# Ability to "Check the Denominator"

- Issue: Identify relevant ongoing and completed trials, published and unpublished
- Approach: Search the ClinicalTrials.gov registry for all studies conducted about Intervention X for Condition Y in Population Z
- Limitations:
  - Ambiguous intervention names
  - "World Chaos" in Registration

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**Weight-Loss Efficacy of Lorcaserin (Belviq) and Phentermine plus Extended-Topiramate (Qsymia) at 1 Year.***

| Drug, Study, and Treatment | Mean Percentage Change in Body Weight (Mean Efficacy Criterion) | Proportion of Pa ≥5% of Bod (Categorical Effic |
|---|---|---|
| Belviq† | | |
| Studies 1 and 2 combined | | |
| 10 mg BID | −5.8 | 47 |
| Placebo | −2.5 | 23 |
| Study 3 | | |
| 10 mg BID | −4.5 | 38 |
| Placebo | −1.5 | 16 |
| Qsymia‡ | | |
| Study 1 | | |
| 15 mg/92 mg | −10.9 | 67 |
| Placebo | −1.6 | 17 |
| Study 2 | | |
| 7.5 mg/46 mg | −7.8 | 62 |
| 15 mg/92 mg | −9.8 | 70 |
| Placebo | −1.2 | 21 |

## Unambiguous Identification of Obesity Trials

TO THE EDITOR: Colman et al. (Oct. 25 issue)[1] describe trial results underlying approval of two weight-management drugs by the Food and Drug Administration. However, their table included noninformative terms (e.g., "study 1") without citing publications or ClinicalTrials.gov records. The materials that were referenced[2,3] used only acronyms (e.g., BLOOM) and internal identifiers (e.g., OB-301) — neither of which could be linked to the terms in the table. Using ClinicalTrials.gov (www.clinicaltrials.gov), we identified six studies of lorcaserin for obesity[4] and nine studies of phentermine and topiramate for obesity[5] (as of October 15, 2012). Only Colman et al. could confirm the likely matches (Table 1).

This is an important example of why listing ClinicalTrials.gov identifiers (NCT numbers) would provide unambiguous access to trial-design infor-

**Table 1. Different Identifiers for the Same Clinical Studies.***

| Drug, Identifier Used by Colman et al., and Identifier Used in References Cited by Colman et al. | Probable ClinicalTrials.gov Identifier | Publication (PubMed Identifier) Associated with Probable ClinicalTrials.gov Identifier |
|---|---|---|
| Belviq | | |
| Studies 1 and 2 combined | | |
| BLOOM | NCT00395135 | Smith et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. N Engl J Med 2010; 363:245-56 (20647200) |
| BLOSSOM | NCT00603902 | Fidler et al. A one-year randomized trial of lorcaserin for weight loss in obese and overweight adults: the BLOSSOM trial. J Clin Endocrinol Metab 2011; 96:3067-77 (21795446) |
| Study 3 | | |
| BLOOM-DM | NCT00603291 | O'Neil et al. Randomized placebo-controlled clinical trial of lorcaserin for weight loss in type 2 diabetes mellitus: the BLOOM-DM study. Obesity (Silver Spring) 2012;20:1426-36 (22421927) |
| Qsymia | | |
| Study 1 | | |
| OB-302 | NCT00554216 | NA |
| Study 2 | | |
| OB-303 | NCT00553787 | Gadde et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomized, placebo-controlled, phase 3 trial. Lancet 2011;377:1341-52 (21481449) |

* BLOOM denotes Behavioral Modification and Lorcaserin for Overweight and Obesity Management, BLOOM-DM Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus, BLOSSOM Behavioral Modification and Lorcaserin Second Study for Obesity Management, and NA not applicable.

N ENGL J MED 368;6 NEJM.ORG FEBRUARY 7, 2013

**Source**: Zarin DA, Tse T. N *Engl J Med*. 2013; 368:580-1

# Editor's Note

"Zarin and Tse are correct. It is our policy to refer to clinical trials by their registration number or to reference a publication in which they can be unequivocally identified, and we should have done so for the ones they mentioned in their letter."

