



Title: [DHHS Regulation for Clinical Trials Registration and Results Information Submission \(Final Rule\)](#)

Date of Last Revision: 07/17/2017

Audience: Office of Research HRP

Scope

Element	Final Rule
Scope/Applicability	<p>Applicable clinical trials of FDA-regulated drug, biological, and device products and pediatric post-market surveillance studies of devices required by the FDA under the FD&C Act.</p> <p>Does not apply to phase 1 trials or small feasibility device studies.</p> <p>Applicable clinical trials are (1) clinical trials of drug and biological products that are controlled, clinical investigations, other than phase 1 investigations, of a product subject to FDA regulation; and (2) prospective clinical studies of health outcomes comparing an intervention with a device product against a control in humans (other than small feasibility studies) or any pediatric post-market surveillance studies required by FDA under the FD&C Act.</p> <p>Applies to public and private sector sponsors and other entities who meet the definition of a responsible party.</p> <p>https://www.nih.gov/news-events/summary-table-hhs-nih-initiatives-enhance-availability-clinical-trial-information</p>

Continuing Review

https://www.gpo.gov/fdsys/pkg/ Government ... gpo.gov

141 / 177 85%

Fill & Sign

Certified by Superintendent of Documents, United States Government Printing Office, certificate issued by VeriSign CA for Adobe CDS. Signatu

https://www.gpo.gov/fdsys/pkg/FR-2016-09-21/pdf/2016-22129.pdf

APPLICABILITY OF REQUIREMENTS IN 42 CFR PART 11

Initiation date	Primary completion date	Registration information submission required?		Results information submission required?	
		Approved, licensed, or cleared products	Unapproved, unlicensed, or uncleared products	Approved, licensed, or cleared products	Unapproved, unlicensed, or uncleared products
On or before September 27, 2007	After December 26, 2007 and before Effective Date of Final Rule.	Yes, as specified in section 402(j)(2)(A)(ii) of the PHS Act.	Yes, as specified in section 402(j)(2)(A)(ii) of the PHS Act.	Yes, as specified in section 402(j)(3)(C) and section 402(j)(3)(I) of the PHS Act.	No.
After September 27, 2007 and before the Effective Date of the Final Rule.	Before Effective Date of Final Rule.	Yes, as specified in section 402(j)(2)(A)(ii) of the PHS Act.	Yes, as specified in section 402(j)(2)(A)(ii) of the PHS Act.	Yes, as specified in section 402(j)(3)(C) and section 402(j)(3)(I) of the PHS Act.	No.
After September 27, 2007 and before Effective Date of Final Rule.	On or after Effective Date of Final Rule.	Yes, as specified in section 402(j)(2)(A)(ii) of the PHS Act.	Yes, as specified in section 402(j)(2)(A)(ii) of the PHS Act.	Yes, as specified in 42 CFR part 11.	Yes, as specified in 42 CFR part 11.
On or after Effective Date of Final Rule	On or after Effective Date of Final Rule.	Yes, as specified in 42 CFR part 11.	Yes, as specified in 42 CFR part 11.	Yes, as specified in 42 CFR part 11.	Yes, as specified in 42 CFR part 11.

The table above does not apply to voluntary submissions under § 402(j)(4)(A) of the PHS Act and § 11.60. The registration and results information submission requirements for the voluntary submission of clinical trial information are addressed in § 11.60.

if the trial is not initiated until after the effective date of the final rule, the responsible party will be required to comply with the registration provisions as specified in the final rule and to update the registration information for that applicable clinical trial. In a situation such as this, we would expect

information required as specified in the final rule prior to the effective date). However, if the applicable clinical trial actually was initiated one week before the effective date of the final rule, the trial would instead be subject to the registration requirements as specified in section 402(j)(2)(A)(ii) of the PHS Act

DHHS: Voluntary Submission of a non-ACT, and an ACT that is not otherwise required to submit clinical trial registration information

- Subpart D - Additional submissions of Clinical Trial Information: <https://www.federalregister.gov/d/2016-22129/p-1566>
- Submission of results to ClinicalTrials.gov for a non-ACT: <https://clinicaltrials.gov/ct2/manage-recs/faq#applicable>

