INSTRUCTIONS FOR FILLING OUT FORM FDA 1571
INVESTIGATIONAL NEW DRUG APPLICATION (IND)

(The field numbers below correspond to the numbered boxes on the Form FDA 1571)

Field 1: SELECT APPROPRIATE CENTER

Field 2: NAME OF SPONSOR

The sponsor is the person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual, pharmaceutical company, governmental agency, academic institution, private organization or other organization (21 CFR 312.3(b)). A Sponsor-Investigator is an individual who both initiates and conducts a clinical investigation and under whose immediate direction the investigational drug is being administered or dispensed (21 CFR 312.3(b)). For administrative reasons, only one individual should be designated as sponsor-investigator.

If a pharmaceutical company will be supplying the drug, but will not itself be submitting the IND, the company is not the sponsor.

Field 3: 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 4–5: SPONSOR ADDRESS AND TELEPHONE NUMBER.

Provide the address and telephone number of the sponsor identified in field 1 (21 CFR 312.23(a)(1)(i)). If this address is a post office box number, a street address should also be provided on line 2.

The telephone number is the number where the sponsor is usually available during normal working hours.

Field 6: NAME(S) of DRUG

For name(s) of drug (21 CFR 312.23(a)(1)(i)), list the established name(s) and trade name, if available. Also, provide the dosage form(s), and the unique ingredient identifier (UNII) term and code for active substances (if applicable). Use the Continuation Page if additional space is needed.

Field 7A: IND NUMBER

Provide the IND number if it was previously assigned. If an IND number has not been assigned, leave the field blank. For IND numbers less than six digits, the IND number should be preceded using leading zeros (i.e., for IND 12345 enter 012345).

Field 7B: IND TYPE

Select Commercial IND if the product under investigation is intended to be commercialized at a later date. (21 CFR 312.320).

Select Research IND* if the product under investigation is not intended to be commercialized at a later date. Research INDs are generally sponsored by individual investigators, academic institutions and non-profit entities. Includes INDs for emergency use or other expanded access. (21 CFR 312.310, 312.315 and 312.320).

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* When a sponsor that generally submits Research INDs, then submits either a Phase 2 or Phase 3 protocol, they should select “Commercial” (eCTD requirements will apply). However, when the sponsor believes the Phase 2 or Phase 3 protocol is still solely for research, the sponsor may submit a justification explaining their rationale in the cover letter, along with the protocol. If the FDA agrees, then the IND will remain a “Research” IND and the eCTD requirements will not apply. Note that in all cases, expanded access INDs and protocols should be marked as “Research” on the Form 1571 and are exempt from eCTD requirements.

Field 8A: PROPOSED INDICATION FOR USE

Provide the proposed indication. Indicate if the proposed indication is for a rare disease (prevalence <200,000 U.S. patients). If the sponsor for the submission is the holder of the Orphan Designation Number, select "Yes" and provide the four or five digit identifier listed after the year in the Designation Number (e.g., for DRU-YYYY-1234, provide 1234). For Designation Numbers with an identifier shorter than four digits, please add zeros before the first digit of the identifier to increase the length of the identifier to four digits (e.g., for DRU-YYYY-123, provide 0123).

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.

Field 8B-C: SNOMED CT INDICATION TERM(S)

SNOMED CT terms should provide the underlying or, target diseases, associated symptoms, and/or procedures referenced for each provided indication. The underlying/target disease term should be entered as the Primary Term and any associated conditions should be entered as the Secondary Term(s). If an indication describes a procedure (therapeutic or diagnostic), then the procedure SNOMED CT term is the Primary Term and any condition or symptom terms the procedure is designed to diagnose or treat are the associated Secondary Term(s).

For each original IND submission (including resubmissions to this submission type), provide one SNOMED CT Primary Term **(Field 8B)** and, if applicable, one or more associated SNOMED CT Secondary Term(s) **(Field 8C)** for the verbatim indication provided in **Field 8A** (multiple Secondary Term(s) shall be separated by a semicolon). To specify additional Primary Terms for an indication and corresponding Secondary Term(s), use the continuation page and duplicate all indication information in **Field 8A,** including the proposed indication and rare and orphan designation information.

