

**Updates to FDA Forms 356h & 1571:
Commercial vs. Research
SNOMED CT
Combination Products**



- **Part I**
 - Review of the following updates to forms 356h & 1571:
 - Commercial vs. Research
 - SNOMED CT
 - Combination Products
- **Part II**
 - **LIVE** walk-through of forms 356h & 1571 with mock data
- **Part III**
 - Contact Information
 - Acknowledgments

1571 Form: Commercial vs. Research

Mia Prather

Supervisory Program Analyst

Office of Business Informatics (OBI)

Division of Data Management Services & Solutions

Center for Drug Evaluation and Research

U.S. Food and Drug Administration



1571 Form: Commercial vs. Research



Beginning May 5, 2018, Commercial INDs will be required in eCTD format.

The latest fillable Form FDA 1571, found on the FDA Forms Website, allows the submitter to identify an IND submission as either Commercial or Research.

Where will it be on the form?

The new identifier is located in field 6B.

6A. IND Number <i>(If previously assigned)</i>	
<input type="text"/>	
6B. Select One:	Commercial <input type="checkbox"/>
	Research <input type="checkbox"/>

1571 Form: Commercial vs. Research



How will I obtain this information so I can successfully complete the form?

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

OR

✓ Select Research (IND) if the product under investigation is not intended to be commercialized at a later date.

Note: Instructions for completing the form can be found on the FDA's Forms website:
<https://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/ListFormsNumerically/default.htm>

1571 Form: Commercial vs. Research



Who do I contact if I have questions?

- For further questions, please contact:

CDER Division of Drug Information
U.S. Food and Drug Administration

druginfo@fda.hhs.gov

Tel: 855-543-3784 or 301-796-3400

Fax: 301-431-6353



SNOMED CT

Leposava Antonovic, PhD

Science Policy Analyst

Office of New Drugs (OND) – Immediate Office (IO)

Center for Drug Evaluation and Research

U.S. Food and Drug Administration



What is SNOMED CT and why is it being implemented?

- **SNOMED CT** stands for Systematized Nomenclature of Medicine Clinical Terms.
- The most comprehensive clinical healthcare terminology in the world with more than 30 countries actively contributing to its development and maintenance.
- Supported by National Library of Medicine (NLM), Center for Disease Control (CDC) and Prevention and the Office of the National Coordinator (ONC) for Health Information Technology.
- Required FDA terminology standard for coding study data indications of the IND, NDA, BLA and ANDA submissions.
- Additional tracking and metrics analysis.

SNOMED CT in FDA 1571 and FDA 356h Forms

Where are the changes located on the Forms?



- **Form 1571:**

- Field 7 changed to 7A
- Field 7B added to capture the SNOMED CT Indication Disease Term

7A. (Proposed) Indication for Use	Is this indication for a rare disease (prevalence <200,000 in U.S.)? <input type="checkbox"/> Yes <input type="checkbox"/> No	
	Does this product have an FDA Orphan Designation for this indication? <input type="checkbox"/> Yes <input type="checkbox"/> No	If yes, provide the Orphan Designation number for this indication: <input type="text"/>
Continuation Page for #7		
7B. SNOMED CT Indication Disease Term <i>(Use continuation page for each additional indication and respective coded disease term)</i>		

- **Form 356h:**

- Field 15 changed to 15A
- Field 15B added to capture the SNOMED CT Indication Disease Term

15A. Proposed Indication for Use	Is this indication for a rare disease (prevalence <200,000 in U.S.)? <input type="checkbox"/> Yes <input type="checkbox"/> No	
	Does this product have an FDA Orphan Designation for this indication? <input type="checkbox"/> Yes <input type="checkbox"/> No	If yes, provide the Orphan Designation number for this indication: <input type="text"/>
Continuation Page for #15		
15B. SNOMED CT Indication Disease Term <i>(Use continuation page for each additional indication and respective coded disease term)</i>		

SNOMED CT in FDA 1571 and FDA 356h Forms

How will I get SNOMED CT information?



