDA Labeling Workshop
September 11, 2013
Agenda

• Overview of the Labeling Review Process
• Updates
• Reminders

Disclaimer: This presentation reflects the views of the author and should not be construed to represent FDA’s views or policies.
OVERVIEW
Responsibilities

• Ensure that the generic labeling is the “same as” the labeling for the product’s reference listed drug (RLD), except for differences allowed under
  – Section 505(j)(2)(A)(v) of the Act
  – 21 CFR 314.94(a)(8)

• Ensure that the labels and labeling are clear and accurately reflect the drug product information
Labeling Review Process

- **Primary Review** (Labeling Reviewer)
- **Secondary Review** (Team Leader)
- **Finalize Review**
  - Communicate Comments to Firm
    - (RPM or Labeling Reviewer)

(Consults)
Labeling Review Process

- Side-by-Side Comparisons
- Regulations and Guidance Documents
- USP Requirements
- REMS
- Nomenclature Differences
- Consults
- Patents and Exclusivities
- Clinical Experience
- Petitions
- USP Requirements
- Petitions
- Patents and Exclusivities
- Clinical Experience
- Consults
- Nomenclature Differences
- Regulations and Guidance Documents
Labeling Review Template

REMS required? (OTC do NOT require)
- Medications and/or PPIs (505-1(e))
- Communication plan (505-1(e))
- Elements to assure safe use (ETASU) (505-1(f)(3))
- Implementation system if certain ETASU (505-1(f)(4))
- Timetable for assessment (505-1(d))

ANDA REMS acceptable?
- Yes
- No
- n/a

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NOTES/QUESTIONS TO THE CHEMIST/BIO REVIEWER/MICRO REVIEWER

FOR THE RECORD:
1. MODEL LABELING
2. USP & PF
3. PATENT AND EXCLUSIVITY
   Patient Data – NDA

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Exclusivity Data – NDA

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4. INACTIVE INGREDIENTS
5. MANUFACTURING FACILITIES
6. FINISHED PRODUCT DESCRIPTION
   - RLD:
   - ANDA:
7. STORAGE STATEMENT AND DISPENSING RECOMMENDATIONS
   - RLD:
   - ANDA:
8. PRODUCT LINE
   - RLD:
   - ANDA:
9. CONTAINING CLOSURE
10. MEDICATION GUIDES/PATIENT PACKAGE INSERT
11. RELATED APPLICATIONS
12. SPL DATA ELEMENTS
13. CITIZENS PETITION/PROPRIETARY NAME/CONSULTS

Date of Review:
Primary Reviewer:
Team Leader:
UPDATES

• Generic Drug User Fee Amendments of 2012 (GDUFA)
• Guidance Documents
• Manual of Policies and Procedures (MAPPs)
• USP Requirements
Labeling Review Branch

- 4 Labeling Review Teams
- GDUFA New Hires
  - 5 Labeling Reviewers
  - 3 Labeling Project Managers
- By January 2014
  - 23 Labeling Reviewers
  - 4 Project Managers
- Training new staff
GDUFA and Labeling

• Identify and implement changes to the current review process to achieve GDUFA timeframes

• Labeling PM and RPM
  – Identify priorities
  – Coordinate issuance and tracking of labeling deficiencies
Draft Guidance Documents on Minimizing Medication Errors

• Safety Considerations for Product Design to Minimize Medication Errors
  – Recommendations for minimizing risks associated with the design of the drug product and its container closure system

• Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
  – Recommendations for ensuring that critical elements of a product’s container labels and carton labeling are designed to promote safe dispensing, administration, and use of the product
Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation*

- Guidelines and criteria by which a scored tablet’s characteristics are evaluated
- Products that meet the criteria can be labeled as having *functional scoring*
DRAFT GUIDANCE: Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex

• FDA recommends:
  – “Not made with natural rubber latex” or
  – “The <vial stopper> is not made with natural rubber latex”

• Manufacturers currently using statements such as "latex-free" or "does not contain latex" should submit revised labels and labeling as a CBE-0 supplement

• [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm340972.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm340972.htm)
MAPP: Generic Drug Labeling Revisions Covered Under Section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act

• Section 505(j)(10) of the FD&C Act permits the FDA to approve an ANDA with labeling that differs from that of the RLD if all of the criteria are met

• ANDA sponsor must provide a letter of commitment to submit a “Supplement – Changes Being Effected” to update the labeling within 60 days of notification

• [link to additional information]
MAPP: Naming of Drug Products Containing Salt Drug Substances

- USP Salt Policy became official on May 1, 2013
- When an active ingredient in a drug product is a salt:
  - Nonproprietary name of the drug product should contain the name of the active moiety (not the name of the salt)
  - Strength should be expressed in terms of the active moiety
- Policy includes exceptions that allow retaining the salt form in the name and strength (CDER review issue)
- Apply to new USP drug product monographs
USP: Ferrules and Cap Overseals

• “Labeling on Ferrules and Cap Overseals” section of USP General Chapter <1> Injections will become official on December 1, 2013

• Restricts the labeling on ferrules and cap overseas to important safety messages critical for the prevention of imminent life-threatening situations
  – Only cautionary statements may appear on the top (circle) surface of the ferrule and/or cap overseal of a vial containing an injectable product.
  – If no cautionary statement is necessary, the top surface of the vial, including the ferrule and cap overseal, must remain blank.

