

Day one-presentation-session III  
Toigo, Theresa

Regulation & other governmental influences on  
clinical research

**Toigo, Theresa**

This presentation will focus on some of the provisions included in the most recent revision to the FD&C Act, i.e., the 2007 Food and Drug Administration Amendments Act (FDAAA), including Risk Evaluation and Mitigation Strategies (REMS) and Clinical Trials Registries and Results Databases (ClinicalTrials.gov); discuss the Sentinel Initiative; review some examples of existing registries for drugs and devices; and provide an overview of the Orphan Drug Act and the Orphan Products Grant program administered by FDA.



## ***Uniting Rare Diseases***

### ***Advancing Rare Disease Research: The Intersection of Patient Registries, Biospecimen Repositories and Clinical Data***

#### ***Session III***

### ***Clinical Research, Patient Care and Disease Management:***

## **Regulatory and Other Governmental Influences on Clinical Research**

**Theresa Toigo, RPh, MBA**  
Director, Office of Special Health Issues  
Food and Drug Administration





# Goals

- Topics to Address
  - ❖ Legal Framework
  - ❖ FDA Amendments Act (FDAAA) of 2007
  - ❖ Risk Evaluation and Mitigation Strategies (REMS)
  - ❖ Post-marketing requirements (PMR)
  - ❖ Research transparency (ClinicalTrials.gov)
  - ❖ Other “registry” examples
  - ❖ Orphan drug designation
- With 15 minutes to cover multiple FDA legal and regulatory topics, none of which can be covered in 15 minutes, the goal of this presentation is to raise awareness about FDA topics and show you where to find more detailed information.



# Legal Framework

- Federal Food, Drug, and Cosmetic Act (FD&C Act)
- Code of Federal Regulations (CFR)
- Guidance



# Regulatory Influences on Clinical Research

The screenshot shows the FDA website page for "Running Clinical Trials". A red arrow points from the text "The U.S. Food & Drug Administration (FDA) recently redesigned the FDA Web site." to the "Running Clinical Trials" link in the "Science and Research Special Topics" sidebar. Another red arrow points from the text "Contributes to leadership and direction through participation in FDA's Human Subject Protection/Bioresearch Monitoring Council" to the "Resources for You" section.

**Science and Research Special Topics**

- ▶ **Running Clinical Trials**
- Bioresearch Monitoring Program (BIMO)
- Regulations
- Report Problems to FDA
- Complaints relating to Clinical trials
- Guidances, Information Sheets, and Notices
- Proposed Regulations and Draft Guidances
- Compliance & Enforcement
- Educational Materials
- Replies to Inquiries to FDA on Good Clinical Practice

**Resources for You**

- Laws Enforced by FDA
- Freedom of Information
- Dockets Management
- Approvals of FDA-Regulated Products
- Websites with Information About Clinical Trials

**Running Clinical Trials**

✉ Sign up for Good Clinical Practice/Human Subject Protection e-mail updates

The U.S. Food & Drug Administration (FDA) recently redesigned the FDA Web site. As a result, the Good Clinical Practice Program was moved.

Additionally, some Web links (URLs) embedded within Guidance documents, Rules, and other documents are no longer valid. If you find a link that does not work, please try searching for the document using the document title. For more assistance, go to [Contact FDA](#)

We apologize for any inconvenience this redesign might have caused.

**Good Clinical Practice Program Mission**

The Good Clinical Practice Program is the focal point within FDA for Good Clinical Practice issues arising in human research trials regulated by FDA. In relation to Good Clinical Practice, the Good Clinical Practice Program:

- Coordinates FDA policies
- **Contributes to** leadership and direction through participation in FDA's Human Subject Protection/Bioresearch Monitoring Council
- Coordinates FDA's Bioresearch Monitoring program with respect to clinical trials, working together with FDA's Office of Regulatory Affairs (ORA)
- Contributes to international Good Clinical Practice harmonization activities

**In The News**

- Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects (PDF - 163KB)
- FDA Issues Final Rules to Help Patients Gain Access to Investigational Drugs
- FDA Enhances Speed and Transparency of Actions Taken Against Misconduct in Drug and Device Development
- FDA, European Medicines Agency Launch Good Clinical Practices Initiative
- Frequently Asked Questions - IRB Registration (PDF - 181KB)
- FDA's HSP/BIMO Initiative Accomplishments - Update
- Adverse Event Reporting to IRBs - Improving Human Subject Protection (PDF - 79KB)
- Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials - Information Sheet (PDF - 399KB)
- FDA Imposes Restrictions on Certain IRBs



# Regulatory Influences on Clinical Research

**FDA U.S. Food and Drug Administration** A-Z Index Search  go

[Home](#) | [Food](#) | [Drugs](#) | [Medical Devices](#) | [Vaccines, Blood & Biologics](#) | [Animal & Veterinary](#) | [Cosmetics](#) | [Radiation-Emitting Products](#) | [Tobacco Products](#)

**Science & Research** Share Email this Page Print this page Change Font Size

[Home](#) > [Science & Research](#) > [Science and Research Special Topics](#) > [Running Clinical Trials](#)

**Science and Research Special Topics**

- Running Clinical Trials**
- Bioresearch Monitoring Program (BIMO)
- Regulations**
- Report Problems to FDA
- Complaints relating to Clinical trials
- Guidances, Information Sheets, and Notices
- Proposed Regulations and Draft Guidances
- Compliance & Enforcement
- Educational Materials
- Replies to Inquiries to FDA on Good Clinical Practice

## Regulations

[FDA Regulations Relating to Good Clinical Practice and Clinical Trials | Preambles to GCP Regulations](#)

### FDA Regulations Relating to Good Clinical Practice and Clinical Trials

Get e-mail updates when this information changes.

