Instructions for Use — Patient Labeling for Human Prescription Drug and Biological Products — Content and Format

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Combination Products (OCP)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2022
Labeling

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Instructions for Use — Patient Labeling for Human Prescription Drug and Biological Products — Content and Format Guidance for Industry[1]

> This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I.   INTRODUCTION

This guidance provides recommendations for developing the content and format of a patient Instructions for Use (IFU) document for human prescription drug and biological products, as well as drug-led or biologic-led combination products[2] submitted under a new drug application (NDA) or a biologics license application (BLA).[3,4,5] The IFU is written for patients (or their

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[1] This guidance has been prepared by the Office of Medical Policy in the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER) and the Office of Combination Products and in consultation with the Center for Devices and Radiological Health at the Food and Drug Administration.

[2] See 21 CFR 3.2(e).

[3] In this guidance, the terms *drug, drug product*, and *product* refer to human prescription drug and biological products and drug-led or biologic-led combination products that are regulated by CDER and CBER. However, the term *biological product* is used in order to distinguish between human prescription drug products and biological products (e.g., where there is a difference in regulatory treatment).

[4] For information specific to abbreviated new drug application (ANDA) submissions, please refer to the guidance for industry *Acceptability of Draft Labeling to Support ANDA Approval* (October 2015). (We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.) An ANDA is required to contain information to show that the labeling proposed for the generic drug is the *same* as the labeling for the reference listed drug (RLD), except for certain permissible differences required because of differences approved under a suitability petition (see section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 314.93) or because the generic drug and the RLD are produced or distributed by different manufacturers (see section 505(j)(2)(A)(v) of the FD&C Act)).

[5] For information specific to biosimilar and interchangeable biosimilar products licensed under section 351(k) of the Public Health Service Act, refer to the guidance for industry *Labeling for Biosimilar Products* (July 2018), and the draft guidance for industry *Biosimilarity and Interchangeability: Additional Draft Q&As on Biosimilar*

caregivers) who use drug products that have complicated or detailed patient-use instructions.[6] The recommendations in this guidance are intended to help ensure that patients receive clear and concise information that is easily understood for the safe and effective use of such products. The recommendations in this guidance are also intended to help provide consistency to the content and format of IFU documents.[7]

The recommendations in this guidance do not apply to labeling for stand-alone devices or for device constituent parts of cross-labeled combination products if the device constituent is marketed under a device authorization[8,9] (i.e., devices that are not constituent parts of drug-device, biologic-device, or biologic-drug-device combination products submitted under BLA or NDA), labeling for combination products for which the device constituent part provides the primary mode of action, or labeling intended for use by health care providers.[10] The recommendations in this guidance also do not apply to stand-alone devices regulated under a BLA, such as devices associated with blood collection and processing procedures.

This guidance is one of several documents FDA is issuing to fulfill the performance goals under the fifth reauthorization of the prescription drug user fee program, the Prescription Drug User

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Development and the BPCI Act (November 2020). When final, this guidance will represent FDA's current thinking on this topic.

[6] The IFU is considered part of the product user interface. The need for an IFU may be informed by following a human factors (HF) engineering process, which includes conducting comprehensive use-related risk analyses (URRA). The inclusion of an IFU document as a part of prescription drug labeling may be implemented as a mitigation for use-related risks. A comprehensive URRA helps to determine if an IFU is warranted. Additional data, such as data from HF studies, could be used to inform the development and design of the IFU, including the content to be included under the headings recommended in this guidance for a product regulated under an NDA or BLA. Additional discussions of HF considerations in the development of an IFU are outside the scope of this guidance. For additional information on development of the user interface and HF considerations, see the draft guidance for industry and FDA staff *Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development* (February 2016). When final, this guidance will represent FDA's current thinking on this topic. If alternatives to the recommendations in this guidance are proposed for an IFU based on HF studies, applicants should consult with FDA early in the development process.