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# Does the Search Engine Enable You to Find the Trials You Want?

- Spelling correction and relaxation of search terms
- Use of synonymy
- Fielded search
- Use of hierarchy from MeSH
- Relevancy ranking

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# Naming Drugs

- After Approval
  - Generic name (USAN, USP), links to chemical structure
- Before Approval
  - Chemical structure (name, drawing)
  - Company serial number
    - No public record or oversight
    - No guaranteed one-to-one correspondence

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# Names/Identifiers Are Critical

- Search engines depend on known names, lists of synonyms, and hierarchies: e.g., Paxil
  - Aropax - Ldmp
  - Asimia - Paroxetine
  - brl-29060 - Pexeva
  - fg-7051 - Seroxat
- "Code" names, without "de-coders," lead to "hidden" trials
- Non-specific names may also prevent the search engine from retrieving a useful list of trials
- Biologic, device, and other irregular intervention names challenge the system:
  - Vaccine: ALVAC-HIV MN120TMG (vCP205)
  - Device: IT LEISH (rK39); Device: galyfilcon AP 8.3 BC; Device: BD/33G

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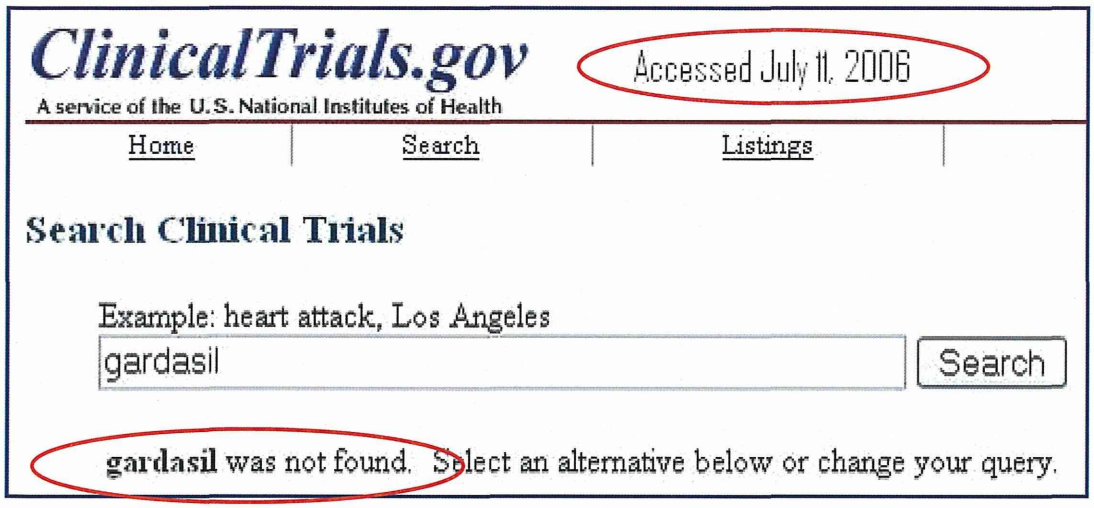
# Drug Serial #s = "Hidden" Trials