To look up the indication's SNOMED CT coded term(s):

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 search term in the search field.
5. Check the box 'Group by concept'.
6. Select the most appropriate and specific term for the indication that does not introduce incorrect information regarding 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 Primary Term into **Field 8B** of Form FDA 356h (e.g., "102449007 | Tardive dyskinesia (disorder)").
10. If applicable, repeat the process in Steps 1–8 to provide one or more associated SNOMED CT Secondary Term(s) into **Field 8C** for the single Primary Term provided in **8B.** If multiple Secondary Term(s) are to be entered, separate each term by a semicolon. To provide more Secondary Term(s) for a given Primary than the space in **Field 8C** permits, please use a continuation page and duplicate all the indication and Primary information from **Fields 8A** and **8B,** respectively.
11. For additional indications, use the continuation page for #8 and repeat these steps.

Field 9: PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED

Identification of the phase or phases of the clinical investigation to be conducted (21 CFR 312.23(a)(1)(ii)).

Field 10: CROSS REFERENCE

It is necessary for the sponsor to submit certain information with an IND (such as manufacturing and controls information, pharmacology and toxicology data, or data from prior human studies) unless that information

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has previously been submitted to FDA. If the sponsor of the previously submitted information is not the same as the sponsor listed in **Field 2,** the sponsor of the previously submitted information must provide a letter authorizing FDA to refer to the information (21 CFR 312.22(d)), (21 CFR 312.23 (b)). The sole exception to this requirement is when a marketed drug is used in the study, without modification to its approved packaging, in which case the marketed drug product must be identified by trade name, established name, dosage form, strength, and lot number (21 CFR 312.23(a)(7)(d)).

Field 11: SERIAL NUMBER

IND submissions should be consecutively numbered. The initial IND should be numbered "Serial Number: 0000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 0001." Submissions should be numbered consecutively in the order in which they are submitted.

Field 12A: SUBMISSION INFORMATION

Initial Investigational New Drug Application (IND): Should only be checked for an original IND submission. For subsequent submissions, check ALL the boxes below that apply because the submission may contain more than one type of information:

Response to Clinical Hold: A submission addressing deficiencies previously cited in a Clinical Hold letter (21 CFR 312.42(e))

Response to FDA Request for Information: A submission containing responses to information requests (21 CFR 312.41)

Request for Reactivation or Reinstatement: A request to resume clinical investigation under an IND placed on inactive status (21 CFR 312.45(d)); or, terminated by FDA (21 CFR 312.44(d))

Annual Report: A brief report of the progress of the investigation submitted within 60 days of the anniversary date that the IND went into effect (21 CFR 312.33)

General Correspondence: Any communication between the sponsor and FDA pertinent to the IND (21 CFR 312.41)

Development Safety Update Report (DSUR): A report that provides information to assure that sponsors are adequately monitoring and evaluating the evolving safety profile of the investigational drug; may be used in place of the Annual Report

Other: Any submission that does not fit in the other categories.

Protocol Amendment(s):

- *New Protocol:* A protocol for a study not covered by a protocol already contained in the IND (21 CFR 312.30(a))
- *Change in Protocol:* A submission describing changes in a protocol (21 CFR 312.30(b)), including changes to investigators (21 CFR 312.30(e))
- *New Investigator:* A new investigator added to carry out a previously submitted protocol (21 CFR 312.30(c))
- *PMR/PMC Protocol:* A protocol related to a postmarketing requirement or postmarketing commitment
- HF Validation Protocol: A protocol for a human factors (HF) validation study
- *Use Related Risk Analysis*: Used to analyze product tasks, risks, harms, and associated mitigations for the proposed product, can be used to support design of a HF validation study, or to support a justification that an HF validation study does not need to be submitted for Agency review.

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Information Amendment(s): Select the review discipline(s) to which the submission applies (21 CFR 312.31)

Request For: Select the type(s) of request(s) contained within the submission.

IND Safety Report(s):

- *Initial Written Report:* 21 CFR 312.32(c)
- *Follow-up to a Written Report:* 21 CFR 312.32(d)

Field 12B Does the submission contain:

Digital Health Technology (DHT) data or a proposal to collect DHT data? Select 'Yes' if the submission contains or proposes to collect clinical data acquired remotely from trial participants using a DHT. This information may be contained in meeting-related documents, study protocols, study reports, etc.

DHTs are systems that use computing platforms, connectivity, software, and/or sensors for remote clinical data acquisition from participants in a clinical investigation. Examples of DHTs include wearable sensors, environmental sensors, or mobile applications to measure clinical events or characteristics. FDA's guidance on DHTs represents the Agency's current thinking on the use of DHTs: https://www.fda.gov/media/155022/download.