[7] The format recommendations presented in this guidance are written to apply to an IFU document presented in portrait orientation on letter size paper (8.5 x 11). We recommend that IFU documents presented in other formats aim to carry over as many format recommendations as practical unless information or data, such as data from HF studies, would support otherwise.

[8] See generally sections 510(k), 513(f), and 515 of the FD&C Act.

[9] For information on developing patient labeling for devices, including in vitro diagnostic products, please see 21 CFR parts 801 and 809 and the FDA web page on device labeling at https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/DeviceLabeling/default.htm.

[10] FDA also approves IFU documents intended specifically for use by health care providers. These documents include instructions on how to administer a product safely and effectively to patients. However, the recommendations provided in this guidance apply to IFU documents intended for use by patients and do not apply to IFU documents intended specifically for use by health care providers.

Fee Act (PDUFA) VI. In particular, this guidance relates to the PDUFA VI performance goal regarding guidance on patient-oriented labeling (e.g., IFU documents).

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II.   BACKGROUND

The IFU is a form of prescription drug labeling.[11] For drugs for which self-administration may be complicated (such as requiring the patient to perform multiple steps to prepare, administer, store, and/or dispose the drug), the IFU is intended to give directions that are clear and understandable for patients, and therefore, promote the safe and effective use of that drug. For a drug-led or biologic-led combination product that includes a device constituent part, the IFU provides directions on the use of the device (e.g., regarding device preparation, injection of the drug or biologic, and product storage of the device or combination product as a whole). Also, an IFU may be appropriate for a product with one set of dosing instructions for adult patients and another set for pediatric patients; in this situation, two separate IFU documents may be appropriate. The IFU is developed by the applicant, reviewed and approved by FDA, and provided to patients when the product is dispensed.

Applicants must submit true representations of both the content and format of the IFU, including page layout, graphic design, and color, for FDA's review and approval.[12] In general, before implementing and distributing changes to an FDA-approved IFU, applicants should refer to 21 CFR 314.70 or 601.12 for the requirements on submitting changes to previously approved labeling. The Agency encourages applicants to meet with FDA as early as the investigational new drug application (IND)/pre-IND phase, if appropriate, to discuss the development of any IFU.

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[11] Patients may receive one or more forms of FDA-approved written patient prescription drug product information (i.e., patient labeling) when they receive a prescription drug, including (1) a Medication Guide, (2) a Patient Package Insert, and/or (3) an IFU. This guidance provides content and format recommendations only for IFU documents.

[12] See 21 CFR 314.50(e)(2)(ii).

III. CONTENT

A. General Content Recommendations

The IFU guides the patient on how to safely and effectively use a prescription drug product and commonly includes instructions on preparation, administration, handling, storage, and disposal. The primary purpose of an IFU is to provide detailed, step-by-step written instructions, including visuals if appropriate, in a patient-friendly manner, as visuals can complement written instructions.

1. Consistency With the FDA-Approved Prescribing Information

When reviewing the contents of an IFU, FDA looks for accuracy and consistency with the FDA-approved Prescribing Information (PI) or in the case of a pending NDA or BLA, the to-be-approved version of the PI. The IFU must not be false or misleading and must be updated when new information causes the IFU to become inaccurate, false, or misleading.[13]

FDA recommends that the IFU include pertinent information from the PI that describes how to use the drug product. FDA also recommends that the IFU include additional details not typically discussed in the PI where those details are important for the safe and effective use of the drug product by patients (for example, step-by-step instructions and visuals for how to self-administer the drug product using a co-packaged syringe).

The following sections of the PI[14] will generally contain the pertinent information for the IFU:

- DOSAGE AND ADMINISTRATION

- HOW SUPPLIED/STORAGE AND HANDLING

- PATIENT COUNSELING INFORMATION

Information from other sections of the PI may also be useful to include in the IFU, as appropriate.

2. Language and Readability

FDA suggests writing the IFU in terms that patients, including those with low literacy skills, are likely to understand. The IFU should be written at or below the national average reading level to

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[13] See section 502(a) of the FD&C Act (21 U.S.C. 352(a)).