## ClinicalTrials.gov Gardasil® Search

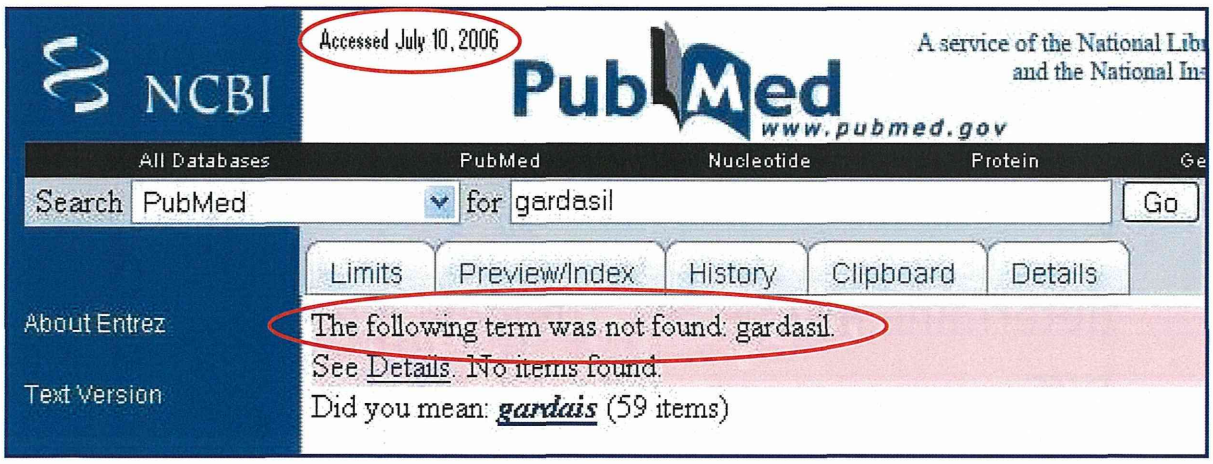
**Gardasil® was approved on June 8, 2006**




75

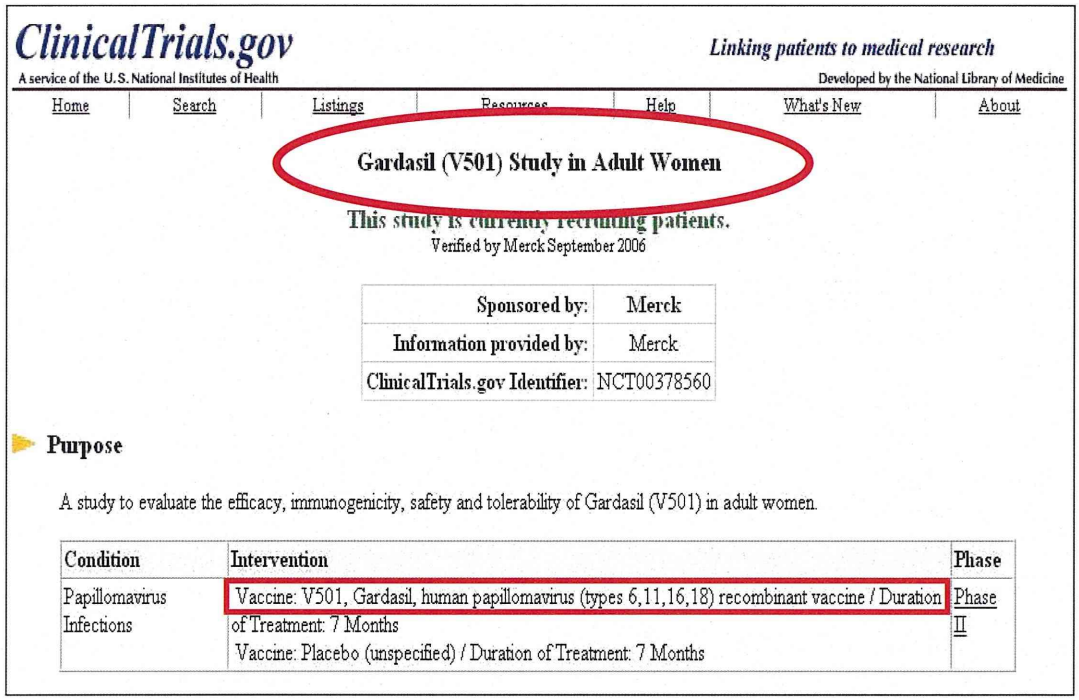
# PubMed Gardasil® Search

**One month after approval (and promotion)**




76

# Study NCT00378560



ClinicalTrials.gov

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

*Linking patients to medical research*

Developed by the National Library of Medicine

Home | Search | Listings | Resources | Help | What's New | About

**Gardasil (V501) Study in Adult Women**

This study is currently recruiting patients.