APPLICABLE DEVICE CLINICAL TRIAL

The following elements are all required:

- Protocol includes [human subjects](#)
- Protocol meets the definition of a [clinical study](#)
- Protocol is prospective in nature
- Protocol includes ascertaining health [outcomes](#) as an endpoint
- Protocol [compares](#) an [intervention](#) with a device
- Protocol includes a [control](#) population
- Protocol includes a [device](#) product subject to FD&C Act [[21 U.S.C. 321\(h\)](#)]
- Study occurs within the US (or US territory); or, the device is manufactured in the US (or US territory) and is exported for study in another country
- Protocol is not a feasibility study

OR

- Protocol is a [pediatric postmarket surveillance](#) of devices

LR Responsibilities:

- Informed Consent documents will include a specific statement relating to posting of clinical trial information at *ClinicalTrials.gov*
- Each clinical trial will only have one entry in *ClinicalTrials.gov* that contains its registration and results information
- Registration:** [Not later than 21 days after enrollment of the first participant](#)
- Results:** [Not later than 12 months after primary completion date](#)

APPLICABLE DRUG CLINICAL TRIAL

The following elements are **all** required:

- Protocol meets definition of a [controlled clinical investigation](#)
- Protocol is **not** a [Phase 1 trial](#)
- Protocol includes a drug [[Chapter II Section 201\(g\), page 4](#)] (or biologic [[42 USC 262\(i\)](#)]) that is subject to [FD&C Act](#) [has an IND, NDA or BLA]
OR
Protocol includes a drug (or biologic) that is [exempt from IND requirements](#)
- Study occurs within the US (or US territory); or, the drug is manufactured in the US (or US territory) and is exported for study in another country under an IND

LR Responsibilities:

- Informed Consent documents will include a specific statement relating to posting of clinical trial information at *ClinicalTrials.gov*
- Each clinical trial will only have one entry in *ClinicalTrials.gov* that contains its registration and results information
- Registration:** [Not later than 21 days after enrollment of the first participant](#)
- Results:** [Not later than 12 months after primary completion date](#)

Registration Steps

Steps 1 and 2

1. Responsible Party (RP) will register at ClinicalTrials.gov: system will prompt questions to help determine whether a study is an ACT (applicable clinical trial)
2. PRS (ClinicalTrials.gov team) will review the registration information: 2-5 business days

Steps 3 and 4

3. PRS will provide comments to the RP: completion time depends on the comments and the response time from the RP and PRS *[this is an opportunity to verify the study is an ACT or not]*

*** a registration record can only be deleted if it has not yet been assigned an NCT#**

4. After review of comments are accepted, PRS will assign the registration record an NCT #: study will be posted publicly within 2 business days

Step 5

5. After an NCT # has been assigned (regardless of ACT/non-ACT status), there are obligations for providing system *updates*; and there are obligations for providing *results* (*results only for ACTs*)

* Only the RP can approve/release transactions (i.e., register, update, results) in the system; a designated/assigned individual can *prepare* the transactions

ELABORATIONS OF DEFINITIONS OF AN APPLICABLE CLINICAL TRIAL

Applicable Device Trial: *All 4 elements must be met*

Element 1 Prospective clinical study of health outcomes: *all parts of the definition must be met*

The agency considers a "clinical study" of a device to be an investigation in which a device is used in one or more human subjects. For device studies, the term **"subject"** is defined in the Food and Drug Administration (FDA) regulations as a **"human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease."** (See [21 CFR § 812.3\(p\)](#)).

For purposes only of the requirements under 402(j) of the PHS Act [\[page 588\]](#), *this definition of human subject does not apply to de-identified human specimens.* (See, Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, April 25, 2006 (<http://www.fda.gov/cdrh/oivd/guidance/1588.html>))

- The term "study" is often used interchangeably with the term "investigation". As pertaining to devices, **"investigation"** is defined as **"a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device."** ([21 CFR §812.3\(h\)](#)). Although FDA's regulations pertaining to devices do not specifically define the term **"clinical investigation,"** that term is defined in FDA regulations pertaining to clinical investigations of drugs and biological products as any **"experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects,"** where "experiment" is defined as **"any use of a drug except for the use of a marketed drug in the course of medical practice."** (See 21 CFR § [312.3](#)).

