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## INSTRUCTIONS FOR FILLING OUT FORM FDA 356h – APPLICATION TO MARKET A NEW OR ABBREVIATED NEW DRUG OR BIOLOGIC FOR HUMAN USE

*(The field numbers below correspond to the numbered boxes on the Form FDA 356h)*

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**NOTE: Please submit a new Form FDA 356h with each submission. Complete the pages of the form sequentially using continuation pages as needed. If continuation pages are not needed, click on the 'Remove Continuation Page' button at top/bottom of form.**

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### **Field 1: DATE OF SUBMISSION**

Enter the date the submission is being submitted to the FDA. The date entered should match the date of the cover letter for the submission.

### **Fields 2–6: APPLICANT INFORMATION**

This section should include the name, street address, applicant Data Universal Numbering System (DUNS) number, telephone and facsimile numbers of the person or legal entity submitting the application. For biologic products, the name of applicant in **Field 2** is the name of the person or legal entity to whom the license will be issued. Enter the U.S. license number, if previously issued, in the appropriate field. Enter the name, street address, applicant DUNS number, US Agent DUNS and telephone number of the person and legal entity authorized to represent a non-U.S. applicant in **Field 6**.

### **Fields 7–15: PRODUCT DESCRIPTION**

This section should include all the information necessary to identify the product that is the subject of this application or submission.

### **Field 7: NDA, ANDA, OR BLA APPLICATION NUMBER**

Provide the six-digit application number. For application numbers less than six-digits, the application number should be preceded using zeros (i.e., for NDA 12345 enter 012345).

### **Field 8: SUPPLEMENT NUMBER**

Provide the four-digit supplement number with preceding zeros for supplement numbers that are less than four-digits (i.e., for Supplement 1 enter 0001).

### **Field 15A: PROPOSED INDICATION FOR USE**

For original and efficacy supplemental applications only (including resubmissions to these application types), provide the indication(s) proposed within the application. Indicate if the proposed indication is for a rare disease (prevalence <200,000 U.S. patients). Indicate if the product proposed within the application (i.e. not the reference listed drug for an ANDA) has an FDA Orphan Drug Designation and if so; provide the six-digit Orphan Designation number. If the submission is not an original application or efficacy supplement, select 'No' in response to 'Is this indication for a rare disease?' Use the Continuation Page if there are more than one proposed indications for use by adding one indication per entry and providing rare disease/Orphan Drug Designation information for each entry, as applicable. If continuation pages are not needed, click on the 'Remove Continuation Page' button at top/bottom of form.

### **Field 15B: SNOMED CT INDICATION DISEASE TERM(S)**

For each original and efficacy supplemental applications only (including resubmissions to these application types), provide the SNOMED CT coded disease term (e.g., 38341003 | Hypertensive disorder, systemic arterial (disorder) |) for the indication provided in **Field 15A**. To look up the indication's SNOMED CT coded disease term:

1. Navigate to <http://browser.ihtsdotools.org/>.
2. Under Local Extensions, select 'Go Browsing United States edition'.
3. Select the 'Search' tab located in the upper left hand of page.
4. Enter the disease term in the search field.
5. Check the box 'Group by concept'.

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6. Select the single most appropriate term for the indication.
7. Select the 'Expression' tab located in the upper right hand of page.
8. Copy the entire text that appears under the heading 'Pre-coordinated Expression.
9. Paste the copied SNOMED CT disease term into **Field 15B** of Form FDA 356h.
10. For additional indications, use the continuation page for #15 and repeat these steps.

### **Fields 16–30: APPLICATION INFORMATION**

Fields 16–18: Identify the appropriate application type.

#### **Field 19: 351(k) BASIS FOR SUBMISSION**

If the application is a 351(k) BLA, provide the name of the biological reference product that is the basis for the application and the holder of the licensed application.