Verified by Merck September 2006

| | |
|---|---|
| Sponsored by: | Merck |
| Information provided by: | Merck |
| ClinicalTrials.gov Identifier: | NCT00378560 |

**Purpose**

A study to evaluate the efficacy, immunogenicity, safety and tolerability of Gardasil (V501) in adult women.

| Condition | Intervention | Phase |
|---|---|---|
| Papillomavirus Infections | Vaccine: V501, Gardasil, human papillomavirus (types 6,11,16,18) recombinant vaccine / Duration of Treatment: 7 Months<br>Vaccine: Placebo (unspecified) / Duration of Treatment: 7 Months | Phase II |

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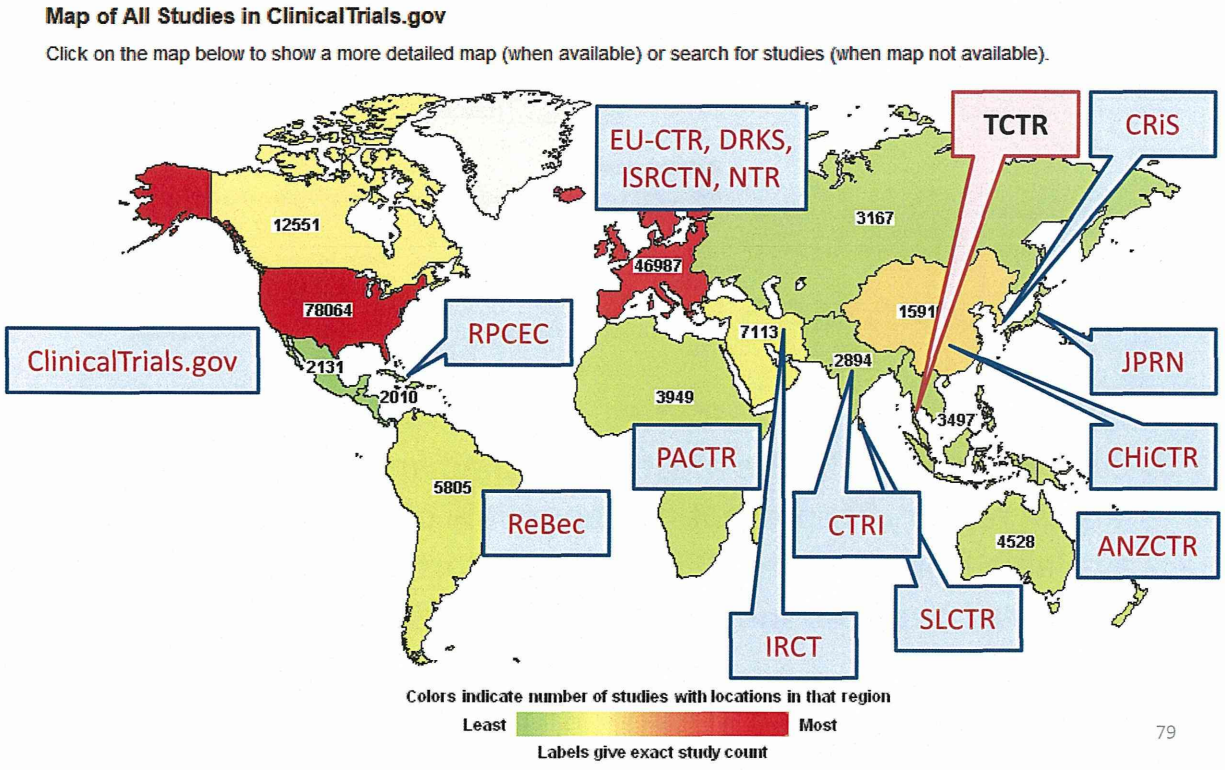
# The Problem of Undetected Duplicate Trial Records