[14] The labeling sections noted are pertinent to drug product labeling that must meet the content and format requirements of the final rule "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products," (71 FR 3922, January 24, 2006), available at https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources. (See also 21 CFR 201.56 and 201.57.)

facilitate understanding. FDA recommends that the IFU be written in nontechnical language. Overly technical language may deter patients from reading and understanding important information in the IFU. For example, for products with dosage form terminology that may not be recognizable to patients, consider defining the dosage form terminology in patient-friendly terms after its first use in the body of the IFU, e.g., "transdermal system (referred to as a "patch" in this document)."

FDA recommends that the IFU be written in active voice and command language and that sentences or phrases in the IFU begin with an action verb when possible. For instance, the IFU should state "Wash your hands" (rather than "You should wash your hands") and "Shake the vial until the solution dissolves and is clear" (rather than "You should shake the vial until the solution dissolves and is clear").

In general, FDA recommends avoiding abbreviations in the IFU because they may be misinterpreted, which could result in medication errors that may harm a patient. The Agency also recommends writing dose designations (amount and volumetric units) clearly, to help avoid medication errors. For instance, FDA suggests avoiding trailing zeros after a decimal point for doses expressed in whole numbers (e.g., state 1 mg rather than 1.0 mg).[15]

3.   *Headings*

Standardized headings in patient labeling materials enhance readability and usefulness (Lorch et al. 2001; Kools et al. 2008; Cowburn and Stockley 2004). Headings and subheadings help organize and differentiate topics so patients can quickly locate information in the IFU. Thus, FDA recommends that headings and subheadings clearly identify the focus of each topic in the IFU. FDA generally recommends organizing information under each heading such that related topics are consolidated within a single heading, though FDA recognizes that repeating certain information can be an important tool for comprehension. FDA also generally recommends using subheadings (under headings) in the IFU, to group related tasks that accomplish a single objective.

Section III.B of this guidance provides recommended headings to organize content in the IFU. The appendix lists the recommended order of all headings described in section III.B. Additional headings and subheadings can also be useful to include in the IFU.

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[15] See also the List of Error-Prone Abbreviations at the Institute for Safe Medication Practices website (https://www.ismp.org/recommendations/error-prone-abbreviations-list).

B.   Specific Content Recommendations[16]

FDA recommends that the following information, if applicable, appear in the order listed to ensure consistency and to help patients become familiar with the type and location of information in the IFU.

1.   *Title*

FDA recommends that the title **INSTRUCTIONS FOR USE** appear centered prominently at the top of the first page of the IFU, in bold uppercase letters, as follows:

<div align="center">

INSTRUCTIONS FOR USE

</div>

2.   *Product Title*

FDA recommends that the product title[17] in the IFU include the product's proprietary name, nonproprietary name,[18] dosage form,[19] route of administration (ROA),[20] and when applicable, the controlled substance schedule. The Agency also recommends that the product title appear beginning on the line immediately below the title INSTRUCTIONS FOR USE and that the product title appear centered in bold letters across one, two, or three lines.

For drug products *with a proprietary name*, FDA recommends that the information appear in the following order:

> Line 1: Proprietary name in uppercase letters, followed by the pronunciation spelling in brackets and, if applicable, the controlled substance schedule

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[16] Text appearing in brackets in the examples provided in this section indicates a placeholder and should be replaced with the appropriate product-specific information.

[17] See the draft guidance for industry *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018). When final, this guidance will represent FDA's current thinking on this topic.

[18] In this guidance, the *nonproprietary name* refers to the established name of the drug (if any) or for biological products, the proper name. (See section 502(e)(3) of the FD&C Act (21 U.S.C. 352(e)(3)); 21 CFR 600.3(k)). For more information related to biological products, see the guidance for industry *Nonproprietary Naming of Biological Products* (January 2017). See also the draft guidance for industry *Nonproprietary Naming of Biological Products: Update Guidance for Industry* (March 2019). When final, this guidance will represent FDA's current thinking on this topic.