In NIH's view, these definitions can be applied to device trials by defining a **"clinical study of a device"** as **"any experiment in which a device is administered, dispensed to, or used involving, one or more human subjects,"** defining an **"experiment"** as **"any use of a device except for the use of a marketed device in the course of medical practice,"** and using the definition of "subject" described above (from [21 CFR § 812.3\(p\)](#)). This interpretation helps improve consistency between definitions of the terms "applicable device clinical trial" and "applicable drug clinical trial" (defined below).

This definition of a **clinical study of a device** would **include studies in which subjects are assigned to specific interventions in a clinical investigation according to a study protocol.** Studies in which a device is used on a patient as part of routine medical care and not under a study or protocol would not be considered "clinical investigations" for purposes of [Title VIII of PL 110-85](#). Examples of studies that might fall under this description include situations in which, after a device has been administered to a patient in the course of routine medical practice by a healthcare provider, a researcher not associated with the administration of the device reviews the records of the patients to assess certain effects or interviews the patients to assess certain impacts, or collects longitudinal data to assess health outcomes.

- Turning to the interpretation of "prospective," a **"prospective" clinical study** is considered by the agency to be **any study that is not retrospective** or, in other words, is one in which subjects are followed forward in time from a well defined point, i.e., the baseline of the study. A "prospective clinical study" also **may have non-concurrent (e.g., historical) control groups.** A "prospective clinical study" **may also include studies in which subjects are provided an intervention and assessed at the same time.** An example of a retrospective study, and thus not an applicable device clinical trial, is a study in which subjects are selected based on the presence or absence of a particular event of interest from hospital records or other data sources.

For purposes of this definition, a prospective study of health outcomes is a study in which the primary purpose is to evaluate a defined clinical outcome directly related to human health. For example, a study of a diagnostic device (such as an in vitro diagnostic (IVD)) in which the primary purpose is to evaluate the ability of the device to make a diagnosis of a disease or condition is directly related to human health and, therefore, would be considered a study of health outcomes for purposes of [Title VIII of PL 110-85](#).

Element 2 Comparing an intervention with a device against a control in human subjects:

The agency interprets an "intervention with a device" to be one in which a device is used on a human subject in the course of a study. As stated above, the term "subject" is defined consistent with [21 CFR § 812.3\(p\)](#). As noted previously, for purposes only of the requirements under 402(j) of the PHS Act [[page 588](#)], however, this definition of human subject does *not apply to de-identified human specimens*. The agency interprets the term "intervention" broadly to include various techniques using the device such as, among other things, device regimens and procedures, and use of prophylactic, diagnostic, or therapeutic agents.

A clinical study is considered to "compare an intervention with a device against a control in human subjects" when it compares differences in the clinical outcomes (or diagnosis) between subjects who received an intervention that included a device and control subjects (who received other interventions, or no intervention). The intervention may be with a device that has never been cleared or approved, or with an already marketed device, whether or not the device has been cleared or approved for the indication being studied. Such controlled clinical studies include not only concurrent control groups, but also non-concurrent controls such as historical controls (e.g., literature, patient records), validated objective outcomes using objective performance criteria (criteria based on broad sets of data from historical databases (e.g., literature or registries) that are generally recognized as acceptable values, or patients as their own control.

Expanded access protocols under section 561 of the FDC Act [[page 408](#)], under which investigational devices are made available to individuals under certain conditions, are not controlled clinical investigations and, therefore, are not applicable device clinical trials. Similarly, a continued access protocol, under which an investigational device continues to be made available after completion of a controlled trial and while a marketing application is being prepared or reviewed, is, by definition, not a controlled clinical investigation and, therefore, is not an applicable device clinical trial.