- Navigate to <http://browser.ihtsdotools.org/>
- Make sure to select **US Edition** extension.
- Instructions on how to fill out Forms FDA 1571 and FDA 356h may be found at <https://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/ListFormsNumerically/default.htm>

SNOMED CT in FDA 1571 and FDA 356h Forms

How will I get SNOMED CT information? *Cont.*



1. Navigate to <http://browser.ihtsdotools.org/>

2. Select 'Go browsing United States edition'

The screenshot shows a web browser window displaying the SNOMED International SNOMED CT Browser. The browser's address bar shows the URL <http://browser.ihtsdotools.org/>. The page title is "SNOMED International SNOMED CT Browser". The main heading is "SNOMED International SNOMED CT Browser". Below the heading, there is a paragraph of text: "The SNOMED International SNOMED CT Browser provides ways to browse and search SNOMED CT. The browser has been implemented as part of development within the SNOMED International Open Tooling Framework, by the SNOMED International and its development partners". Another paragraph states: "The Browser is provided by SNOMED International to anyone for reference purposes. The interface and REST APIs are **not** to be used as part of production systems in health care settings. Any abuse of the REST APIs will result in the offending IP address being banned from accessing the browser." A third paragraph says: "Please provide any feedback on the browser by clicking on the feedback button at the top of the page. Your feedback is essential to the evolution and improvement of this service. Please visit the [SNOMED CT Content Request Service](#) to provide content feedback." Below this, there is a section titled "International Editions" with two buttons: "Go browsing... International edition January 2018" and "Ir al Navegador... Edición en español 2017-10-31". Underneath is a section titled "Local Extensions" with several buttons: "Go browsing... Australian edition 2017-09-30", "Go browsing... Belgian edition 2018-03-15", "Go browsing... Canadian edition 2017-10-31", "Gå til browser-siden D...", "Go browsing...", "Börja söka... Swedish edition 2017-11-30", "Go browsing... United Kingdom edition (hosted by the UK)", "Go browsing... United States edition 2018-03-01", and "Go browsing... Uruguay edition 2017-12-15". At the bottom left, there is a link "OR take the Tour...".

SNOMED CT in FDA 1571 and FDA 356h Forms

How will I get SNOMED CT information? *Cont.*



3 Select 'Search' tab in left hand panel.

4 Enter your disease term in the search field.

5 Check the box 'Group by concept'

6 Select the most appropriate SNOMED CT term.

7 In the right hand panel, select the 'Expression' tab.

8 Copy the entire text under the heading 'Pre-coordinated Expression.'

The screenshot shows the SNOMED International website search interface. The search field contains "high blood pressure". The search results are grouped by concept, showing four results. The first result is selected. The 'Expression' tab is selected in the right hand panel, showing the pre-coordinated expression: "38341003 |Hypertensive disorder, systemic arterial (disorder)|".

Options	Type at least 3 characters	Example: shou fra
<input type="checkbox"/> Group by concept	<input type="radio"/> High blood pressure	Hypertensive disorder, systemic arterial (disorder)
<input type="checkbox"/> Filter results by Language	<input type="radio"/> On examination - check high blood pressure	On examination - blood pressure (finding)
<input type="checkbox"/> Filter results by Semantic Tag	<input type="radio"/> On examination - initial high blood pressure	On examination - blood pressure (finding)
<input type="checkbox"/> finding	<input type="radio"/> On examination - blood pressure reading very high (finding)	On examination - blood pressure reading very high (finding)
<input type="checkbox"/> disorder		

```
<<< 49601007 |Disorder of cardiovascular system (disorder)| :
363705008 |Has definitional manifestation (attribute)| = 24184
363698007 |Finding site (attribute)| = 51840005 |Systemic circ
```

SNOMED CT in FDA 1571 and FDA 356h Forms

How do I enter SNOMED CT information?