[19] Established names for drug products typically include the dosage form. We include the dosage form separately in the product title in certain instances because proper names for biological products typically do not include a dosage form.

[20] For some drug products (other than biological products), the route of administration is also part of the nonproprietary name.

Line 2: Nonproprietary name in lowercase letters[21] in parentheses
Line 3: Dosage form in lowercase letters followed by the ROA in lowercase letters if the nonproprietary name does not include the dosage form or the ROA; or ROA in lowercase letters if the nonproprietary name contains the dosage form but does not include the ROA

Example A: For the fictitious drug product MYDRUG (drugoxide injection), for intramuscular use, in which the nonproprietary name contains the dosage form but does not include the ROA, FDA recommends that the product title appear as follows:

<div align="center">

MYDRUG [mye-drug]
(drugoxide injection)
for intramuscular use

</div>

Example B: For the fictitious biological product MYBIOLOGIC (drugimab-hjxf) injection, for subcutaneous use, FDA recommends that the product title appear as follows:

<div align="center">

MYBIOLOGIC [mye-bye-oh-LAH-jik]
(drugimab-hjxf)
injection, for subcutaneous use

</div>

For drug products *without a proprietary name*, FDA recommends that the product title appear in the following order:

Line 1: Nonproprietary name in title case letters, followed by the pronunciation spelling of the chemical portion of the nonproprietary name in brackets and, if applicable, the controlled substance schedule; or for biological products, generally, the proper name in title case letters, followed by the pronunciation spelling of the proper name in brackets and, if applicable, the controlled substance schedule
Line 2: Dosage form in lowercase letters followed by the ROA in lowercase letters if the nonproprietary name does not include the dosage form or the ROA; or ROA in lowercase letters if the nonproprietary name contains the dosage form but does not include the ROA

Example C: For the fictitious drug product Drugoxide Injection, for intramuscular use, which does not have a proprietary name (the nonproprietary name contains the dosage form but does not include the ROA), FDA recommends that the product title appear as follows:

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[21] FDA recommends that the location of the parentheses associated with the nonproprietary name mirror the location of the parentheses associated with the nonproprietary name on the carton and container labeling and the product title in the Highlights of Prescribing Information. See the draft guidance for industry *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018).

Drugoxide Injection [drug-OX-ide]
for intramuscular use

> **Example D:** For the fictitious product Drugoxide Transdermal System (the nonproprietary name contains the dosage form and the ROA), a combination product, FDA recommends that the product title appear as follows:

Drugoxide Transdermal System [drug-OX-ide]

> 3. *Purpose Statement*

FDA recommends that the following purpose statement appear below the product title, flush with the left margin:

> This Instructions for Use contains information on how to [insert applicable action verb[22]] [insert Drug Name[23]].

For example:

> This Instructions for Use contains information on how to inject MYDRUG.

> 4. *Visual of Drug Product*

Following the purpose statement, FDA generally recommends that the IFU display a visual of the drug product and, if the drug is a constituent part of a drug-led, drug-device combination product, a visual of the device or devices used to administer the drug. Choose the best type of visual that clearly depicts the drug product, such as a photograph, simple illustration, or line drawing. If a product consists of multiple parts, FDA recommends visually identifying and clearly labeling each part of the product, including the device constituent part(s) if applicable. In some cases, it can also be useful to include further explanation of the purpose or function of the parts of the product, including the device constituent part(s) if applicable.

Generally, FDA recommends that IFU documents include a visual of a drug product for an oral dosage form (such as capsules, tablets, oral solution, or oral suspension) only if manipulation is necessary to prepare and administer a dose (for example, opening and sprinkling the contents of a capsule). In other instances of drug products with oral dosage forms, patients could likely comprehend the instructions without a visual of the drug product.

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[22] Insert the appropriate action verb as determined by the product's dosage form; for example, "take" (oral products), "use" (inhalation, ear or eye products), "inject" (injectable products), "apply" (topical or transdermal products), or "insert" (suppositories).

[23] Drug Name is the proprietary name (if any) or the nonproprietary name of the drug product.

