Common Deficiencies in Container Labels and Carton Labeling for Biological Products

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Objectives

• Identify common deficiencies for container labels and carton labeling for biological products

• Discuss appropriate labeling with regard to proper name, dosage form, strength, route of administration, and manufacturer information
Common Deficiencies

Common deficiencies observed in CDER during review of products regulated under the Public Health Service Act:

- Dosage form
- Placement of dosage form alongside proper name
- Strength
- Route of Administration
- Manufacturer Information
Example #1

License Bio submits a BLA for Mybio (biolomab)

- Injectable solution of 200 mg in 0.5 mL in a prefilled syringe
- Subcutaneous use
- Supplied in cartons containing 1, 2, and 4 prefilled syringes
Proposed Carton Labeling #1

Mybio
(biolomab) for injection
200 mg
Contains 4 single-dose prefilled syringes
For Subcutaneous Use Only
Deficiency: Dosage Form

- [DRUG] Injection. Liquid preparations that are drug substances or solutions thereof.

- [DRUG] for Injection. Dry solids that, upon the addition of suitable vehicles, yield solutions conforming in all respects to the requirements for Injections.

Note: these are the primary dosage forms applicable to OBP products. USP

USP General Chapters: <1> Injections, Nomenclature and Definitions, Nomenclature.
Proper Name Definition

• Defined in 21 CFR 600.3(k) as applied to a product, means the name designated in the license for use upon each package of the product.

• Does not include a dosage form
Deficiency: Placement of Proper Name & Dosage Form

- The proper name should not include the dosage form.
- The dosage form can appear on the line below the proper name.

Correct Proper Name & Dosage Form Placement Options

• NDA

- Mydrug (drugozide) injection

• BLA

- Mydrug (drugozide) injection
- drugozide Mydrug injection

Deficiency: Strength Presentation

• For containers holding a volume of less than 1 mL, the strength per fraction of a mL should be the only expression of strength.

- USP General Chapters: <1> Injections, Labels and Labeling, Strength and Total Volume for Single- and Multi-Dose Injectable Drug Products.
- Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
Deficiency: Prominence of Route of Administration

- Route of administration should appear more prominently than the quantity of prefilled syringes

- 21 CFR 610.61(k) and 21 CFR 201.15
- Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
Revised Carton Labeling #1

**Before**

NDC 12345-6789-12  Rx Only

**Mybio**
(biolomab) for injection
200 mg
Contains 4 single-dose prefilled syringes
For Subcutaneous Use Only

**After**

NDC 12345-6789-12  Rx Only

**Mybio**
(biolomab) injection
200 mg/0.5 mL
For Subcutaneous Use Only
Single-Dose
Contains 4 prefilled syringes
Example #2

License Bio submits a BLA for Yourbio (biolamase)

- 200 mg/0.25 mL, 400 mg/0.5 mL, and 600 mg/0.75 mL solution
- Subcutaneous injection
- Single-dose vials
Proposed Carton Labeling #2

Yourbio
(biolamase)
injection

200 mg/0.25 mL
(800 mg/mL)

For Subcutaneous Use Only

Contains 10 single-dose vials
Deficiency: Strength Presentation

- For containers holding a volume of less than 1 mL, the strength per fraction of a mL should be the only expression of strength.

- USP General Chapters: <1> Injections, Labels and Labeling, Strength and Total Volume for Single- and Multi-Dose Injectable Drug Products.
- Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
Deficiency: Prominence of Route of Administration

- Route of administration should appear more prominently than the quantity of prefilled syringes
- Color can be used for strength differentiation
- Consider other warnings and critical information
Revised Carton Labeling #2

Before

NDC 12345-5644-12 Rx Only

Yourbio
(biolamase) injection

200 mg/0.25 mL
(800 mg/mL)
For Subcutaneous Use Only

Contains 10 single-dose vials

After

NDC 12345-5644-12 Rx Only

Yourbio
(biolamase) injection

200 mg/0.25 mL
For Subcutaneous Use Only
Single-Dose Vial. Discard Unused Portion
Contains 10 single-dose vials
License Bio submits a BLA for Ourbio (biocept)

- 300 mg lyophilized powder in a single-dose vial
- Intravenous Infusion
- Contract manufacturer in CMO, Inc.
- Distributed by Distribio Pharm
Proposed Carton Labeling #3

Ourbio
(biocept)
injection

300 mg
For Intravenous Infusion Only
Single-Dose Vial. Discard Unused Portion

Mfd by: CMO, City, Country
Distributed by: Distribio Pharm, Anycity, Anystate
Deficiency: Strength Presentation

- Dry powder products should express the strength in terms of the total amount of drug per vial.