- Duplicates occur when multiple parties register the same trial
  - 47% of trials are multi-site
  - 10% have > 25 locations
- Distort search results, making it impossible to determine #s of trials, subjects, etc.
- Difficult to detect
  - False positives and false negatives

78

# International Landscape

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# ClinicalTrials.gov Records in Regions with WHO Primary Registries (as of 11/17/14)

| WHO Primary Registry | Number of Records | |
|---|---|---|
| | WHO Primary Registry: Total # Studies | ClinicalTrials.gov: Total # Studies in Region |
| EU | 24,296 | 49,650 |
| Australia/New Zealand (ANZCTR) | 14,536 | 4,699 |
| ISRCTN (*Many in UK*) | 12,965 | 9,784 (UK) |
| Iran | 6,972 | 663 |
| China | 5,198 | 5,520 |
| Netherlands | 4,660 | 5,750 |
| India | 5,190 | 2,542 |
| Germany | 2,958 | 12,250 |
| Brazil | 2,517 | 4,153 |
| Korea | 1,267 | 5,805 |
| Africa | 380 | 4,176 |
| Thailand | 261 | 1,609 |
| Cuba | 191 | 39 |
| Sri Lanka | 145 | 38 |
| Japan (UMIN) | 17,310 *records* | 3,412 |

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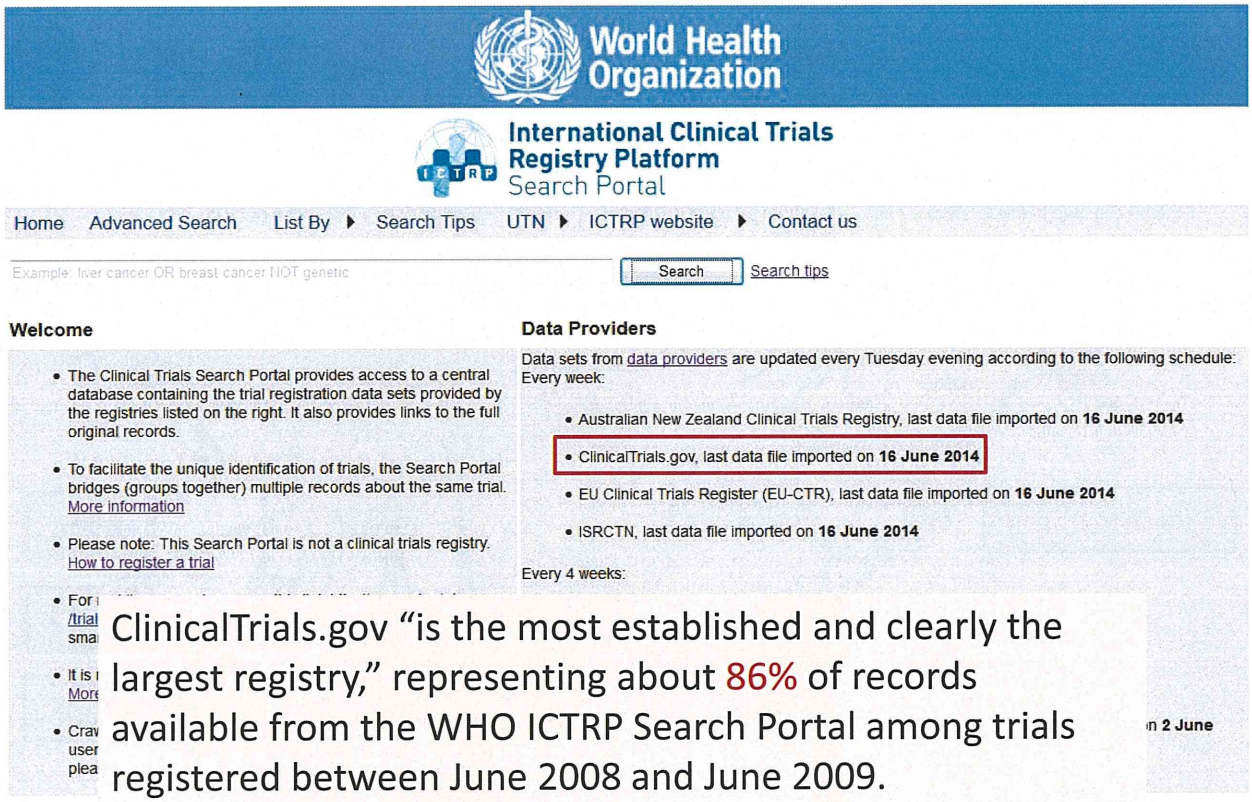