If a drug product is dispensed in or with multiple components or constituent parts (such as cartridges, blister cards or packs), FDA recommends that the IFU provide information about all the components or constituent parts and include the following, if applicable:

- A list or visual representation of all components or constituent parts, each clearly identified and labeled

- A list of items needed to use the drug product that are not included within the drug product package

   5.   Important Information for Patients

FDA recommends that important information for patients to know before using the drug product be described under the following heading:

Important Information You Need to Know Before [Insert Applicable Action Verb[24]] [Insert Drug Name]

For example, FDA recommends that the heading for this section of the IFU for the fictitious drug product MYDRUG appear as follows:

Important Information You Need to Know Before Injecting MYDRUG

FDA recommends that the IFU include this heading when patients should take specific actions to prepare, administer, store, and/or dispose of the drug product to prevent or reduce potentially serious outcomes that might occur if the specific action is not followed. FDA recommends that information under this heading highlight important instructions and information to alert patients about the appropriate uses, techniques, and routes of administration that, if not followed, could result in injury or impair efficacy.

If confusion could occur about the route of administration based on the dosage form, such as capsules for inhalation that may be mistaken for oral capsules, FDA recommends that the first statement in this section explain how the drug product should be administered. For example:

- **For oral use only** (take by mouth)

- **For subcutaneous injection only** (inject directly under the skin)

- **For topical use only** (apply on top of skin)

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[24] Insert the appropriate action verb ending in "ing" as determined by the product's dosage form; for example, "taking" (oral products), "using" (inhalation, ear or eye products), "injecting" (injectable products), "applying" (topical or transdermal products), or "inserting" (suppositories).

Subsequent content that FDA recommends be placed under this heading includes, but is not limited to, the following:

- The timing of a dose relative to a behavior or action specified in labeling; for example:

Take [Insert Drug Name] 1 hour before eating.

  - Apply [Insert Drug Name] after bathing.

  - Wait at least 2 hours after applying [Insert Drug Name] before showering or swimming.

- Safety information or other important instructions specifically related to administration. For example:

  - Swallow tablet whole. Do not cut, crush, or chew tablet.

  - Inject [Insert Drug Name] into the thigh. Do not inject [Insert Drug Name] into any other area of the body.

  - Check to see if the safety seal is in place. Do not use [Insert Drug Name] if the safety seal is broken.

  - [Insert Drug Name] is for one-time use only. Do not reuse [Insert Drug Name]. Throw away (discard) unused portion.

- Instructions to prevent or mitigate the risk of secondary exposure to a drug; for example:

  - To prevent the transfer of [Insert Drug Name] from your body to others, avoid direct skin contact or cover the areas of your body where [Insert Drug Name] has been applied.

    6.   Preparation Instructions

FDA recommends that instructions on preparing the product for use be described under the following heading:

Preparing to [Insert Applicable Action Verb[25]][Insert Drug Name]

For example, FDA recommends that the heading for this section of the IFU for the fictitious drug product MYDRUG appear as follows:

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[25] See footnote 22.

Preparing to Inject MYDRUG

Content that FDA recommends be placed under the preparation instructions section includes, but is not limited to, the following:

- Information about supplies and materials for administering the dose (for example, a bowl and spoon for mixing a drug product with food; alcohol wipes to prepare an injection; an adhesive bandage to cover an injection site)

- Information about the time needed to allow a refrigerated product to warm to room temperature or the maximum amount of time the product may remain unrefrigerated before use

- Instructions to check the drug product for particles or discoloration and to check the expiration date on the product's label

- Directions for assembling constituent parts or components of the product at the time of first use, and if applicable, assembly instructions for subsequent uses

- Instructions for priming topical or inhaled products for first use or priming for subsequent use

- Directions for products requiring reconstitution and/or dilution

- Directions for drawing a drug product into a syringe

- Instructions on how to insert a co-packaged bottle adaptor

   7.   *Administration Instructions*

FDA recommends that instructions for administering the drug product be described under the following heading:

[Insert Applicable Action Verb[26]] [Insert Drug Name]

For example, FDA recommends that the heading for the administration instructions section of the IFU for the fictitious drug product MYDRUG appear as follows:

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[26] Insert the appropriate action verb ending in "ing" concerning administration as determined by the product's dosage form; for example, "taking" (oral products), "using" (inhalation, ear or eye products), "injecting" (injectable products), "applying" (topical or transdermal products), or "inserting" (suppositories).