Real-world evidence (RWE) or a proposal to use RWE?: Select 'Yes' if the submission contains real-world evidence (RWE) (i.e. analyses of real-world data (RWD) to generate evidence regarding a medical product's potential benefits or risks) or contains a proposal to use RWE and the submission contains a meeting request or meeting-related documents; protocol; statistical analysis plan; interim or final clinical study report; or original or supplemental marketing application. Select 'No' if the submission does not contain RWE or a proposal to use RWE (e.g., if the submission only includes or proposes analyses of RWD that would not provide evidence about the potential benefits or risks of a medical product), or the submission is not one of the submission types above.

RWD are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Examples of RWD include data from electronic health records; medical claims; product, disease, or other registries; and data from digital health technologies in non-research settings. For recommendations on providing information about the RWE or proposal to use RWE contained in the submission, see the Guidance for Industry: Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drug and Biological Products.

Field 13: COMBINATION PRODUCTS

Field 12A (Submission Information) should be filled out before attempting to fill out **Field 13. Field 13** is only fillable for original submissions [i.e., the Initial Investigational New Drug Application (IND)]. Indicate if the product proposed within the submission is a combination product [e.g., drug-device, drug-biological product, drug-device-biological 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
6: Drug/Biologic Combination
7: Separate Products Requiring Cross Labeling
8: Possible Combination Based on Cross Labeling of Separate Products
9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)

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If the product in the submission is not a combination product, select 'No' and leave the Combination Product Type blank. If the submission relates to both combination product and non-combination product configurations (e.g., the submission relates to a drug product in a vial and is also in a pre-filled syringe presentation), 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 14. SUBMISSIONS REQUIRING A JUSTIFICATION STATEMENT

Select the following only if applicable. A justification statement must be submitted with the application for any items selected. Refer to the cited CFR section for further information.

Expanded Access Use, 21 CFR 312.300: Note that Treatment INDs and Treatment Protocols are not intended for single patient use. Before checking this box, the sponsor should be thoroughly familiar with the cited regulations and contact the appropriate FDA review division to discuss the proposed treatment use (21 CFR 312.320).

Field 15: CONTENTS OF APPLICATION

This section contains items 1 through 12 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.

- For a Sponsor-Investigator IND, Items 2–4 may be briefly addressed in the cover letter or in a summary.
- When the investigational drug is obtained from a supplier in a final dosage form, Items 5, 7, 8 and 9 may be referenced if authorization is given by the supplier (see explanation in field 9 above). If the investigational drug is prepared or altered in any way after shipment by the supplier, complete manufacturing (or compounding) and controls information, including information on sterility and pyrogenicity testing for parenteral drugs, must be submitted for that process in Item 7.
- Item 6 requires that a protocol be submitted, along with information on the investigators, facilities, and Institutional Review Board. Completed Form(s) FDA 1572 with attachments would suffice for Items 6 b–d.
- Item 7 also requires submission of either a claim of categorical exclusion from the requirement to submit an environmental assessment or an environmental assessment (21 CFR 25.15(a)). When claiming a categorical exclusion, the sponsor should include the following statements: "I claim categorical exclusion (under 21 CFR 25.31(e)) for the study(ies) under this IND. To my knowledge, no extraordinary circumstances exist."
- In certain applications, information on special topics may be needed (Item 10). Refer to the cited CFR section for further information. Additional information may also include the Generic Drug User Fee (GDUFA) Coversheet (Form FDA 3794) for GDUFA Master Files (Type II APIs), when applicable.
- Include the Biosimilar User Fee Cover Sheet (Form FDA 3792) (Item 11) and / or the Clinical Trials Certification of Compliance (Form FDA 3674) (Item 12) as applicable.

Field 16: CONTRACT RESEARCH ORGANIZATIONS (CROs)

Check the appropriate box to indicate if the clinical study will be conducted by a CRO.

Use the Continuation Page to provide a statement containing the name and address of the CRO, identification of the clinical study and a listing of the obligations transferred (21 CFR 312.23(a)(1)(viii)).

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Field 17: Provide the Name and Title of the person responsible for monitoring the conduct and progress of the clinical investigations (21 CFR 312.23(a)(1)(vi)). For Sponsor-Investigator INDs, the investigator has this responsibility.