ClinicalTrials.gov "is the most established and clearly the largest registry," representing about 86% of records available from the WHO ICTRP Search Portal among trials registered between June 2008 and June 2009.

Source: Viergever RF, Ghersi D (2011) *PLoS ONE*.

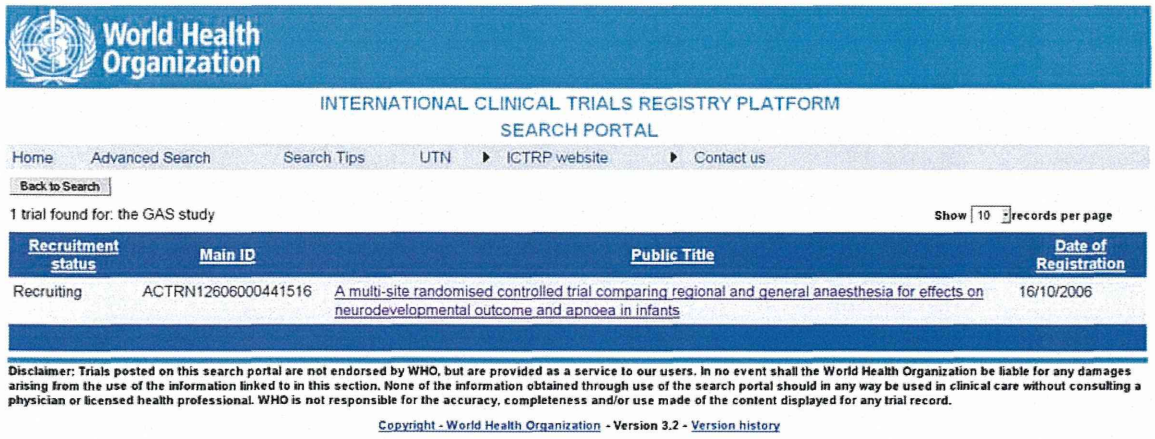
81

# Case Study – the GAS Study

- Registered in (at least) three registries
  - ISRCTN, ClinicalTrials.gov, ANZCTR
- Three different PIs (US, UK, Aus); three different "sponsors."
- ANZCTR and ClinicalTrials.gov records have same title; ISRCTN lists ANZCTR as secondary ID
- WHO portal lists two records, but does not recognize them as duplicates; does not have the ISRCTN record

82

# On WHO Portal Site: Basic Search for "The GAS Study"



World Health Organization

INTERNATIONAL CLINICAL TRIALS REGISTRY PLATFORM
SEARCH PORTAL

Home | Advanced Search | Search Tips | UTN | ICTRP website | Contact us

Back to Search

1 trial found for: the GAS study

Show 10 records per page

| Recruitment status | Main ID | Public Title | Date of Registration |
|---|---|---|---|
| Recruiting | ACTRN12606000441516 | A multi-site randomised controlled trial comparing regional and general anaesthesia for effects on neurodevelopmental outcome and apnoea in infants | 16/10/2006 |

Disclaimer: Trials posted on this search portal are not endorsed by WHO, but are provided as a service to our users. In no event shall the World Health Organization be liable for any damages arising from the use of the information linked to in this section. None of the information obtained through use of the search portal should in any way be used in clinical care without consulting a physician or licensed health professional. WHO is not responsible for the accuracy, completeness and/or use made of the content displayed for any trial record.