Injecting MYDRUG

FDA recommends that the IFU clearly state the sequence of actions (e.g., information appears as logically ordered, detailed, step-by-step instructions) so that patients can safely and effectively take or administer the drug product.

For drug products with more than one method of administration (for example, sprinkle capsule contents into food or drink; administer by feeding tube for patients who have difficulty swallowing), FDA recommends using distinct sections to separate the instructions for each administration method.

Content that FDA recommends be placed under the administration instructions heading includes, but is not limited to, the following:

- Instructions and illustrations specifying which areas of the body are appropriate and inappropriate for potential injection sites

- Instructions for injecting the drug product

- Instructions for rotating the site of application or injection, such as describing the manner of rotation and the importance of keeping track of injection sites to ensure an injection is not given in the same spot for consecutive doses

- Instructions on how to actuate an inhaler to ensure appropriate dosing

- Instructions on how to administer a dose with an auto-injector

- Instructions on how to apply and remove a transdermal system

  8. *Storage Instructions*

FDA recommends that instructions on appropriate storage be described under the following heading:

Storing [Insert Drug Name]

For example, FDA recommends that the heading for this section for the fictitious drug product MYDRUG appear as follows:

Storing MYDRUG

Content that FDA recommends be placed under this heading includes, but is not limited to, the following:

- Instructions on how to prepare the product for storage (for example, disassembly instructions, washing or cleaning)

- A description of storage conditions (for example, refrigerating the drug product or storing away from light)

- A "Keep out of reach of children" statement

  9.   Disposal Instructions

FDA recommends that disposal instructions be described under the following heading:

Disposing of [Insert Drug Name]

For example, FDA recommends that the heading for this section of the IFU for the fictitious drug product MYDRUG appear as follows:

Disposing of MYDRUG

Generally, FDA recommends including this heading only when there are specific disposal instructions to prevent the risk of unintended exposure to or harm from products (for example, certain transdermal systems). Under this heading, FDA recommends that, where appropriate, the IFU explain how to dispose of the drug product when it is no longer needed, has expired, or is otherwise unusable.

Content that FDA recommends be placed under this heading includes, but is not limited to, the following:

- For items that present a risk of needle stick injury or infection (for example, auto-injectors, pens, syringes), this section should include the appropriate safe sharps disposal language.[27]

- For drug products that require special disposal procedures (for example, outpatient chemotherapeutic drug products, drug products on FDA's flush list[28]), this section should provide specific information for patients on how to appropriately dispose of these drug products.

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[27]Appropriate language to include for safe sharps disposal is available at www.fda.gov/safesharpsdisposal.

[28] Information concerning how to safely dispose of unused or expired medicine is available at https://www.fda.gov/drugs/safe-disposal-medicines/disposal-unused-medicines-what-you-should-know.

10.   *Additional Information*

At the bottom of the last page of the IFU, FDA recommends that the following information be placed in the order listed below:

(1)   Resources for additional information on the product, if applicable (for example, a telephone number that patients can call to speak with a customer service representative, a telephone number for more product information and to report problems with the product, and/or a telephone number to report adverse reactions to FDA).

(2)   For products marketed under an NDA or ANDA, include the name and place of business of the manufacturer, packer, and/or distributor.[29]

(3)   For products marketed under a BLA, include the name, address, and license number of the manufacturer (and may include the distributor).[30]

(4)   On the last line of the IFU, include the following:

a.   The verbatim statement, written as follows:

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

b.   The verbatim statement is followed by the:

(1) month and year of initial FDA approval of the IFU (for example, Approved: May 2023)

or

(2) month and year of the subsequent revision to the IFU (for example, Revised: December 2023).