#### **Field 20: ANDA OR 505(b)(2) BASIS FOR SUBMISSION**

If the application is a 505(b)(2) NDA, provide the name(s) and application number(s) of the listed drug(s) that you are relying on. If you are submitting an ANDA, please provide the name and application number for the reference listed drug (RLD). If the reference standard (RS) for the ANDA (generally identified in the Orange Book) differs from the RLD, information about the RS should not be provided on the 356h, but should be included elsewhere in the application (e.g., sections 1.12.11)."

#### **Field 21: SUBMISSION TYPE**

For original applications, select 'Original'. For all other submission types, select any of the submission types listed that apply, or specify the type of submission under "Other" if otherwise not listed. See also 21 CFR 314.3(b).

**Original:** An application for which FDA has never issued an approval letter;

**Labeling Supplement:** A supplemental application for labeling changes to an approved product as described under 21 CFR 314.70 and 21 CFR 601.12 that does not otherwise qualify as another type of supplement (e.g., Efficacy, CMC, REMS);

**CMC Supplement:** A supplemental application for chemistry, manufacturing, and control (CMC) changes to an approved product as described under 21 CFR 314.70, 21 CFR 314.71, 21 CFR 314.72, and 21 CFR 601.12, including CMC supplements with corresponding labeling changes;

**Efficacy Supplement:** A supplemental application for changes to an approved product from among the following changes: new or modified indication; new or revised dose or dosing regimen; new route of administration; comparative efficacy claim naming another product; significant alteration in the patient population; switch of marketing status from prescription to over-the-counter use; traditional approval of a product originally approved under Subpart H (Accelerated Approval) or Subpart I (Animal Rule); labeling or manufacturing change requiring clinical data for approval;

**Annual Report:** See 21 CFR 314.81(b)(2) for NDAs and 21 CFR 601.12(d) for BLAs;

**Product Correspondence:** Any communication or general correspondence related to an application (e.g., routine administrative changes, donor re-entry requests, lot distribution reports, license reissuance requests, meeting requests) that is not an amendment to a pending application. Provide a description of the content or intent of the Product Correspondence in **Field 27** (Reasons for the Submission);

**REMS Assessment Methodologies and Study Protocols:** A submission containing information on methodological approaches and study protocols use to assess a REMS program;

**REMS Assessment Report:** A submission containing information and data to support if the goal of each strategy is being met; modifications to the REMS or revisions to the REMS assessment plan are

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needed, including the timing of the REMS assessments; and whether the REMS is still necessary to ensure the benefits outweigh the risks of the drug;

**REMS Supplement:** A supplemental application proposing a new Risk Evaluation and Mitigation strategy (REMS) or modifications (major and/or minor) to an approved REMS;

**Post Marketing Requirements or Commitments:** A submission containing information related to post marketing requirements or commitments (e.g., nonclinical protocol, final study report);

**Periodic Safety Report:** Periodic reports (Periodic Adverse Drug Experience Reports (PADERs)) of adverse drug or biological product experience as described under 21 CFR 314.80(c)(2), 21 CFR 314.98, and 21 CFR 600.80(c)(2), including those in Periodic Safety Update Report (PSUR) format;

**Request for Proprietary Name Review:** A submission containing a request for proprietary name review;

**Human Factors (Specify Type):** Select check box and specify what type of HF information is being submitted in "Specify Type" (e.g. HF Protocol, HF Study Report, Use-Related Risk Analysis, Justification for no HF Validation Study, Comparative Analysis, etc.);

**Other (specify):** State the submission type if it is not one of the previous submission types listed above (e.g., formal dispute resolution request, REMS revisions). If this box is checked, provide the Reasons for the Submission in **Field 27**.

#### **Field 22: SUBMISSION SUB-TYPE**

Select one of the submission sub-types listed. See also 21 CFR 314.3(b).