- [Electronic Records; Electronic Signatures \(21 CFR Part 11\)](#)
- [Protection of Human Subjects \(Informed Consent\) \(21 CFR Part 50\)](#)
- [Financial Disclosure by Clinical Investigators \(21 CFR Part 54\)](#)
- [Institutional Review Boards \(21 CFR Part 56\)](#)
- [FDA IRB Registration Rule \(21 CFR 56.106\)](#)
- [FDA IRB Registration Rule \(21 CFR 56.106\) \(printable PDF version\)](#)
- [Investigational New Drug Application \(21 CFR Part 312\)](#)
- [Foreign Clinical Trials not conducted under an IND \(21 CFR 312.120\)](#)
- [Expanded Access to Investigational Drugs for Treatment Use \(pdf - 216KB\)](#)
- [Charging for Investigational Drugs \(pdf - 204KB\)](#)
- [Form 1571 \(Investigational New Drug Application\)](#)
- [Form 1572 \(Statement of Investigator\)](#)
- [Applications for FDA Approval to Market a New Drug \(21 CFR Part 314\)](#)
- [Bioavailability and Bioequivalence Requirements \(21 CFR Part 320\)](#)
- [Applications for FDA Approval of a Biologic License \(21 CFR Part 601\)](#)
- [Investigational Device Exemptions \(21 CFR Part 812\)](#)

# Some Recent Changes in the Regulatory & Legal Frameworks

- The most recent revision to the FD&C Act is the 2007 Food and Drug Administration Amendments Act (FDAAA) provides FDA with additional requirements, authorities, and resources with regard to both pre- and postmarket **drug safety**.
  - ❖ **Title IX** gives FDA authority to require postmarket studies and clinical trials, safety labeling changes, and Risk Evaluation and Mitigation Strategies (REMS).
  - ❖ **Title VIII** provides for an expanded **clinical trials registry and results database** and requires greater FDA involvement in ensuring that clinical trials information is provided to the National Institutes of Health (NIH) [ClinicalTrials.gov](http://ClinicalTrials.gov).



## **FDAAA Title IX- Enhanced Authorities Postmarket Safety of Drugs**

- New authorities took effect March 25, 2008.
- As of September 14, 2009 (FDA's Two Year Report to Congress)
  - ❖ FDA issued 74 letters with postmarketing requirements to assess safety issues.
  - ❖ FDA used its new authorities to require safety label changes 22 times. Most of the required safety label changes were invoked for classes of drugs or biologics.
  - ❖ FDA has approved 78 REMS, 59 REMS that include only a Medication Guide, and 19 that include elements other than a Medication Guide (e.g., a communication plan and/or elements to assure safe use)
- In May 2008, FDA launched the Sentinel Initiative, a long-term FDA effort to create a national electronic system for monitoring product safety.



# Postmarket Safety of Drugs

U.S. Department of Health & Human Services [www.hhs.gov](http://www.hhs.gov)

**FDA U.S. Food and Drug Administration** A-Z Index Search  go

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**Drugs** [Share](#) [Email this Page](#) [Print this page](#) [Change Font Size](#)

Home > Drugs > Drug Safety and Availability > Postmarket Drug Safety Information for Patients and Providers

**Drug Safety and Availability**

- ▶ **Postmarket Drug Safety Information for Patients and Providers**
- Index to Drug-Specific Information
- Approved Risk Evaluation and Mitigation Strategies (REMS)
- Postmarketing Safety Evaluation of New Molecular Entities: Final Report
- Drug Safety Information for Healthcare Professionals

## Postmarket Drug Safety Information for Patients and Providers

In accordance with Section 915 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), this website contains links to postmarket drug safety information to improve transparency and communication to patients and healthcare providers.

**Studies and Clinical Trials of Approved Products Required by FDA or Agreed to by the Application Holder**

- [Postmarket Study Requirements and Commitments](#)  
Searchable database of CDER and CBER commitments. (updated quarterly)

**Registries and Clinical Trials**

- [ClinicalTrials.gov Registry and Results Databank](#)  
ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world. These trials are designed primarily to evaluate the premarket efficacy and safety of drugs and biologics, as well as for new indications for products currently marketed.

**Memorandum of Agreement Between the Office of New Drugs and the Office of Surveillance and Epidemiology in the Center for Drug Evaluation and Research**

- [The Memorandum](#)

**Latest Safety Information**

- [Index to Drug-Specific Information](#) For patients, consumers, and healthcare professionals, provides links to safety sheets with the latest risk information about particular drugs, related press announcements, and other

**Recalls & Alerts**

- [Import Alerts](#)
- [Recalls, Market Withdrawals, & Safety Alerts](#)
- [Warning Letters](#)

**MedWatch**

- [Reporting Serious Problems to FDA](#)

<http://www.fda.gov/Drugs/Drugsafety/Postmarketdrugsafetyinformationforpatientsandproviders/default.htm>



# Postmarket Safety of Drugs

U.S. Department of Health & Human Services [www.hhs.gov](http://www.hhs.gov)

**FDA U.S. Food and Drug Administration** A-Z Index Search  go

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FDA Home

## Postmarket Requirements and Commitments

[Introduction](#) | [FAQ](#)

Postmarket requirement and commitment studies and clinical trials occur after a drug or biological product has been approved by FDA. For more information, please read: "Report to Congress: Reports on Postmarketing Studies [FDAMA 130]" and the Guidance for Industry (PDF - 456KB). A separate Web site is available for post approval studies for medical devices.