Example: 38341003 | Hypertensive disorder, systemic arterial (disorder) |

- **Form FDA 1571**

7A. (Proposed) Indication for Use For the treatment of hypertension, to lower the blood pressure.	Is this indication for a rare disease (prevalence <200,000 in U.S.)? <input type="checkbox"/> Yes <input type="checkbox"/> No
	Does this product have an FDA Orphan Designation for this indication? <input type="checkbox"/> Yes <input type="checkbox"/> No
	If yes, provide the Orphan Designation number for this indication: <input type="text"/>
	Continuation Page for #7
7B. SNOMED CT Indication Disease Term (Use continuation page for each additional indication and respective coded disease term) 38341003 Hypertensive disorder, systemic arterial (disorder)	

- **Form FDA 356h**

15A. Proposed Indication for Use For the treatment of hypertension, to lower the blood pressure.	Is this indication for a rare disease (prevalence <200,000 in U.S.)? <input type="checkbox"/> Yes <input type="checkbox"/> No
	Does this product have an FDA Orphan Designation for this indication? <input type="checkbox"/> Yes <input type="checkbox"/> No
	If yes, provide the Orphan Designation number for this indication: <input type="text"/>
	Continuation Page for #15
15B. SNOMED CT Indication Disease Term (Use continuation page for each additional indication and respective coded disease term) 38341003 Hypertensive disorder, systemic arterial (disorder)	

FAQs: Do I need to provide SNOMED CT code for every proposed indication?



- **Yes.** A single SNOMED CT coded disease term (Concept ID and Concept Term) should be provided for each proposed indication.
- Consistent with the instructions for the Proposed Indication for Use; the Continuation Page should be used if there are more than one proposed indication and respective SNOMED CT Indication Disease Term per entry.

FAQs: How do I submit multiple indications and respective SNOMED CT codes?



- **Form 1571:**

- Use the “Continuation Page for #7” button located in this field to provide additional indications and respective SNOMED CT codes.

7A. (Proposed) Indication for Use

Is this indication for a rare disease (prevalence <200,000 in U.S.)? Yes No

Does this product have an FDA Orphan Designation for this indication? Yes No

If yes, provide the Orphan Designation number for this indication:

7B. SNOMED CT Indication Disease Term *(Use continuation page for each additional indication and respective coded disease term)*

Continuation Page for #7

- **Form 356h:**

- Use the “Continuation Page for #15” button located in this field to provide additional indications and respective SNOMED CT codes.

15A. Proposed Indication for Use

Is this indication for a rare disease (prevalence <200,000 in U.S.)? Yes No

Does this product have an FDA Orphan Designation for this indication? Yes No

If yes, provide the Orphan Designation number for this indication:

15B. SNOMED CT Indication Disease Term *(Use continuation page for each additional indication and respective coded disease term)*

Continuation Page for #15

FAQs: When are new versions of SNOMED CT US Edition released?



- New versions of SNOMED CT US Edition are generally available in **March** and **September** of **each year**.
- <http://browser.ihtsdotools.org/>

FAQs: Do I need to update SNOMED CT coded disease terms when a new version is released?