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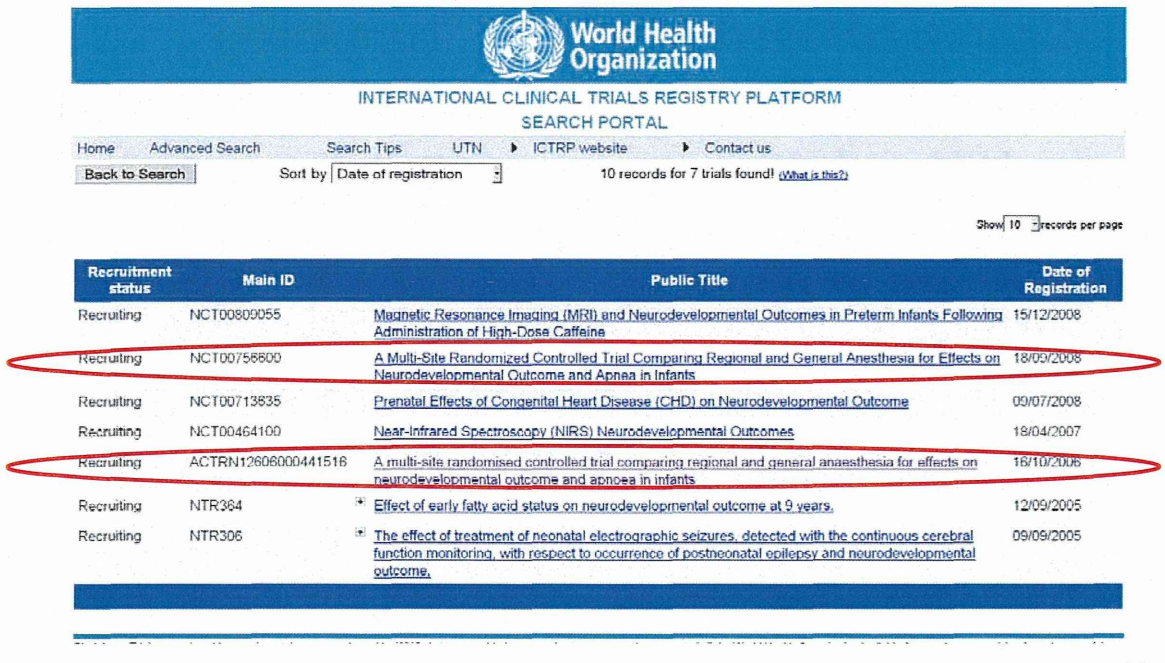
# On WHO Portal Site: Title Field Search for "Neurodevelopmental Outcome"



World Health Organization

INTERNATIONAL CLINICAL TRIALS REGISTRY PLATFORM
SEARCH PORTAL

Home | Advanced Search | Search Tips | UTN | ICTRP website | Contact us

Back to Search | Sort by Date of registration | 10 records for 7 trials found! (What is this?)