**Center:**  Both CBER and CDER  CBER  CDER

**Applicant:**

**Product:**

**NDA/ANDA/BLA Number:**

**Requirement/Commitment Status:** All Statuses Status Definitions

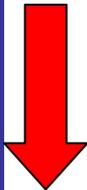
**Required Under:**

- Accelerated Approval
- Animal Efficacy Rule
- Pediatric Research Equity Act
- FDAAA Section 505(o)(3)

**NDA/ANDA/BLA Approval Date:** Date format: mm/dd/yyyy

**From:**  **To:**

[Downloadable Database File](#)



**1 of 98 Application(s)/Supplement(s)** Previous | Next

**You searched for: Both CBER and CDER; All Statuses; FDAAA Section 505(o)**

**(3)** First | Last



# Postmarket Safety of Drugs

<b>Applicant</b>	Amgen, Inc.
<b>Product</b>	Nplate, Romiplostim
<b>NDA/BLA Number</b>	125268
<b>NDA/BLA Approval Date</b>	08/22/2008
<b>Annual Report Due Date (must be submitted within 60 days of this date)</b>	08/22/2010
<b>Annual Report Received</b>	09/30/2009
<b>Requirement/Commitment Number 1</b>	
<b>Required Under</b>	FDAAA Section 505(o)(3)
<b>Description</b>	To conduct an "Antibody Registry Study" that will enroll subjects who have received romiplostim and whose blood samples contain antibodies to either romiplostim or thrombopoietin. The antibody assays will be performed by Amgen in response to spontaneously submitted requests for the post-marketing blood tests. As described in the romiplostim prescribing information, a lack or loss of response to romiplostim should prompt the healthcare provider to search for causative factors, including neutralizing antibodies to romiplostim. In these situations, healthcare providers are to submit blood samples to Amgen for detection of antibodies to romiplostim and thrombopoietin. The Antibody Registry Study will collect follow-up platelet count and other clinical data sufficient to assess the long term consequences of the detected antibodies. Patients will be followed until the detected antibodies resolve or stabilize in titer over a several month period of time. You will conduct this study according to the following timetable: Protocol Submission: November 2008; Study Start: May 2009; First interim report submission: May 2010 then annually; Final Report Submission: Within six months of FDA notification that sufficient data has been collected
<b>Current Status</b>	Ongoing
<b>Requirement/Commitment Number 2</b>	
<b>Required Under</b>	FDAAA Section 505(o)(3)
<b>Description</b>	To develop and maintain a prospective, observational pregnancy exposure registry study conducted in the United States that compares the pregnancy and fetal outcomes of women exposed to romiplostim during pregnancy to an unexposed control population. The registry will detect and

## Postmarket Requirements/Commitments



# Postmarket Safety of Drugs

U.S. Department of Health & Human Services [www.hhs.gov](http://www.hhs.gov)

**FDA U.S. Food and Drug Administration**

Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products

**Drugs**

Home > Drugs > Drug Safety and Availability > Postmarket Drug Safety Information for Patients and Providers

**Drug Safety and Availability**

**Postmarket Drug Safety Information for Patients and Providers**

[Index to Drug-Specific Information](#)

[Approved Risk Evaluation and Mitigation Strategies \(REMS\)](#)

[Postmarketing Safety Evaluation of New Molecular Entities: Final Report](#)

[Drug Safety Information for Healthcare Professionals](#)

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**Resources for You**

- [FDA Issues Draft Guidance on Risk Evaluation and Mitigation Strategies](#)
- [Format and Content of Proposed Risk Evaluation and Mitigation Strategies \(REMS\), REMS Assessments, and Proposed REMS Modifications \(PDF - 316KB\)](#)
- [Medication Guides](#)
- [Drugs@FDA](#)
- [Index to Drug-Specific Information](#)

## Approved Risk Evaluation and Mitigation Strategies (REMS)

Name	Application	Date REMS Approved	REMS Components (All REMS include timetable for assessment)
Actoplus Met (pioglitazone hydrochloride and metformin hydrochloride) Tablets (PDF - 13KB) <i>Updated!</i>	NDA 21-842/S-011, 22-024	9/14/2009; modified 10/21/2009	medication guide
Actoplus Met XR (pioglitazone and metformin) Extended-Release Tablets (PDF - 79KB)	NDA 22-024	5/12/2009	medication guide
Actos (pioglitazone hydrochloride) Tablets (PDF - 61KB)	NDA 21-073/S-037	9/9/2009	medication guide
Advair Diskus (fluticasone propionate and salmeterol xinafoate inhalation powder) (PDF - 35KB)	NDA 21-077/S-029	4/30/2008	medication guide
Advair HFA (fluticasone			

## Risk Evaluation and Mitigation Strategies (REMS)

# Postmarket Safety of Drugs

BL 125268 Nplate™ (romiplostim)  
REMS Submission August 12, 2008

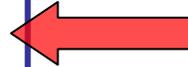
Amgen Inc.

## BLA 125268 Nplate (romiplostim)

### RISK EVALUATION AND MITIGATION STRATEGY (REMS)

#### I. GOALS

- To promote informed risk-benefit decisions before initiating treatment and while patients are on treatment to ensure appropriate use of Nplate (romiplostim)
- To establish the long-term safety and safe use of Nplate (romiplostim) through periodic monitoring of all patients who receive Nplate (romiplostim) for changes in bone marrow reticulin formation and bone marrow fibrosis, worsened thrombocytopenia after cessation of Nplate, thrombotic/thromboembolic complications, hematological malignancies and progression of malignancy in patients with a pre-existing hematological malignancy or myelodysplastic syndrome (MDS), and medication errors associated with serious outcomes.



Nplate (romiplostim) for Subcutaneous Injection (PDF - 3250KB)

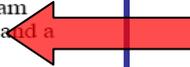
BLA 125268

8/22/2008;  
modified  
8/14/2009

medication guide,  
communication plan,  
elements to assure  
safe use,  
implementation  
system

#### 4. Each patient treated with Nplate is subject to certain monitoring.

- a. Safety Monitoring - Prescribers must complete a Nplate™ NEXUS Program Patient Baseline Data Form for each patient within 30 days of enrollment and a Nplate™ NEXUS Program Safety Questionnaire every six months during treatment with Nplate. The Nplate™ NEXUS Program Safety Questionnaire also requires the prescriber to authorize continued treatment with Nplate. The Nplate™ NEXUS Program Call Center will remind the Nplate prescriber when it is time to complete the questionnaires for each patient. All reported serious adverse events will be further investigated and followed by Amgen Global Safety. These forms and questionnaires can be completed and faxed to Nplate™ NEXUS Program at 1-877-NPLATE0 (1-877-675-2830), or completed over the telephone. Please see appended [Nplate™ NEXUS Patient Safety Registry](#).
- b. Patient Discontinuation - At the time the prescriber determines that a patient should be discontinued from Nplate, the Nplate™ NEXUS Program Discontinuation/Post-Discontinuation Follow-up Form must be completed at the time of discontinuation and 6 months later.