Element 3 A Device Subject to [Section 510\(k\)](#) [[page 284](#)], [515](#) [[page 329](#)], or [520\(m\)](#) [[page 369](#)] of the Federal Food, Drug, and Cosmetic Act:

In the view of the agency, a device (including a [significant risk device](#) for which approval of an investigational device exemption (IDE) is required under section [520\(g\)](#) of the FDC Act; a [non-significant risk device](#) that is considered to have an approved IDE in accordance with 21 CFR § [812.2\(b\)](#); or a device that is exempt from the submission requirements of 21 CFR [Part 812](#)) is subject to section 510(k), 515, or 520(m) of the FDC Act if any of the following is required before it may be legally marketed: (1) a finding of substantial equivalence under section 510(k) permitting the device to be marketed; (2) an order under section 515 of the FDC Act approving a premarket approval application for the device; or (3) a humanitarian device exemption under section 520(m) of the FDC Act.

When a clinical study includes sites both within the U.S. (including any territory of the U.S.) and outside of the U.S., if any of those sites is using (for purposes of the clinical study) a device that is subject to section 510(k), 515, or 520(m) of the FDC Act, then the agency will consider the entire clinical study to be an applicable device clinical trial (assuming that it meets the rest of the statutory definition).

OR

A clinical study that is being conducted entirely outside of the U.S. (i.e., does not have any sites in the U.S. or in any territory of the U.S.) may be an applicable device clinical trial, depending on where the device being used in the clinical study is manufactured. If the device is manufactured in the U.S. or any territory of the U.S., and is exported for study in another country (whether it is exported under section 801(e) [page 590] or section 802 [page 603] of the FDC Act), then the device is considered to be subject to section 510(k), 515, or 520(m) of the FDC Act.

If the device is manufactured outside of the U.S. or its territories, and the trial sites are all outside of the U.S. and/or its territories, then it would **not** be considered to be subject to section 510(k), 515, or 520(m) of the FDC Act.

Element 4 *Other Than a Small Clinical Trial to Determine the Feasibility of a Device, or a Clinical Trial to Test Prototype Devices Where the Primary Outcome Measure Relates to Feasibility and Not to Health Outcomes:*

Protocol is **not** a feasibility study

Trials or studies designed primarily to determine the feasibility of a device or to test a prototype device (feasibility studies) are considered by the agency to be trials conducted to confirm the design and operating specifications of a device before beginning a full clinical trial. Feasibility studies are sometimes referred to as phase 1 studies, pilot studies, prototype studies, or introductory trials. Feasibility studies are not considered applicable device clinical trials under the statutory definition.

AND/OR

The second part of the statutory definition specifies that an “applicable device clinical trial” includes “pediatric postmarket surveillance” of devices “as required under section 522 of the Federal Food, Drug, and Cosmetic Act.” Postmarket surveillances can take many forms, from literature reviews to controlled clinical trials. Based on the statutory language, any pediatric postmarket surveillance under section 522 of the FDC Act [page 372], regardless of its form, is an applicable device clinical trial.

Section 520(g) = Section [360j](#)