**Presubmission:** Information submitted prior to the submission of a complete original application (e.g., submission of partial application (rolling submission));

**Amendment:** A submission to a pending original application, or pending supplemental application, including responses to Information Request letters, Discipline Review letters, or other FDA communications. Amendments also include submissions that contain additional supportive material intended to augment or revise information previously submitted in a submission type listed under **Field 21** (e.g., amendment to an annual report);

**Initial submission:** A submission type under **Field 21** that has never before been submitted (excluding presubmissions);

**Resubmission:** A complete response to an action letter, or submission of an original application that has been the subject of a withdrawal before FDA action or a refusal to file action.

#### **Field 23: SUPPLEMENT CATEGORY**

Select the appropriate type of supplemental application, if applicable.

**CBE (Changes Being Effected):** A supplemental application proposing certain changes for which distribution of the product made using the change(s) can occur upon FDA receipt of the application as described under 21 CFR 314.70(c)(6) and 21 CFR 601.12(c)(5);

**CBE-30 (Changes Being Effected in 30 Days):** A supplemental application proposing certain changes requiring submission at least 30 days prior to distribution of the product made using the change(s) as described under 21 CFR 314.70(c) and 21 CFR 601.12(c);

**Prior Approval (PA):** A supplemental application proposing a major change for which distribution of the product made using the change(s) cannot occur prior to FDA approval as described under 21 CFR 314.70(b) and 21 CFR 601.12(b).

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## Field 24: COMBINATION PRODUCTS

**Field 21** (Submission Type) should be filled out before attempting to fill out **Field 24**. **Field 24** is only fillable for original submissions and supplements (Labeling, CMC, Efficacy, REMS), including resubmissions and amendments to these types. Indicate if the product proposed within the submission is a combination product (e.g., drug-device, drug-biologic product, drug-device-biologic product, see 21 CFR 3.2(e)) by selecting 'Yes' and entering the number below that best identifies the type:

1. Convenience Kit or Co-Package
2. Prefilled Drug Delivery Device/System
3. Prefilled Biologic Delivery Device/System
4. Device Coated/Impregnated/Otherwise Combined with Drug 5: Device Coated or Otherwise Combined with Biologic
5. Drug/Biologic Combination
6. Separate Products Requiring Cross Labeling
7. Possible Combination Based on Cross Labeling of Separate Products
8. Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)

If the product(s) in the submission is not a combination product, select 'No' and leave the Combination Product Type blank. If the submission relates to a drug product available in both combination product (e.g., pre-filled syringe presentation) and non-combination product (e.g., vial presentation) configurations select 'Yes' and identify the type that applies to the combination product configuration. If the submission relates to a product configuration that has multiple combination product types (e.g., a submission is for a product that contains a prefilled syringe (Type 2) and is co-packaged with other devices and drugs (Type 1)), select type '9'.

If this is the initial submission for a product for which a Request for Designation (RFD) was submitted, provide the six-digit RFD number.

### Field 25: Does the submission contain:

**Only Pediatric data?:** If the submission identified in **Field 21** of this form contains data only from pediatric studies, select 'Yes'. If the submission does not contain data from pediatric studies, or is an original application or efficacy supplement that contains data from both adult and pediatric studies, select 'No'.

**Digital Health Technology (DHT) Data?:** If the submission contains Digital Health Technology (DHT) data, select 'Yes'. DHTs are systems that use computing platforms, connectivity, software, and/or sensors, (e.g., activity trackers, mobile medical applications) for remote data acquisition from participants in a clinical investigation. Although not final, FDA's guidance on DHTs represents the Agency's current thinking on the use of DHTs: <https://www.fda.gov/media/155022/download>.

### Field 26: PROPOSED MARKETING STATUS

Select the appropriate Proposed Marketing Status.

### Field 27: REASONS FOR SUBMISSION

This section should contain a brief explanation of the contents of, or rationale for, the submission (e.g., "manufacturing change from roller bottle to cell factory" or "response to Information Request Letter of mm/dd/yy" or "pediatric exclusivity determination request" or "to fulfill a Subpart H postmarketing requirement"). If you selected 'Yes' for human factors information, specify what type of HF information is being submitted (e.g., HF protocol, HF study report, use-related risk analysis, justification for no HF validation study). If you selected 'Yes' for REMS Assessment Methods and Study Protocols, specify what type of methodologies and protocols are being submitted (e.g., survey methodologies, audit plans, drug use study, epidemiology studies).