Please see the following appended documents:

- [Nplate™ NEXUS Program Patient Baseline Data Form](#)
- [Nplate™ NEXUS Program Safety Questionnaire](#)
- [Nplate™ NEXUS Program Discontinuation/Post-Discontinuation Follow-up Form](#)

# Sentinel Initiative

In May 2008, FDA launched the Sentinel Initiative, a long-term FDA effort to create a national electronic system for monitoring product safety.

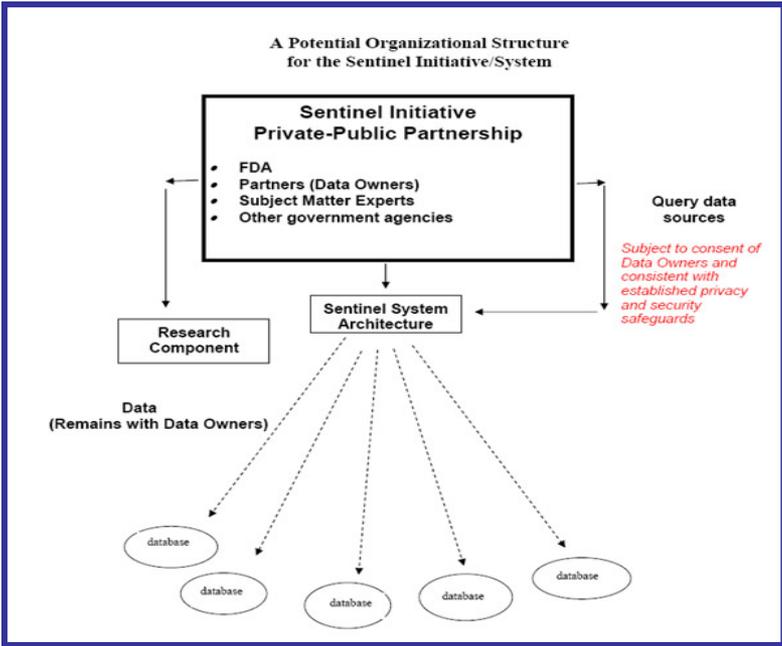
**Sentinel Initiative - Transforming How We Monitor Product Safety**

A national electronic system that will transform FDA's ability to track the safety of drugs, biologics, medical devices--and ultimately all FDA-regulated products once they reach the market--is now on the horizon. Launched in May 2008 by FDA, the Sentinel Initiative aims to develop and implement a proactive system that will complement existing systems that the Agency has in place to track reports of adverse events linked to the use of its regulated products.

Monitoring the safety of its regulated products is a major part of FDA's mission to protect public health. The Sentinel System would enable FDA to actively query diverse automated healthcare data holders—like electronic health record systems, administrative and insurance claims databases, and registries—to evaluate possible medical product safety issues quickly and securely.

Sentinel will be developed and implemented in stages. As the system is envisioned, data would continue to be managed by its owners and questions would be sent to the participating data holders. Within pre-established privacy and security safeguards, these data holders would evaluate their information and send summary results to FDA. It is also anticipated that Sentinel will facilitate the development of

The Sentinel System will enable queries of automated healthcare data systems (e.g., electronic health record systems, administrative claims databases, registries) quickly and securely for relevant product safety information.



# Other Registry Examples

The screenshot shows the NCDR website with the following content:

- Header:** NCDR® National Cardiovascular Data Registry, www.ncdr.com, Quality Improvement. Quantified.®
- Navigation:** Home, About Us, Program Requirements, Latest News, Research, How to Join, Software Vendors, ACTION Registry® - GWTG™, CARE Registry®, CathPCI Registry®, ICD Registry™, IMPACT Registry™, PINNACLE Registry™ (IC<sup>3</sup> Program®), SPECT-MPI Pilot, Participant Login
- Main Content:**
  - Introduction:** The NCDR®, an initiative of the American College of Cardiology Foundation®, began in 1997 to help health care provider groups and institutions respond to increasing requirements to document their processes and outcomes of care in the cath lab setting. Today, the NCDR is the most comprehensive, outcomes-based quality improvement program in the United States, encompassing both hospital-based registries and a practice-based program.
  - Mission:** As a trusted, patient-centered resource, the NCDR is uniquely positioned to help participating facilities and other medical professionals identify and close gaps in quality of care; reduce wasteful and inefficient care variations; and implement effective, continuous quality improvement processes.
  - News:** NCDR in the News. Register now for the 11th Annual NCDR Meeting.
  - Hospital-based cardiovascular registries:**
    - ACTION Registry®-GWTG™:** For acute coronary syndrome patients
    - CARE Registry®:** For carotid artery revascularization and endarterectomy procedures
    - CathPCI Registry®:** For diagnostic cardiac catheterizations and percutaneous coronary interventions
    - ICD Registry™:** For implantable cardioverter defibrillators
    - IMPACT Registry™:** For Improving Pediatric and Adult Congenital Treatment
  - Announcing:** PINNACLE Registry™ Practice INNOVation AND CLInical Excellence

The American College of Cardiology manages the National Cardiovascular Data Registry (NCDR). This registry collects information from institutions nationwide on factors such as patient demographics, revascularization procedures, and procedural medications. CDHR obtained registry data from April 2003-April 2004 to gather information on drug-eluting stent procedures, including the utilization of antiplatelet therapy.