Applicable Drug Trial: *All 4 elements must be met*

Element 1	<p><i>Clinical Investigation:</i></p> <p><input type="checkbox"/> FDAAA states that "clinical investigation" has the meaning given that term in 21 CFR § 312.3, which defines "<u>clinical investigation</u>" as <u>any "experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects."</u> The regulation further defines an "experiment" as <u>"any use of a drug except for the use of a marketed drug in the course of medical practice."</u></p> <p>This definition of a clinical investigation of a drug would <u>include studies in which subjects are assigned to specific interventions in a clinical investigation according to a study protocol.</u></p> <p>A study in which a drug is administered or provided to a patient as part of routine medical care and not under a study or protocol would <u>not</u> be considered a "clinical investigation" for purposes of Title VIII of PL 110-85. Examples of studies that might fall under this description, include situations in which, after a drug has been administered to a patient in the course of routine medical practice by a healthcare provider, a researcher not associated with the administration of the drug reviews the records of the patients to assess certain effects, interviews the patients to assess certain impacts, or collects longitudinal data to track health outcomes. Similarly, a situation in which a healthcare provider only observes and records the effects of the use of a marketed drug in the course of his or her routine medical practice would <u>not</u> be considered a clinical investigation under this definition. Because these activities would <u>not</u> be considered "clinical investigations" under 21 CFR § 312.2 <u>these, therefore, would not be considered "applicable drug clinical trials."</u></p>
Element 2	<p><i>Controlled:</i></p> <p><input type="checkbox"/> The agency considers a <u>controlled clinical investigation</u> to be one that is <u>designed to permit a comparison of a test intervention with a control to provide a quantitative assessment of the drug effect.</u> The purpose of the control is to distinguish the effect of a drug from other influences, such as the spontaneous change in the course of the diseases, placebo effect, or biased observation. The control will provide data about what happens to human subjects who have not received the test intervention or who have received a different intervention. Generally, the <u>types of control</u> that are used in clinical investigations are: (1) placebo concurrent control; (2) dose-comparison control; (3) no intervention concurrent control; (4) active intervention concurrent control; and (5) historical control (See 21 CFR § 314.126(b)).</p> <p>OR</p> <p><input type="checkbox"/> In the agency's view, a <u>clinical investigation designed to demonstrate that an investigational drug product is bioequivalent to a previously approved drug product, or to demonstrate comparative bioavailability of two products</u> (such as for purposes of submitting an <u>abbreviated new drug application/ANDA</u> under 21 USC § 355(j) or a <u>new drug application/NDA</u> as described in 21 USC § 355(b)(2)) <u>is considered to be a controlled clinical investigation.</u> In this case, the control generally would be the previously approved drug product.</p> <p>In the agency's view, similar to investigational devices, the <u>use of an investigational drug under an expanded access program</u> under section 561 of the FDC Act [page 408] <u>does not meet the definition of a "controlled clinical investigation" and therefore would not be considered an "applicable drug clinical trial."</u></p>

We note that FDAAA does require, for certain applicable drug clinical trials, the submission of certain information regarding whether there is expanded access to the drug or biological product under section 561 of the FDC Act [\[page 408\]](#).

Element 3 **Other than a phase I clinical investigation:**

- Protocol is **not** a Phase 1 trial

An "applicable drug clinical trial" is defined in FDAAA to exclude Phase 1 clinical investigations, as that term is defined in 21 CFR § [312.21](#). Under 21 CFR § [312.21](#), Phase 1 includes the initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. The total number of subjects and patients included in Phase 1 studies varies with the drug, but is generally in the range of 20 to 80. Phase 1 studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. **Studies that meet the definition of "Phase 1" are not "applicable drug clinical trials."**

Under certain circumstances, a clinical investigation designed to demonstrate that an investigational drug product is bioequivalent to a previously approved drug product, or to demonstrate comparative bioavailability of two products (such as for purposes of submitting an abbreviated new drug application under 21 USC § [355\(i\)](#) or a new drug application as described in 21 USC § [355\(b\)\(2\)](#)) will be considered to be a Phase 1 clinical investigation under 21 CFR § [312.21](#) for purposes of determining whether a particular clinical trial is an "applicable drug clinical trial" under [Title VIII of PL 110-85](#) (section 402(j)(1)(A)(iii) of the PHS Act [\[page 588\]](#)). Although Phase 1 clinical investigations are generally designed to fit sequentially within the development plan for a particular drug, and to develop the data that will support beginning Phase 2 studies, 21 CFR § [312.21\(a\)](#) does not limit Phase 1 trials to that situation. Bioequivalence or comparative bioavailability studies that fall within the scope of the studies described in 21 CFR § [320.24\(b\)\(1\)](#), (2), and (3) share many of the characteristics of Phase 1 clinical investigations as described in 21 CFR § [312.21\(a\)](#), and therefore will be considered to be Phase 1 trials for purposes of [Title VIII of PL 110-85](#). However, bioequivalence or comparative bioavailability trials that fall within the scope of 21 CFR § [320.24\(b\)\(4\)](#) do not share the characteristics of Phase 1 trials as described in 21 CFR § [312.21\(a\)](#), and thus would not be considered to be Phase 1 trials for purposes of [Title VIII of PL 110-85](#).