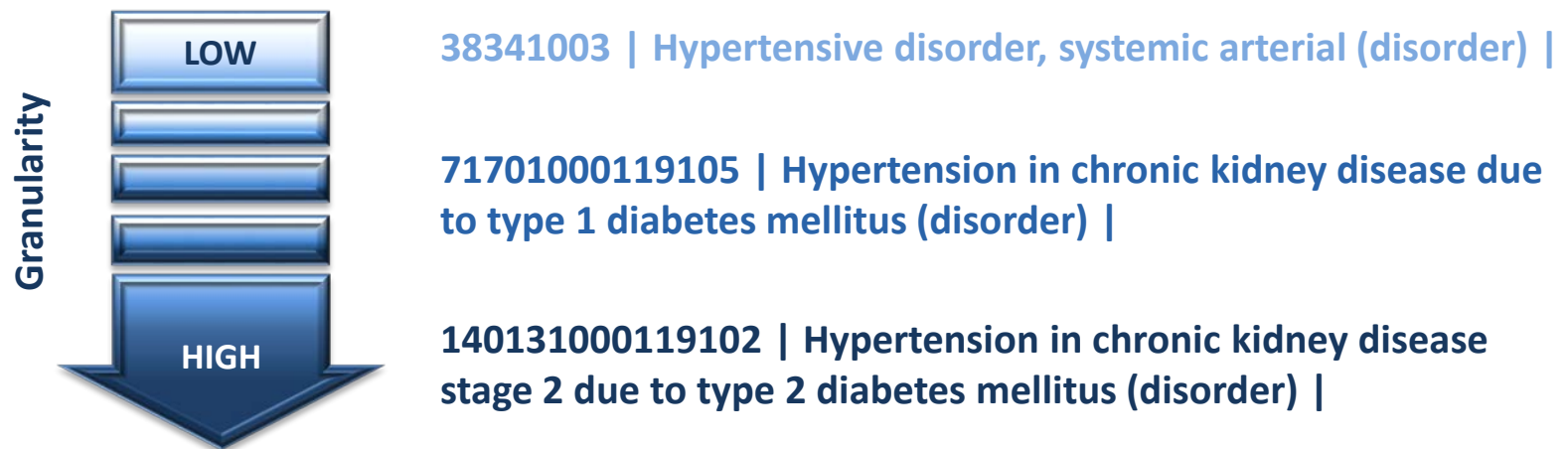


- In cases where SNOMED CT coded indication disease term(s) for given application/submission have changed, the updated SNOMED CT coded indication disease term(s) should be provided.
- The updated information should be provided with next additional information or supplement submission.

FAQs: What should I do if I cannot find the Target Disease I am looking for?



- SNOMED CT terminology can have multiple levels of “granularity”. Some indication disease terms may be high level terms (low granularity) while some may be low level terms (high granularity).
- Use the lowest level (high granularity) term as possible.



FAQs:

Who do I contact if I have questions?



- For further questions, please contact:

CDER Division of Drug Information
U.S. Food and Drug Administration
druginfo@fda.hhs.gov

Tel: 855-543-3784 or 301-796-3400

Fax: 301-431-6353



Combination Products

Melissa Burns

Senior Program Manager

CAPT, US Public Health Service

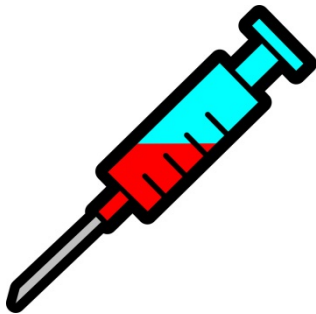
Office of Combination Products

Office of Special Medical Programs

U.S. Food and Drug Administration

What is a Combination Product?

- A “combination product” is:
 - A product comprised of two or more different types of medical products (e.g., drug and device, drug and biological product, device and biological product, or all three together)
- Combination Products are assigned to a “Lead Center” having primary responsibility for their review (e.g., either CBER or CDER for companies submitting NDA/BLA/ANDA/IND)





What is NOT a combination product?

- A combination product is NOT:
 - A product comprised of only two or more of the *same* type of medical product (e.g., drug and drug, device and device, or biologic and biologic).
 - A medical product combined *only* with a non-medical product (e.g., drug and food, drug and cosmetic). See 21 USC 353(g).
- The following ARE NOT combination products:
 - Drugs combined only with each other, such as fixed dose combination drugs
 - Kits of JUST devices, JUST drugs, or JUST biological products
 - Separately distributed general use delivery devices (e.g. syringes) and drugs or biologics with which they can be used.