# Other Registry Examples

The FDA's Office of Women's Health (OWH) maintains a [Pregnancy Registry Webpage](#) that lists all active pregnancy registries. See sample below.

**Science and Research Special Topics**

**Women's Health Research**

- What is a pregnancy exposure registry?
- How can you participate in a pregnancy exposure registry?
- What should you expect when you participate?
- Learn more about taking medicines while you are pregnant
- See list of pregnancy exposure registries

- About 50% of all U.S. pregnancies are unplanned.
- Many women enter pregnancy with medical conditions that require treatment.
- New medical problems may develop or old ones may worsen during pregnancy.
- It is common for pregnant women to take medication during pregnancy because
  - The woman is unaware of her pregnancy.
  - It may be medically necessary to continue treatment.

In response to these facts, FDA began requiring some pharmaceutical companies to sponsor pregnancy exposure registries. The results of these studies will provide their health care providers' better understanding of drug effects on pregnancy. FDA has also developed a master directory of pregnancy registries to aid pregnant women in finding registries to participate in these important studies.

**What is a pregnancy exposure registry?**

FDA defines a pregnancy exposure registry as a prospective observational study that collects information on women who take medicines and/or use devices during pregnancy.

**List of Pregnancy Exposure Registries**

This list is sorted by:

General Information about Pregnancy Registries

- Registries that study medicines for specific medical conditions
- Registries that study specific medical products
- Drugs used in a registry focused on a specific disease

The \* symbol means your doctor will enroll you in the registry.

**Specific Medical Conditions**

Medical Condition	Medical Products Studied	Registry Name	Contact Information
HIV/AIDS	HIV/AIDS Medicines	Antiretroviral Pregnancy Registry	Kendle International North America: Phone: 1-800-258-4263 (toll-free) Fax: 1-800-800-1052 Outside North America: Phone: 910-256-0238 (call collect) Fax: 910-256-0637 <a href="http://www.kendle.com/LS_Pregnancy_Registries.php">http://www.kendle.com/LS_Pregnancy_Registries.php</a>
Cancer	Cancer Medicines	Cancer and Childbirth Registry	Cooper Health Phone: 1-877-635-4499 (toll-free) Phone: 856-757-7876 Phone: 856-342-2491 <a href="http://www.cooperhealth.org/content/pregnancyandcancer.htm">www.cooperhealth.org/content/pregnancyandcancer.htm</a>
Epilepsy	Epilepsy Medicines	AED (antiepileptic drug) Pregnancy Registry	Genetics and Teratology Unit Massachusetts General Hospital Phone: 1-888-233-2334 (toll-free) Fax: 617-724-8307 <a href="http://www.massgeneral.org/aed/">www.massgeneral.org/aed/</a>
Transplant	Anti-rejection Medicines	National Transplantation Pregnancy Registry (NTPR)	National Transplantation Pregnancy Registry (NTPR) Thomas Jefferson University 1025 Walnut St. 605 College Bldg. Philadelphia, PA 19107 Phone: 215-955-4820 Fax: 215-923-1420 E-Mail: <a href="mailto:NTPR.Registry@jefferson.edu">NTPR.Registry@jefferson.edu</a>



# FDAAA Title VIII- Expanded Clinical Trial Registry and Results Data Bank

- FDAMA Section 113 (1997): Mandates a registry of trials for serious or life-threatening diseases or conditions conducted under an IND
- ClinicalTrials.gov launched in February 2000
- FDAAA 801 (2007):
  - ❖ Expands the registry to require submission of a broader scope of trials and more information for each trial.
  - ❖ Creates a results database
  - ❖ Includes devices
  - ❖ Failure to comply has consequences
  - ❖ Link from registry to specified FDA & NIH results information



# ClinicalTrials.gov Statistics

(as of 01/04/2010)

	<u>Number</u>	<u>Percent</u>
Total	83,540	100%
Type of Trial*		
Observational	13,717	16%
Interventional	69,471	83%
– Drug & Biologic	50,460	
– Surgical Procedure	8,886	
– Behavioral, Gene Transfer, Other	13,579	
– Device**	4,995	
International Sites (171 countries)		
US only	38,797	46%
Non-US only	30,161	36%
US & Non-US mixed	5,865	7%
Missing	8,717	10%

\*91 Expanded Access records; 261 missing Study Type

\*\*261 applicable device clinical trials – “delayed posting”



# ClinicalTrials.gov Statistics (cont.)

(as of 01/04/2010)

	<u>Number</u>	<u>Percent</u>
Trials by Data Provider		
US Federal (including NIH)	19,258	23%
Industry	26,257	31%
University, Other	38,025	46%
Total	83,540	

## User Statistics

Page Views per month	50 Million
Unique Visitors per day	65,000



# ClinicalTrials.gov: Registry Record

Study 1 of 1 for search of: NCT00364858

← Previous Study [Return to Search Results](#) Next Study →

**Full Text View**

[Tabular View](#)

[Study Results](#)

[Related Studies](#)

## Safety and Efficacy of Cerezyme® Infusions Every 4 Weeks Versus Every 2 Weeks in Type 1 Gaucher Disease

**This study has been completed.**

First Received: August 15, 2006 Last Updated: September 3, 2009 [History of Changes](#)

Sponsor:	Genzyme
Information provided by:	Genzyme
ClinicalTrials.gov Identifier:	NCT00364858

### ► Purpose

This is a multicenter, randomized trial to compare the safety and efficacy of two dosing frequencies of Cerezyme® in patients with Gaucher Disease, Type 1.

Approximately 90 patients will be randomized in a 2:1 (q4 : q2) ratio to one of two treatment arms at up to 26 study centers worldwide. Patients were receiving prior to study enrollment, however, they will be randomized to receive either their total 4-week dose in two infusions, one in 4 weeks. The randomization scheme will ensure a 2:1 balance between the every 4-week versus every 2-week infusion groups, respectively.