IV.   FORMAT

The following formatting recommendations are intended to make the IFU easier for patients to read and to help them use prescription drug products safely and effectively (Buck 1998; Koo et al. 2003).

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[29] 21 CFR 201.1 and 201.100(e) provide additional information about labeling and about including this information.

[30] 21 CFR 610, subpart G, provides additional information about labeling and about including this information.

A.   Typeface Styling Recommendations

1.   Font and Font Size

FDA recommends using a sans-serif font for all text in the IFU because sans serif is easier to read than a serif type font (American Foundation for the Blind 2020). Recommended sans-serif fonts include, but are not limited to, Verdana and Arial. FDA recommends against the use of any reverse type (such as white or neutral color type on a darker color background), lightface, shading, highlighting, condensed type, or narrow fonts. These techniques can make reading more difficult for patients (Raynor and Dickinson 2009).

Recommendations on font size are intended for easier readability (Buck 1998). Overall, FDA recommends that the font size be no smaller than 10 points (1 point equals 0.0138 inches) for any section of the IFU, except that FDA recommends the following sections or terminology appear in font no smaller than 8 points:

- For products marketed under an NDA or ANDA, the name and place of business of the manufacturer, packer, and/or distributor.

- For products marketed under a BLA, the name, address, and license number of the manufacturer (and, if included, the distributor).

- The verbatim statement: This Instructions for Use has been approved by the U.S. Food and Drug Administration.

- The month and year of initial FDA approval *or* revision of the IFU.

2.   Letter Case

FDA recommends that the title **INSTRUCTIONS FOR USE** appear in all uppercase letters. FDA also recommends that the letter case of the proprietary name or nonproprietary name used in the body of the IFU (excluding the IFU product title) match its appearance in the PI. All other headings in the IFU are recommended to appear in title case. FDA suggests avoiding the use of words or phrases with all uppercase letters in the body of the IFU. The abundant use of uppercased text is difficult to read (Hoffmann and Worrall 2004) and may detract from the prominence of terms that should appear in uppercase text in the IFU.

3.   Bold, Italicized, or Underlined Text

FDA recommends that the following information appear in bold type: **INSTRUCTIONS FOR USE**; **product title** (including **drug name(s), pronunciation spelling**, **dosage form,** and **route of administration,** and (when applicable) the **controlled substance symbol**); **headings**; **step numbers**; and **figure titles**. Bolded headings can help patients find information quickly and easily (Raynor and Dickinson 2009). However, FDA suggests that bolding, italicizing, and underlining in the body of the IFU be used sparingly and be limited to important phrases or

concepts (for example, important information for patients to know before using the drug product, such as **For oral use only)**.

B.   Page Layout and Design Recommendations

1.   Step-by-Step Instructions

FDA recommends that instructions be sequentially numbered, with each step heading appearing in bold type and noted as **Step 1, Step 2,** etc. FDA also recommends using continuous numbering throughout the document. For example, FDA suggests avoiding more than one instance of Step 1.

The Agency recommends that action-oriented instruction appear before any supporting information particular to performing a step. The Agency also suggests that supporting information appear in bulleted text on a separate line immediately following the corresponding step.

For example:

> **Step 4.** Check the liquid by looking through the viewing window (**Figure F**).
>
> - The liquid should be yellow and should have no lumps or particles.
>
> - You may see air bubbles. This is normal.

If a patient needs to skip a specific step or set of steps that are not necessary for each dose, FDA recommends that the IFU refer the patient to the next appropriate step. If a patient needs to repeat a step or steps, FDA recommends that, if appropriate, the IFU refer the patient back to the listed step or steps (for example, "Repeat **Steps 10** to **13 a second time**, then continue to **Step 14**").

For example:

> **Step 6.** Close your eye for one minute and gently press at the corner of that eye nearest your nose.
>
> **Step 7.** If you have been instructed by your health care provider to use drops in both eyes, repeat **Steps 3** to **6** in the other eye. If not, continue to **Step 8**.