Field 18: Provide the Name(s) and Title(s) of the person(s) responsible under 21 CFR 312.32 for review and evaluation of information relevant to the safety of the drug (21 CFR 312.23(a)(1)(vii)). For Sponsor-Investigator INDs, the investigator has this responsibility.

Certain important commitments that the IND sponsor makes by signing Form FDA 1571 are listed below field 17. Under Section 744G (11) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as added by the Biosimilar User Fee Act of 2012 (BsUFA), the term "financial hold" means an order issued by FDA to prohibit the sponsor of a clinical investigation from continuing the investigation if FDA determines that the investigation is intended to support a biosimilar biological product application and the sponsor has failed to pay any required initial biosimilar biological product development (BPD) fee, annual BPD fee, or reactivation fee. The term "financial hold" does not mean that any of the bases for a clinical hold identified in section 505(i)(3) of the FD&C Act have been determined by FDA to exist concerning the investigation.

Field 19: NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

For a sponsor-investigator IND, the sponsor-investigator should be named and must sign the form. For an IND sponsored by a pharmaceutical firm or research organization, the name of the sponsor's authorizing representative should be entered and that individual must sign the form.

Fields 20–22: Provide the telephone number, facsimile number, and full mailing address of the individual identified in field 19.

Field 23: Provide the email address of the person identified in field 19. For INDs submitted to the Center for Biologics Evaluation and Research (CBER), a specific statement authorizing communication via non-secure email should be included in the cover letter as applicable.

Field 24: Provide the date the form is signed by the sponsor or sponsor's authorized representative. This date may be different from the date provided in field 3.

Field 25: NAME OF COUNTERSIGNER

If the person signing the application in field 28 does not reside or have a place of business within the United States, the submission must be countersigned by an attorney, agent, or other authorized official who resides or maintains a place of business within the United States (21 CFR 312.23(a)(1)(ix)).

If applicable, provide the name of the attorney, agent or other authorized official countersigning the application in field 29.

Field 26: ADDRESS OF COUNTERSIGNER

If applicable, provide the full mailing address of the individual identified in field 25. If the sponsor or sponsor's authorized representative identified in field 18 does not reside or have a place of business within the United States, this mailing address is the address to which written correspondence from the FDA should be directed.

Field 27: EMAIL ADDRESS

Enter the email address of the Countersigner named in Field 25.

Field 28: SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

The person identified in field 19 must sign in this field (21 CFR 312.23(a)(1)(ix)).

Field 29: SIGNATURE OF COUNTERSIGNER

If applicable, the person identified in field 25 must countersign in this field.

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FORM FDA 1572

Copies of Form FDA 1572 with its attachments may be sent by the sponsor-investigator to FDA to satisfy Form FDA 1571, field 14, item 6 b–d. Information can be supplied in the form of attachments (such as curriculum vitae) rather than entering that information directly onto the form, but this should be noted under the relevant section numbers.

FORM FDA 3674

The Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85) was enacted on September 27, 2007. Title VIII of FDAAA added new Section 402(j) to the Public Health Service Act (42 USC § 282(j)) and expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.

Title VIII further requires that, at the time of submission of an application under section 505 of the FDCA, including an Investigational New Drug application, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, such certification must include the appropriate National Clinical Trial (NCT) numbers. You may use Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank, to comply with the certification requirement. The form may also be found on the FDA Forms page.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of that subsection apply to any clinical trial(s) referenced in your application. Additional information regarding the certification form is available on the FDAAA Certification to Accompany Drug, Biological Product, and Device Applications or Submissions Web page. Additional information regarding the expansion of ClinicalTrials.gov is available at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html. Additional information on registering your clinical trials is available on the Protocol Registration System Web site.

Please note that FDA has published a guidance, Guidance for Sponsors, Industry, Researchers, Investigators, and FDA Staff – Certifications to Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added by Title VIII of the Food and Drug Administration Amendments Act of 2007. In this guidance, FDA recognizes that certain information and documents submitted to FDA typically bear no relationship to the type of information that Title VIII is designed to capture and that it would not further the purposes of the legislation if a certification were to accompany every type of information or document submitted to the Agency regarding a medical product regulated by FDA. Consequently, FDA identifies in the guidance several types of information and documents that typically need not be accompanied by this certification. For assistance in determining whether your submission of an application under section 505 of the FDCA must be accompanied by a certification, you may consult this guidance.