Condition	Intervention
Gaucher Disease, Type 1 Cerebrosidase Lipidosis Syndrome Glucocerebrosidase Deficiency Disease Glucosylceramide Beta-Glucosidase Deficiency Disease Gaucher Disease, Non-Neuronopathic Form	Drug:

Study Type: Interventional  
Study Design: Treatment, Randomized, Open Label, Uncontrolled, Parallel Assignment, Safety/Efficacy Study

### ► Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00364858

[+ Show 26 Study Locations](#)

#### Sponsors and Collaborators

Genzyme

#### Investigators

Study Director: Edward Kaye, M.D. Genzyme

### ► More Information

Additional Information:

[US FDA Approved Full Prescribing Information for Cerezyme®](#) PDF

No publications provided

Responsible Party: Genzyme Corporation ( Medical Monitor )  
Study ID Numbers: CZ-011-01  
Study First Received: August 15, 2006  
Results First Received: May 28, 2009  
Last Updated: September 3, 2009  
ClinicalTrials.gov Identifier: [NCT00364858](#) [History of Changes](#)  
Health Authority: United States: Food and Drug Administration

Keywords provided by Genzyme:  
Type 1 Gaucher Disease  
Glucocerebrosidase Deficiency Disease

Additional relevant MeSH terms:



# ClinicalTrials.gov: Results Record

ClinicalTrials.gov

[Home](#) [Search](#) [Study Topics](#) [Glossary](#)

A service of the U.S. National Institutes of Health

**Study 1 of 1 for search of: NCT00364858**

[← Previous Study](#)  
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 [Next Study →](#)

Full Text View

Tabular View

**Study Results**

Related Studies

**Safety and Efficacy of Cerezyme® Infusions Every 4 Weeks Versus Every 2 Weeks in Type 1 Gaucher Disease**

This study has been completed.

Study NCT00364858 Information provided by Genzyme  
 First Received: August 15, 2006 Last Updated: September 3, 2009 [History of Changes](#)

<b>Study Type:</b>	Interventional
<b>Study Design:</b>	Randomized, Open Label, Uncontrolled, Parallel Assignment
<b>Conditions:</b>	Gaucher Disease, Type 1 Cerebroside Lipidosis Syndrome Glucocerebrosidase Deficiency Disease Glucosylceramide Beta-Glucosidase Deficiency Disease Gaucher Disease, Non-Neuronopathic Form
<b>Intervention:</b>	Drug: Cerezyme

**▶ Participant Flow**

[Hide Participant Flow](#)

**Recruitment Details**

**Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations**

Eligible patients were randomized 2:1 to receive Cerezyme either once every 4 weeks (Q4) or once every 2 weeks (Q2) for 24 months. The studied period was from 14 December 2001 through 01 February 2007. There were 26 centers worldwide (18 United States, 1 Canada, 6 Europe, and 1 Brazil); 25 centers randomized patients to treatment.

**Pre-Assignment Details**

# ClinicalTrials.gov: Results Record

**Participant Flow**  
[Hide Participant Flow](#)

**Recruitment Details**  
Key information relevant to the recruitment process for the overall study, such as dates of the re  
Eligible patients were randomized 2:1 to receive Cerezyme either once every 4 weeks (Q4) or once every 2007. There were 26 centers worldwide (18 United States, 1 Canada, 6 Europe, and 1 Brazil); 25 centers

**Pre-Assignment Details**  
Significant events and approaches for the overall study following participant enrollment, but pr

	Q2 Cerezyme	Q4 Cerezyme
STARTED	33	62
COMPLETED	26	40
NOT COMPLETED	7	22
Adverse Event	1	5
Withdrawal by Subject	1	1
Pregnancy	1	1
Clinical failure	2	13
Discontinuation at baseline	1	0
Non-compliant	1	0
Return to Q2 regimen	0	1
Clinical baseline issue	0	1

**Baseline Characteristics**  
[Hide Baseline Characteristics](#)

**Reporting Groups**

	Description
Q2 Cerezyme	Patients receiving Cerezyme one infusion every 2 weeks (Q2).
Q4 Cerezyme	Patients receiving Cerezyme one infusion every 4 weeks(Q4).

**Baseline Measures**

	Q2 Cerezyme	Q4 Cerezyme	Total
<b>Number of Participants</b> [units: participants]	33	62	95
<b>Age</b> [units: years] Mean ± Standard Deviation	44.8 ± 17.40	47.8 ± 14.47	46.8 ± 15.53
<b>Gender</b> [units: participants]			
Female	13	34	47
Male	20	28	48

**Outcome Measures**  
[Hide All Outcome Measures](#)

1. **Primary: Number of Participants With Clinical Success at Month 24/Discontinuation** [ Time Frame: Month 24 (or at time of discontinuation)]

Measure Type	Primary
Measure Title	Number of Participants With Clinical Success at Month 24/Discontinuation
Measure Description	Patients are considered to be a clinical success if ALL of the following are met: The patient's hemoglobin does not fall more than 1.25g/dL for w... below the patient's baseline value, platelet count does not fall more than 25% below the patient's baseline value or does not fall below 80,000 mm... volumes are not greater than 20% above the patient's baseline value, no evidence of bone disease progression, including no incidence of patholog... infarctions, lytic lesions or avascular necrosis and has had no bone crises during the study.
Time Frame	Month 24 (or at time of discontinuation)
Safety Issue	No

**Serious Adverse Events**  
[Show Serious Adverse Events](#)

**Other Adverse Events**  
[Show Other Adverse Events](#)



# FDA Office of Orphan Products Development

- FDA's Office of Orphan Products Development administers the major provisions of the Orphan Drug Act (ODA) which provide incentives for sponsors to develop products for rare diseases.
- A rare disease or condition is any disease or condition which
  - a) affects less than 200,000 persons in the U.S. or
  - b) affects more than 200,00 persons in the U.S. but for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such a disease or condition will be recovered from sales in the U.S. of such drug.
- The ODA has been very successful - more than 200 drugs and biological products for rare diseases have been brought to market since 1983.