- USP General Chapters: <1> Injections, Labels and Labeling, Strength and Total Volume for Single- and Multi-Dose Injectable Drug Products.
- Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
Deficiency: Manufacturer Information

• The Applicant or licensed manufacturer is considered the manufacturer

• Licensed manufacturer name, address, and license number

• Contract manufacturer is not required on labeling

• Distributor name and address can appear provided the licensed manufacturer name, address and license number appear

• 21 CFR 600.3(t), 21 CFR 610.60(a)(2), 21 CFR 610.61(b), 21 CFR 610.64
Revised Carton Labeling #3

Before

NDC 12345-1357-12  Rx Only

Ourbio
(biocept) injection
300 mg
For Intravenous Infusion Only
Single-Dose Vial. Discard Unused Portion

Mfd by: CMO, City, Country
Distributed by: Distribbio Pharm, Anycity, Anystate

After

NDC 12345-1357-12  Rx Only

Ourbio
(biocept) for Injection
300 mg/vial
For Intravenous Infusion Only
Reconstitute and Dilute Prior to Use
Single-Dose Vial. Discard Unused Portion

Mfd by: License Bio, Anytown, Anystate, U.S. Lic. No 9999
Distributed by: Distribbio Pharm, Anycity, Anystate
Example #4

License Bio submits a BLA for Webio (biokomab)

• 50 mg/5 mL injectable solution
• Must be diluted
• Intravenous infusion
• Single-dose vial
Proposed Container Label #4

Note: Assume this container label is a partial label - 21 CFR 610.60(c).
Deficiency: Strength Presentation

- Strength per total volume expressed prominently, then strength per mL enclosed by parentheses.

- USP General Chapters: <1> Injections, Labels and Labeling, Strength and Total Volume for Single- and Multi-Dose Injectable Drug Products.

- Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
  [Link](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm349009.pdf)
Partial Label Recommendations

- **Name** (proprietary and proper)
- **Strength**
- **Route of Administration**
- **Warnings or Cautionary Statements**
- **Manufacturer**
- **Lot and expiration**

- 21 CFR 610.60(c) and 21 CFR 201.10(i)
- Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
  
Omissions from Partial Label

- Dosage form, Rx only, NDC, & linear bar code
- Containers bearing partial labels shall be placed in a package which bears all the items required for a package label

NDC 12345-9877-12
Rx Only

Webio (biokomab)
50 mg/5 mL
(10 mg/mL)
Concentrated Solution for Infusion
Lot SBIA-1 Exp JAN2020

- USP General Chapters: <1> Injections, Labels and Labeling, Strength and Total Volume for Single- and Multi-Dose Injectable Drug Products.
- Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors
Revised Container Label #4

**Before**

NDC 12345-9877-12  Rx Only

Webio  
(biokomab)

50 mg/5 mL  
(10 mg/mL)  
Concentrated Solution for Infusion

Lot: SBIA-1  Exp: JAN2020

**After**

NDC 12345-9877-12  Rx Only

Webio  
(biokomab)

50 mg/5 mL  
(10 mg/mL)  
For Intravenous Infusion After Dilution

Lot: SBIA-1  Exp: JAN2020  
Mfd by: License Bio, US Lic No 9999
Summary

Common deficiencies observed in CDER during review of products regulated under the Public Health Service Act:

• Dosage form
• Placement of dosage form alongside proper name
• Strength
• Route of Administration
• Manufacturer Information
Questions?
References
Biologic Labeling Regulations – Subpart G

- 21 CFR 610.60 – Container label
- 21 CFR 610.61 – Package Label
- 21 CFR 610.62 – Proper Name
- 21 CFR 610.63 – Divided Manufacturing
- 21 CFR 610.64 – Name and address of distributor
- 21 CFR 610.67 – Bar Code label requirements
- 21 CFR 610.68 – Exemptions or alternative to labeling requirements for biological products held by Strategic National Stockpile
General Labeling Provisions – Subpart A

• 21 CFR 201.2 – Drugs and devices; National Drug Code numbers
• 21 CFR 201.5 – Drugs; adequate directions for use
• 21 CFR 201.6 – Drugs; misleading statements
• 21 CFR 201.10 – Drugs; statement of ingredients
• 21 CFR 201.15 – Drugs; prominence of required label statements
• 21 CFR 201.17 – Drugs; location of expiration date
• 21 CFR 201.25 – Bar code
Labeling Requirements for Prescriptions Drugs and Insulin – Subpart B

• 21 CFR 201.50 – Statement of identity
• 21 CFR 201.51 – Declaration of net quantity of contents
• 21 CFR 201.55 – Statement of dosage
• 21 CFR 201.100 – Prescription drugs for human use
FDA Guidance


• Cooperative Manufacturing Arrangements for Licensed Biologics

• Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products

• Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex
USP General Chapters

• <1> Injections
• <7> Labeling
• <1091> Labeling of Inactive Ingredients
• <1151> Pharmaceutical Dosage Forms
Presentation of Names

- **Biologic**
  - Proper Name above proprietary name
  - 21 CFR 610.62

- **Specified Biologic (21 CFR 601.2)**
  - Exempt from 21 CFR 610.62
  - Proprietary Name above proper name
  - 21 CFR 201.10(g)(2)