• An ANDA that references a currently approved RLD which includes important safety language on the ferrule and/or cap should include the same language on its ferrule and cap overseal
USP: Heparin

• Revised standards for the labeling section of the *Heparin Lock Flush Solution* and *Heparin Sodium Injection* monographs became official on May 1, 2013

• Strength per total volume (the total number of USP units of heparin per total number of milliliters) followed in close proximity by strength per milliliter enclosed by parentheses (number of USP units of heparin per milliliter)
REMINDERS
Cover Letter

Include information such as:

- Changes in patent/exclusivity statements
- Changes in other sections of the ANDA that may impact the labeling submission
- Dimensions of solid oral dosage form
- Commitment that a sufficient number of Medication Guides will be provided with each packaging size
- Withdraw of REMS plan to be in accordance with the RLD
- Description of tamper evident device for controlled substances
Submissions

- Prescribing information should be submitted as a text-based PDF file (not image based)
- To assist in our review, please also submit the prescribing information in MS Word format
- Content of labeling in structured product labeling (SPL) format should be identical to the proposed/approved labeling (including prescribing information and any patient package insert and/or Medication Guide that may be required)
- Ensure accurate names for file folders (draft vs. final)
- Ensure labeling pieces are submitted in the correct folders
Container Closure

• Unit-dose blister labels should meet the bar code label requirements
• Closure
  – Ensure appropriate special packaging (child-resistant closures) for unit-of-use packaging
  – Unit-dose Carton Labeling: Include a statement as to whether or not the unit-dose package is child-resistant
• Manufactured by/for statements
  – Ensure that no person other than the manufacturer, packer, or distributor is identified on the label of a drug or drug product
  – For a drug product manufactured in a foreign country, include the country of origin on the label
Container Closure

• Replace the simulated drawing of solid oral dosage forms with a picture of the actual product that includes unique markings and scoring configurations.

• Use of "FDA approved" on ANDA labeling is NOT acceptable unless it is on the labeling for the RLD.

• The statement “Meets or exceeds FDA quality standards” should NOT be used.
Container Closure

- Droppers, dosing cups, and syringes should be calibrated to provide the same doses as the RLD
  - Provide pictures of your product with the calibrations
  - Provide side-by-side comparison of the RLD and your proposed product
- Syringes
  - Provide pictures of the container label affixed to the syringe
  - One of the pictures should clearly show the calibrations on the syringe
  - Barcode should be surrounded by enough white space to allow scanners to read the bar code properly
- No calibration markings on pharmacy bulk package containers or labels
Over-the-Counter (OTC)

• Follow the format and content requirements for OTC products (21 CFR 201.66)
  – Include a Labeling Format Information Table with your submission

• Describe the tamper-evident feature in the cover letter and include a statement on the package to alert consumers of the tamper-evident device
Prescribing Information

• Dissolution test pending:
  – Include “USP Dissolution Test Pending” in the Description section
  – Update labeling when dissolution test number has been assigned
• Description section, inactive ingredients:
  – Declare the botanical source of starch and pregelatinized starch on the product label
  – Include all nonviolatilte components of the imprinting ink
• If generic product contains an inactive that includes a labeling warning (e.g., FD&C yellow #5 (tartrazine) & #6, aspartame, sulfites) and the RLD does not:
  – Ensure appropriate warnings appear on the labels and labeling
  – Include the warning at the top of patient package insert or Medication Guide
• Medication Guide:
  – Title: Please include the phonetic spelling of the established name
  – Minimum 10-point font size
Physicians Labeling Rule (PLR)

Highlights of Prescribing Information section

• Product Title:
  – Encourage use of all caps for drug name. If the salt is part of the established name, it is to appear in lower case letters.
  – Route of administration should follow the established name
  – Example: PANTOPRAZOLE sodium for injection for intravenous use

• Initial U.S. Approval: On the line immediately beneath the product title line, the verbatim statement: Initial U.S. Approval must be presented

• Adverse Reactions: Include manufacturer's name and phone number for adverse reaction reporting
Thank you!