# Developing Products for Rare Diseases

U.S. Department of Health & Human Services | www.hhs.gov

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**For Industry** | Share | Email this Page | Print this page | Change Font Size

Home > For Industry > Developing Products for Rare Diseases & Conditions

**Developing Products for Rare Diseases & Conditions**

- Designating an Orphan Product Drugs and Biologics
- Orphan Grants Program
- Designating Humanitarian Use Devices (HUDS)
- Frequently Asked Questions
- Incentives
- Other Sources of Rare Disease/Orphan Products Information
- Overview

**Resources for You**

- Join or Leave OrphanProdInfo ListServ
- Orphan Drug Act

## Developing Products for Rare Diseases & Conditions

The Food and Drug Administration has charged The Office of Orphan Products Development (OOPD) to dedicate its mission to promoting the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. In fulfilling that task, OOPD interacts with the medical and research communities, professional organizations, academia, governmental agencies, and the pharmaceutical industry, as well as rare disease groups.

The OOPD administers the major provisions of the **Orphan Drug Act (ODA)** which provide incentives for sponsors to develop products for rare diseases. The ODA has been very successful - more than 200 drugs and biological products for rare diseases have been brought to market since 1983. In contrast, the decade prior to 1983 saw fewer than ten such products come to market.

In addition, the OOPD administers the Orphan Products Grants Program which provides funding for clinical research in rare diseases. The Office Of Orphan Products Development will also administer a new grant program, the Pediatric Device Consortia (PDC) Grant Program. The PDC Grant Program solicits grant applications from institution/organizations that propose to develop nonprofit consortia to facilitate pediatric medical device development. FDA will provide grants to consortia whose business model and approach to device development will either result in, or substantially contribute

**Spotlight**

- OPD Research Grants Program
- Designating an Orphan Product: Drugs and Biologics
- Designating Humanitarian Use Devices (HUDS)
- Orphan Drug Designation Workshop (PDF - 91KB)

**Related Links**

- Pediatrics
- About the Center for Devices and Radiological Health
- About the Center for Evaluation and Research
- About the Center for Biologics Evaluation and Research

**Contact Us**

Office of Orphan Product Development  
(301) 827-3600  
1-800-368-7088

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**Developing Products for Rare Diseases & Conditions**

- Designating an Orphan Product: Drugs and Biologics
- How to Apply for Designation as an Orphan Product
- 21 CFR PART 316: Final Rule
- Common EMEA/FDA Application for Orphan Medicinal Product Designation
- Pediatric Drug Development and The Orphan Drug Act Incentives
- Definition of Disease Prevalence
- Tips for Applying for Orphan Product Designation

## Designating an Orphan Product: Drugs and Biologics

The Orphan Drug Act (ODA) provides for granting special status to a product to treat a rare disease or condition upon request of a sponsor. The combination of the product to treat the rare disease or condition must meet certain criteria. This status is referred to as orphan designation. Orphan designation qualifies the sponsor of the product for the tax credit and marketing incentives of the ODA. A marketing application for a prescription drug product that has been designated as a drug for a rare disease or condition is not subject to a prescription drug user fee unless the application includes an indication for other than a rare disease or condition.

In order for a sponsor to obtain orphan designation for a drug or biological product, an application must be submitted to OOPD, and the designation approved. The approval of an application for orphan designation is based upon the information submitted by the sponsor. A drug that has obtained orphan designation is said to have "orphan status." Each designation request must stand on its own merit. Sponsors requesting designation of the same drug for the same indication as a previously designated product must submit their own data in support of their designation request. The approval of an orphan designation request does not alter the standard regulatory requirements and process for obtaining marketing approval. Safety and efficacy of a compound must be established through adequate and well-controlled studies.

**Searchable Databases**

Searchable database for Orphan Designated and or Approved Products. Note list will be updated monthly.

- <http://www.accessdata.fda.gov/scripts/opdlisting/opd>

<http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/>



# Orphan Drug Designations

U.S. Department of Health & Human Services | www.hhs.gov

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FDA Home

### FDA Application

#### Search Orphan Drug Designations and Approvals

This page searches the Orphan Drug Product designation database. Searches can be limited to specific dates, products, and indications. Results can be output as a condensed list, detailed list, or an Excel spreadsheet. More detailed instructions are described below. It is highly recommended that large searches be retrieved as an Excel file (selected under Output format) since only a maximum of 75 records can be displayed at one time. The database currently contains more than 1800 records.

**Search Criteria**

Product Name:  (single search term without quote marks)

Orphan Designation:  or wildcard characters; [Instructions](#))

Start Date:  End Date:  (default is all dates; [detailed](#))

Search results:  ([detailed help](#))

Output format:  ([detailed help](#))

Sort results:

Records per page:

**Instructions:**

During searches individual fields are 'anded' together, e.g., searching 'interferon' as a product and as a product name would return 'penicillin', 'aminopenicillin', 'penicillinase', etc. Both generic names available) are searched. Searching designations is similar; searching 'malaria' would return 'Treat

**Product Name or Designation**

Entering a search term will find any occurrence of the term in the product name or designation. as a product name would return 'penicillin', 'aminopenicillin', 'penicillinase', etc. Both generic names available) are searched. Searching designations is similar; searching 'malaria' would return 'Treat

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### FDA Application

#### Results for Orphan Drug Product Designations Search

Total Results: 2113 (85 pages) Go to page:

[Return to Orphan Designation Search Page](#)