Categories of Combination Products

	“Single-entity”	“Co-packaged”	“Cross-labeled”
Description	Chemically or physically combined constituent parts	Constituent parts packaged together	Constituent parts that are packaged separately, but labeled and need to be used specifically with one another to achieve the intended therapeutic effect
Examples	<ul style="list-style-type: none">• Prefilled syringe• Transdermal patch• Drug-eluting stent	<ul style="list-style-type: none">• First-aid or surgical kit• Syringe packaged with vial of drug• Drug + prefilled diluent, reconstitution/transfer device, fillable cartridge and wearable patch	<ul style="list-style-type: none">• Some light activated drug product packaged separately from the light activation device
Reference	21 CFR 3.2(e)(1)	21 CFR 3.2(e)(2)	21 CFR 3.2(e)(3) and 21 CFR 3.2(e)(4)

Types of Combination Products

Type	Description	Common Example(s)
1	<p>Convenience Kit or Co-Package</p> <p>Drug and device are provided as individual constituent parts within the same package</p>	Drug or biological product vials packaged with device or accessory kits (empty syringes, auto-injectors, transfer sets)
2	<p>Prefilled Drug Delivery Device/ System</p> <p>Drug is filled into or otherwise combined with the device AND the sole purpose of the device is to deliver drug</p>	Prefilled drug syringe, auto-injectors, metered-dose inhalers, dry power inhalers, nasal-spray, pumps or spray bottles, transdermal patches, prefilled iontophoresis system or microneedle patch
3	<p>Prefilled Biologic Delivery Device/ System</p> <p>Biological product is filled into or otherwise combined with the device AND the sole purpose of the device is to deliver biological product</p>	Prefilled vaccine or other biological product syringes, autoinjectors, nasal Sprays, dropper bottles, transdermal or microneedle patches pre-coated with biological product
4	<p>Device Coated/ Impregnated/ Otherwise Combined with Drug</p> <p>Device has an additional function in addition to delivering the drug</p>	Drug pills embedded with sensors, contact lens coated with a drug

Types of Combination Products

Type	Description	Common Example(s)
5	<p>Device Coated or Otherwise Combined with Biologic</p> <p>Device has an additional function in addition to delivering the drug</p>	Live cells seeded on a device scaffold
6	Drug/Biologic Combination	Antibody-drug conjugates
7	Separate Products Requiring Cross Labeling	Light-activated drugs or biological products labeled for use with a specific light-activation device
8	Possible Combination Based on Cross Labeling of Separate Products	Drug/biological product labeling discusses a device, but submitter is unsure whether the product constitutes a cross-labeled combination product
9	Other Type of Part 3 Combination Product (e.g., Drug/Device/ Biological Product)	<p>Combination product not otherwise described above</p> <p>All 3 articles are combined in a single product (e.g., a prefilled syringe containing an antibody-drug conjugate)</p>



Request for Designation (RFD)

- An RFD is a written submission to the Office of Combination Products (OCP) that request a determination of:
 - The regulatory identity or classification of a product as a drug, device, biological product, or combination product, and/or
 - The component of FDA that will regulate the product if it is a non-combination product or which Center (CBER/CDER/CDRH) will have primary jurisdiction for premarket review and regulation if it is a combination product.
- Most products do not require an RFD prior to making a premarket submission
 - Submission of an RFD is generally only needed when the classification of a product or the Center to which it should be assigned is unclear or in dispute.

How do I know if my Product is a Combination Product and/or What Type of Combination Product?

- In many cases, FDA will have identified the product as a combination product during meeting and submission interactions.
- Use the examples provided in the previous slides as references.
- For marketed products, the combination product identifiers are also used for Registration and Listing (check your R&L).
- If you are still unsure, contact the Lead Center for assistance:
 - CDER: CDERProductJurisdiction@fda.hhs.gov
 - CBER: CBERProductJurisdiction@fda.hhs.gov

Why do I Need to Include Combination Product Information on the 356h and 1571 Forms?