Element 4 **Drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act [\[page 172\]](#) or section 351 of the Public Health Service Act [\[page 368\]](#):**

- Drug/Biologic product has/requires an NDA or BLA

The term "drug" is defined in FDAAA to mean a "drug as defined in section 201(g) of the Federal Food, Drug and Cosmetic Act [\[page 4\]](#) or a biological product as defined in section 351 of [the Public Health Service] Act" [\[page 368\]](#). In keeping with the requirements of the FDC Act and section 351 of the PHS Act [\[page 368\]](#), **a drug or biological product is considered to be "subject to section 505 of the [FDC] Act [\[page 172\]](#) or section 351 of [the PHS] Act [\[page 368\]](#)" if it is the subject of an approved new drug application (NDA) or biologics license application (BLA) or if an approved NDA or BLA would be required in order for that drug or biological product to be legally marketed.**

A non-prescription drug that is or could be marketed under an existing over-the-counter (OTC) drug monograph (see 21 CFR § [330-358](#)) is **not considered "subject to section 505 of the [FDC] Act [\[page 172\]](#)."**

OR

- Drug/Biologic is [IND Exempt](#)

A drug (including a biological product) that is subject to section 505 of the FDC Act [\[page 172\]](#) or to section 351 of the PHS Act [\[page 368\]](#), and therefore would require an approved NDA or BLA in order to be legally marketed, can be shipped for the purpose of conducting a clinical investigation of that product if an investigational new drug application (IND) is in effect. Drugs (including biological products) that are being studied under an IND are considered "subject to section 505" [\[page 172\]](#) both because (in most situations) the drug being studied would need an approved NDA or BLA to be legally marketed, and because INDs are issued by FDA pursuant to the authority in section 505(i) [\(page 184\)](#) of the FDC Act.

However, whether a drug is subject to regulation under section 505 of the FDC Act [\[page 172\]](#) or section 351 of the PHS Act [\[page 368\]](#) is a different question from whether a clinical investigator would need to obtain an IND from FDA before beginning to enroll human subjects in that clinical investigation. Therefore, a drug (including a biological product) being studied in a clinical investigation can be subject to section 505 of the FDC Act [\[page 172\]](#) or section 351 of the PHS Act [\[page 368\]](#), even if a clinical investigation of that drug is "IND exempt" (i.e., does not require an IND because that clinical investigation falls within 21 CFR § 312.2(b)). Hence (assuming it meets the rest of the statutory definition in 402(j)(1)(A) of the PHS Act [\[page 588\]](#)), a clinical investigation of a drug can be an "applicable drug clinical trial" under FDAAA even if it does not require an IND. Furthermore, if a sponsor chooses to obtain an IND (issued under section 505 [\[page 172\]](#) of the FDC Act) for a clinical investigation of a drug (including a biological product) that is *not* otherwise subject to section 505 [\[page 172\]](#) or to section 351 of the PHS Act [\[page 368\]](#), in doing so the sponsor has *agreed* to regulation under section 505 of the FDC Act [\[page 172\]](#) and that clinical investigation will be *considered to be "an applicable drug clinical trial,"* assuming that it meets the other elements of the statutory definition.

AND

- When a clinical investigation includes sites both within the U.S. (including any territory of the U.S.) and outside of the U.S., if any of those sites is using (for purposes of the clinical investigation) a drug that is subject to section 505 of the FDC Act [\[page 172\]](#), then the agency will consider the entire clinical investigation to be an "applicable drug clinical trial," assuming that it meets the rest of the statutory definition.

A clinical investigation that is being conducted entirely outside of the U.S. (i.e., does not have any sites in the U.S. or in any territory of the U.S.) may be an "applicable drug clinical trial," depending on where the drug being used in the clinical investigation is manufactured. If the drug is manufactured in the U.S. or any territory of the U.S., and is exported for study in another country under an IND, pursuant to 21 CFR § 312.110, or pursuant to section 802 of the FDC Act [\[page 603\]](#), then the drug is considered to be subject to section 505 of the FDC Act [\[page 172\]](#) or section 351 [\[page 368\]](#) of the PHS Act (as applicable), and the clinical investigation may be an "applicable drug clinical trial," if it meets the other statutory criteria.

If the drug is manufactured outside of the U.S. or its territories, the trial sites are all outside of the U.S., and the trial is not being conducted under an IND, then it would not be considered to be subject to section 505 of the FDC Act [\[page 172\]](#) or section 351 of the PHS Act [\[page 368\]](#), and the clinical investigation would not be an "applicable drug clinical trial."

Section 505(i) = Section [355](#)