Row Num	Generic Name	Designation Date	Indication
1	Ascorbic Acid	05-11-2009	Treatment of Charcot-Marie-Tooth disease type 1A.
2	(+/-)-7-[3-(4-Acetyl-3-Methoxy-2-Propylphenoxy)Propoxy]-3,4-Dihydro-8-Propyl-2h-1-Benzopyran-2-Carboxylic Acid	03-31-2003	Prevention of serious adverse events associated with vascular leak syndrome caused by Interleukin-2 therapy
3	(+/-)-Cis-3-(4-Hydroxyphenyl)-4-(4-Methoxyphenyl)-3,4-Dihydro-2h-Cromen-7-Ol	01-10-2008	Treatment of pancreatic cancer
4	(+/-)-Cis-3-(4-Hydroxyphenyl)-4-(4-Methoxyphenyl)-3,4-Dihydro-2h-Cromen-7-Ol	01-10-2008	Treatment of cholangiocarcinoma
5	(+/-)-Cis-3-(4-Hydroxyphenyl)-4-(4-Methoxyphenyl)-3,4-Dihydro-2h-Cromen-7-Ol	02-01-2008	Treatment of Stage IIB through Stage IV malignant melanoma
6	(1r,2r)-Octanoic Acid [2-(2',3'-Dihydrobenzo[1,4]Dioxin-6'-Yl)-2-Hydroxy-L-Pyrrolidin-1-Ylmethyl-Ethyl]-Amide-L-Tartaric Acid Salt	09-17-2008	Treatment of Gaucher disease
7	(1r,2s) 6-Bromo-Alpha-[2-(Dimethylamino)Ethyl]-2-Methoxy-Alpha-(1-Naphthyl)-Beta-Phenyl-3-Quinoloneethanol	01-10-2005	Treatment of pulmonary tuberculosis (active disease)
8	(1s)-1-(9-Deazahypoxanthin-9-Yl)-1,4-Dideoxy-1,4-Imino-D-Ribitol-Hydrochloride	08-13-2004	Treatment of acute lymphoblastic leukemia
9	(1s)-1-(9-Deazahypoxanthin-9-Yl)-1,4-Dideoxy-1,4-Imino-D-Ribitol-Hydrochloride		Treatment of T-cell prolymphocytic leukemia



News & Events

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FDA NOTE TO CORRESPONDENTS

For Immediate Release: Dec. 23, 2009

Media Inquiries: Sandy Walsh, 301-796-4669, sandy.walsh@fda.hhs.gov

Consumer Inquiries: 888-INFO-FDA

**FDA: Orphan Drug Workshops Scheduled For Feb. 25-26 and Aug. 3-4, 2010  
Agency Experts to Provide Guidance on Applying for Orphan Drug Designation**

As part of its continuing effort to make the agency more transparent and accessible, the FDA has scheduled a series of workshops about orphan drug designation for academics, biotechnology companies, and those unfamiliar with the process. The FDA can grant a special status, known as orphan designation, for drug products intended to treat rare diseases.

Orphan drugs are either drug or biologic products used to treat conditions affecting fewer than 200,000 people in the United States. Orphan drugs may be already-approved or experimental drugs.

The workshops will be held Feb. 25-26, 2010, in Claremont, Calif., and Aug. 3-4, 2010, in Minneapolis. At the workshops, participants will propose a specific drug for a specific rare disease and work on an orphan designation application to submit to the FDA at the conclusion of the workshop. To help participants develop strong applications, FDA staff will provide one-on-one regulatory help.

To obtain orphan drug designation, drugs must be for the treatment, prevention or diagnosis of a rare disease or condition. Orphan drug designation requires there be a medical rationale for expecting the proposed drug to be effective in the condition.

Orphan designation qualifies the applicant to receive certain benefits, such as tax credits and priority review, in exchange for developing the drug. After designation, the drug must then be submitted for marketing approval, which evaluates the drug for safety and efficacy.

TO LEARN  
MORE ABOUT  
APPLYING  
FOR ORPHAN  
DRUG  
DESIGNATION

U.S. Food and Drug Administration

<p><b>“DO A DESIGNATION” FDA Orphan Drug Workshops</b></p> <p>FDA announces the launch of its orphan drug workshop series, an opportunity for academics, biotechnology companies and larger pharmaceutical firms to spend two days in creation of applications for orphan status designation. Participants will be expected to bring specific products for at least one candidate orphan drug that holds promise for the treatment of a rare disease. Over two days, FDA staff from the Office of Orphan Products Development (OOPD) will provide regulatory assistance to sponsors to find regulatory paths forward. There will be an introductory lecture, but most of the time will be</p>	<p>status designation, and so should come prepared to work on a particular promising therapy, not just therapies in general. Participants need not be the holders of intellectual property rights of the compounds for which they seek orphan designation, but need only to be a “party of interest” and will be considered to be “sponsors” of designations that may be ultimately granted (though naturally, post-designation product development is dependent upon product access and testing). Sponsors should note that participation in this workshop confers neither expedited processing nor preferential consideration of their applications, however a good-faith effort will be made by FDA staff to</p>	<p>products for people with rare diseases who need them.</p> <p><b>Are you ready for orphan status designation?</b></p> <p>The chief task of the orphan status designation application is to convince FDA/OOPD of two things: that the proposed drug is for a rare disease (i.e. that fewer than 200,000 persons in the US have the rare disease or condition) and that there is a medical rationale for believing that proposed drug has “promise” for treating the rare disease/condition (i.e. clinical data, animal model data OR rarely in vitro data, but not exclusively theoretical considerations). This major content of</p>
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# Summary

- FDA's regulatory activities are governed by a number of Federal laws and regulations.
- The 2007 Food and Drug Administration Amendments Act (FDAAA) provides FDA with additional requirements, authorities, and resources with regard to both pre- and postmarket drug safety.
- FDA's Office of Orphan Products Development (OOPD) is dedicated to promoting the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions.



# Thank You

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