2.   Visuals for Step-by-Step Instructions

Visuals help patients comprehend instructions (Wolf et al. 2010). Visuals can be useful for action tasks and informational text that help a patient understand and safely prepare, administer, store, or dispose of the drug product. FDA recommends that visuals be easy to understand; be of adequate size to allow patients to see the focal point; and demonstrate one concept, single idea,

or point of information. Photographs can be compelling because they show the most accurate visual representation of a product. However, in some instances, the use of line drawings and sketch illustrations may be most helpful to simplify complexities and highlight key components or avoid distracting details.

FDA recommends that visuals be placed immediately adjacent to the related instructional step. The Agency also recommends that visuals be labeled alphabetically in bold type (such as **Figure A**, **Figure B,** etc.). Steps with corresponding figures are recommended to reference the appropriate figure or figures at the end of the step.

For example:

> **Step 10.** Attach the needle to the pen (see **Figure G**).

> | Visual corresponding to **Step 10** |
> | :---: |
>
> **Figure G**

3.   *Spacing*

FDA recommends that the IFU maintain a sufficient balance of text, visuals, and white space. White space can be used carefully to keep the document from appearing cramped, overwhelming, or too spread out (for example, at a minimum, FDA recommends adding a single line before each heading). For ease of reading, FDA suggests using white space or blocks of text to separate concepts and to indicate change. Additionally, consider increasing the amount of white space around important text and visuals for emphasis.

4.   *Color*

FDA recommends that the IFU be presented in black type on a white background to facilitate readability. This combination maximizes contrast and legibility and also facilitates uniform reprinting of the document. Colored text and visuals may be useful as long as all text and visuals maintain clarity and remain legible when the IFU is printed in black and white or in grayscale.

REFERENCES

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APPENDIX: INSTRUCTIONS FOR USE —
RECOMMENDED ORDER OF INFORMATION

Numbers in parentheses correspond to items 1 through 10 in Section III.B, Specific Content Recommendations, of the guidance. The main body of this guidance contains detailed information about each item. This example is for a drug that is not a biological product.

<div align="center">

(1) **INSTRUCTIONS FOR USE**
(2) **[Insert Product Title]**

</div>

(3) This Instructions for Use contains information on how to [insert applicable action verb[a]] [Insert Drug Name[b]]

(4) [Insert visual of drug product]

(5) **Important Information You Need to Know Before [Insert Applicable Action Verb[c]] [Insert Drug Name]**

(6) **Preparing to [Insert Applicable Action Verb[d] [Insert Drug Name]**

(7) **[Insert Applicable Action Verb[e]] [Insert Drug Name]**

(8) **Storing [Insert Drug Name]**

(9) **Disposing of [Insert Drug Name]**

(10) [At the bottom of the last page of the IFU, insert resources for additional information on how to use the drug product (for example, a telephone number that patients can call to speak with a customer service representative)]

 [Insert name and place of business of manufacturer, packer, and/or distributor of drug product]

This Instructions for Use has been approved by the U.S. Food and Drug Administration.   Approved: [insert Month Year]
or
Revised: [insert Month Year]

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[a] Insert the appropriate action verb as determined by the product's dosage form; for example, "take" (oral products), "use" (inhalation, ear or eye products), "inject" (injectable products), "apply" (topical or transdermal products), or "insert" (suppositories).

[b] Drug Name is the proprietary name (if any) or the nonproprietary name of the drug product.

[c] Insert the appropriate action verb ending in "ing" as determined by the product's dosage form; for example, "taking" (oral products), "using" (inhalation, ear or eye products), "injecting" (injectable products), "applying" (topical or transdermal products), or "inserting" (suppositories).

[d] See footnote a.

[e] Insert the appropriate action verb ending in "ing" concerning administration as determined by the product's dosage form; for example, "taking" (oral products), "using" (inhalation, ear or eye products), "injecting" (injectable products), "applying" (topical or transdermal products), or "inserting" (suppositories).