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## Field 28: ESTABLISHMENT INFORMATION

If you selected 'Yes' for REMS Assessment Methods and Study Protocols, specify what type of methodologies and protocols are being submitted (e.g., survey methodologies, audit plans, drug use study, epidemiology studies). For original (initial) applications, efficacy supplements, CMC supplements, and resubmissions to these submission types, this section should include complete information on the locations of all manufacturing, packaging, and control sites for both drug substance and drug product.

Establishment information on bioequivalence testing sites, excipient testing sites, and container/ closure manufacturing and testing establishments is not required in **Field 28**. For presubmissions and amendments to these submission types, complete establishment information should be provided in this section when applicable (e.g., an amendment that describes changes to previously submitted establishment information; an amendment that adds or removes an establishment; a presubmission that includes CMC information including establishment information).

For each site, please include the establishment name, address, registration (FEI) number, Master File (MF) or Drug Master File (DMF) number (for facilities used under a MF), and establishment DUNS number. Indicate whether or not the establishment is new to the application, if applicable. New establishments will have by default a 'pending' status. If it is not a new establishment, indicate its current status (e.g., active, inactive, or withdrawn) in the appropriate box.

For CMC and efficacy supplements indicate whether the establishment is involved in the change of the subject submission in Yes/No checkbox.

Also provide the name, title (optional), address, phone number, fax number and email address for the contact at the site. In the section "Manufacturing Steps, and/or Type of Testing", provide a brief description of the specific manufacturing steps and/or type of testing (e.g., final dosage form, stability testing) conducted at the site (i.e., describe the type(s) of assays or testing completed). Indicate whether the site is ready for inspection, or if not, when it will be ready.

Use the Continuation Page as needed. If continuation pages are not needed, click on the 'Remove Continuation Page' button at top/bottom of form.

See Guidance for Industry: Identification of Manufacturing Establishments in Applications <https://www.fda.gov/media/131911/download>

## Field 29: CROSS REFERENCES

This section should contain a list of all Biologics License Applications (BLAs), Investigational New Drug Applications (INDs), New Drug Applications (NDAs), Premarket Approval Applications (PMAs), Premarket Notifications (510(k)s), Investigational Device Exemptions (IDEs), and/or MFs/DMFs/Master Files for Devices (MAFs) that are cross-referenced in the current application. Use the Continuation Page as needed. If continuation pages are not needed, click on the 'Remove Continuation Page' button at top/ bottom of form.

**Field 30:** This section contains items 1 through 20 which is a checklist that should be used to indicate the types of information contained within a particular application or submission. Check all that apply. A complete index or table of contents should immediately follow the Form FDA 356h and, if applicable, a User Fee Cover Sheet (Forms FDA 3397, 3792, or 3794). Note that the CFR references are provided for most items in order to indicate what type of information should or must be submitted in each section. For further information, the applicant may consult the guidance documents that are available from the Agency. Please note, selecting **Field 30**, item 15 indicates the complete Biological Products establishment description is included at **Field 28**.

## Fields 31–38: CERTIFICATION

Enter the name and title, telephone number, facsimile number, email address, and street address of the applicant's Responsible Official in **Fields 31–36** of the form. This person is responsible for certifying compliance with applicable laws and regulations. The authorized U.S. agent named in **Field 6** of the form may also act as the applicant's Responsible Official. The form must be signed in **Field 37** by the applicant, or the applicant's attorney, agent, or other authorized official. 21 CFR 601.2(a). If the person signing the form in **Field 37** does not reside or have a place of business within the United States, the form must be countersigned in **Field 38** by an attorney, agent, or other authorized official who resides or maintains a place of business within the United States. 21 CFR 314.50(a)(5).