- Combination products typically require consults and collaboration between multiple FDA Medical Product Centers (CBER, CDER, CDRH)
 - Early identification of submissions for combination products helps ensure appropriate expertise is engaged early and that Sponsors receive timely and comprehensive review of their submissions
- Congress recognized the importance of Sponsor’s identifying their products as combination products when interacting with FDA
 - See Section 3038 of the [21st Century Cures Act](#): “In seeking agency action with respect to a combination product, the sponsor of such product—shall identify the product as a combination product.”
 - Use of the combination product fields on FDA 356h and 1571 enables Sponsors to fulfill this requirement

When do I Need to Enter Combination Product Information on the 356h and 1571 Form?

- The Sponsor selects “Yes” or “No” that the product is a combination product for submissions that are:
 - **For 356h:** NDA/ANDA/BLA Originals or Supplements (Labeling, CMC, Efficacy, or REMS)
 - **For 1571:** IND Originals
- If the product is NOT a combination product (e.g., “No” is selected) the Combination Product Type field is not required (leave blank)
- If the product IS a combination product (e.g., “Yes” is selected) a single-digit numeric representing the combination product type is entered into the Combination Product Type field
- If a Request for Designation has been submitted for the product in the submission, the RFD number (six-digit numeric) is entered in the RFD field



Where do I Enter Combination Product Information on the 356h and 1571 Form?

- The combination product fields are located at:
 - Form 356h: Field 24

<input type="checkbox"/> Initial Submission <input type="checkbox"/> Resubmission		<input type="checkbox"/> CBE-30	
24. For Originals and all Supplements, is the product a combination product (21 CFR 3.2(e))? <input type="checkbox"/> Yes <input type="checkbox"/> No	Combination Product Type (See instructions)	Request for Designation (RFD) Number	
25. Does the submission contain:	Human factors information?	26. Proposed Marketing Status (Select one)	

- Form 1571: Field 12

<input type="checkbox"/> Non-investigational <input type="checkbox"/> Human Factors Protocol <input type="checkbox"/> Clinical Pharmacology		<input type="checkbox"/> Special Access <input type="checkbox"/> Formal Dispute Resolution	
12. For Originals, is the product a combination product (21 CFR 3.2(e))? <input type="checkbox"/> Yes <input type="checkbox"/> No	Combination Product Type (See instructions)	Request for Designation (RFD) Number	
13. Select the following only if applicable. (Justification statement must be submitted with application for any items selected below. Refer to the cited CFR section for further information.)			

Where Can I find Additional Information on Combination Products?

- Visit the Office of Combination Products Frequently Asked Questions webpage:
<https://www.fda.gov/CombinationProducts/AboutCombinationProducts/>
- If you still have questions, contact the Lead Center or the Office of Combination Products (OCP) for assistance:
 - CDER: CDERProductJurisdiction@fda.hhs.gov
 - CBER: CBERProductJurisdiction@fda.hhs.gov
 - OCP: combination@fda.gov

LIVE walk-through
of Forms 356h & 1571
with mock data

Elizabeth Chen, PharmD

Science Policy Analyst

Office of New Drugs (OND) – Immediate Office (IO)

Center for Drug Evaluation and Research

U.S. Food and Drug Administration



For More Information

- **FDA Forms Webpage**

<https://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/ListFormsNumerically/default.htm>

- **CDER Division of Drug Information**

U.S. Food and Drug Administration

druginfo@fda.hhs.gov

Tel: 855-543-3784 or 301-796-3400

Fax: 301-431-6353



Thank You!

(In Alphabetical Order)

- Members of the FDA Forms Working Group
- Terry Artman
- Sonja Brajovic
- Eric Brodsky
- Cherryn Chang
- Gregory Chin
- Ishani Chowdhury
- Marc Cohen
- Danita Dixon
- Ronald Fitzmartin
- Fatima Frye
- William Hess
- Virginia Hussong
- Karina Kuhn
- Sherry Lard
- Kristina Lauritsen
- Christopher Leptak
- Mary Ann Slack
- Carla Vincent