Show 10 records per page

| Recruitment status | Main ID | Public Title | Date of Registration |
|---|---|---|---|
| Recruiting | NCT00809055 | Magnetic Resonance Imaging (MRI) and Neurodevelopmental Outcomes in Preterm Infants Following Administration of High-Dose Caffeine | 15/12/2008 |
| Recruiting | NCT00756600 | A Multi-Site Randomized Controlled Trial Comparing Regional and General Anesthesia for Effects on Neurodevelopmental Outcome and Apnea in Infants | 18/09/2008 |
| Recruiting | NCT00713635 | Prenatal Effects of Congenital Heart Disease (CHD) on Neurodevelopmental Outcome | 09/07/2008 |
| Recruiting | NCT00464100 | Near-Infrared Spectroscopy (NIRS) Neurodevelopmental Outcomes | 18/04/2007 |
| Recruiting | ACTRN12606000441516 | A multi-site randomised controlled trial comparing regional and general anaesthesia for effects on neurodevelopmental outcome and apnoea in infants | 16/10/2006 |
| Recruiting | NTR364 | Effect of early fatty acid status on neurodevelopmental outcome at 9 years. | 12/09/2005 |
| Recruiting | NTR306 | The effect of treatment of neonatal electrographic seizures, detected with the continuous cerebral function monitoring, with respect to occurrence of postneonatal epilepsy and neurodevelopmental outcome. | 09/09/2005 |

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## Protocol Registration Status

TransparentCT®
THE INTERNATIONAL CLINICAL TRIAL DISCLOSURE KNOWLEDGE BASE

| Mandatory for Registrant to Post (in effect) | Non-voluntary Post by EC or Government (in effect) | Mandatory for Registrant to Post (pending) | Non-voluntary Post by EC or Government (pending) | Legislation / Regulations (ongoing activity) | Voluntary Registry (in effect) |
|---|---|---|---|---|---|
| Argentina[ReNIS] | Argentina[EFC] | Kenya | Croatia | Canada | Africa |
| Austria NIS[1] | Chile | Mexico | Italy[Integrated Platform] | China | Australia/New Zland |
| Brazil[2] | Colombia[6] | Switzerland[8] | Spain[9] | Poland | China[CFDA] |
| Euro. Union[EU PAS] | Czech Republic | | Zimbabwe | | China[ChiCTR] |
| India | Euro. Union[EU CTR] | | | | Cuba |
| Israel[3] | France | | | | Euro. Union[ENCePP] |
| Malaysia | Germany[PharmNet.Bund] | | | | Germany[DRKS] |
| New Zealand[4] | Korea[MFDS] | | | | Hong Kong |
| Philippines[5] | Netherlands[CCMO] | | | | Iran |
| South Africa | Norway | | | | Japan |
| Taiwan | Peru | | | | Korea[CRiS] |
| United States | Russia | | | | Netherlands[NTR] |
| | Serbia | | | | Poland[INFARMA] |
| | Singapore | | | | Sri Lanka |
| | Slovakia[7] | | | | Taiwan PMS[10] |
| | Venezuela | | | | Tanzania[11] |
| | | | | | Thailand |
| | | | | | United Kingdom[12] |

- This table is not intended to be exhaustive
- It is not guaranteed to be accurate
- Red indicates changes since April 2012
- Last updated April 2013

[1] Non-interventional studies
[2] Register Phase 1 - 4 trials in ReBEC
[3] Register in ClinicalTrials.gov
[4] Required for ethics approval (WHO/CTgov)
[5] Register Phase 1 - 4 trials in PHRR
[6] Posts PDF lists of trials
[7] Replaced database with PDF file
[8] In any WHO/ICMJE registry plus national database
[9] NCA loads XML; sponsor adds summary
[10] Post-marketing studies
[11] In public user test phase (since Jul 2011)
[12] NRES, ISRCTN, and PROSPERO





## Policies that Help Avoid World Chaos

- **Ministry of Health, Israel**: "...controlled prospective clinical trials must be registered at the NIH website, http://www.clinicaltrials.gov."
- **Health Canada:** "...registration of clinical trials ... within 21 days of the trial's onset ... in ClinicalTrials.gov or ISRCTN [UK registry]"

# Country-Specific Trial Portal

- New Zealand Clinical Trials Portal (http://clinicaltrials.health.nz/)
- Leverages two existing trial registries
  - ClinicalTrials.gov (at least one site in New Zealand)
  - Australian New Zealand Clinical Trials Registry (ANZCTR)
  - Not a trial registry



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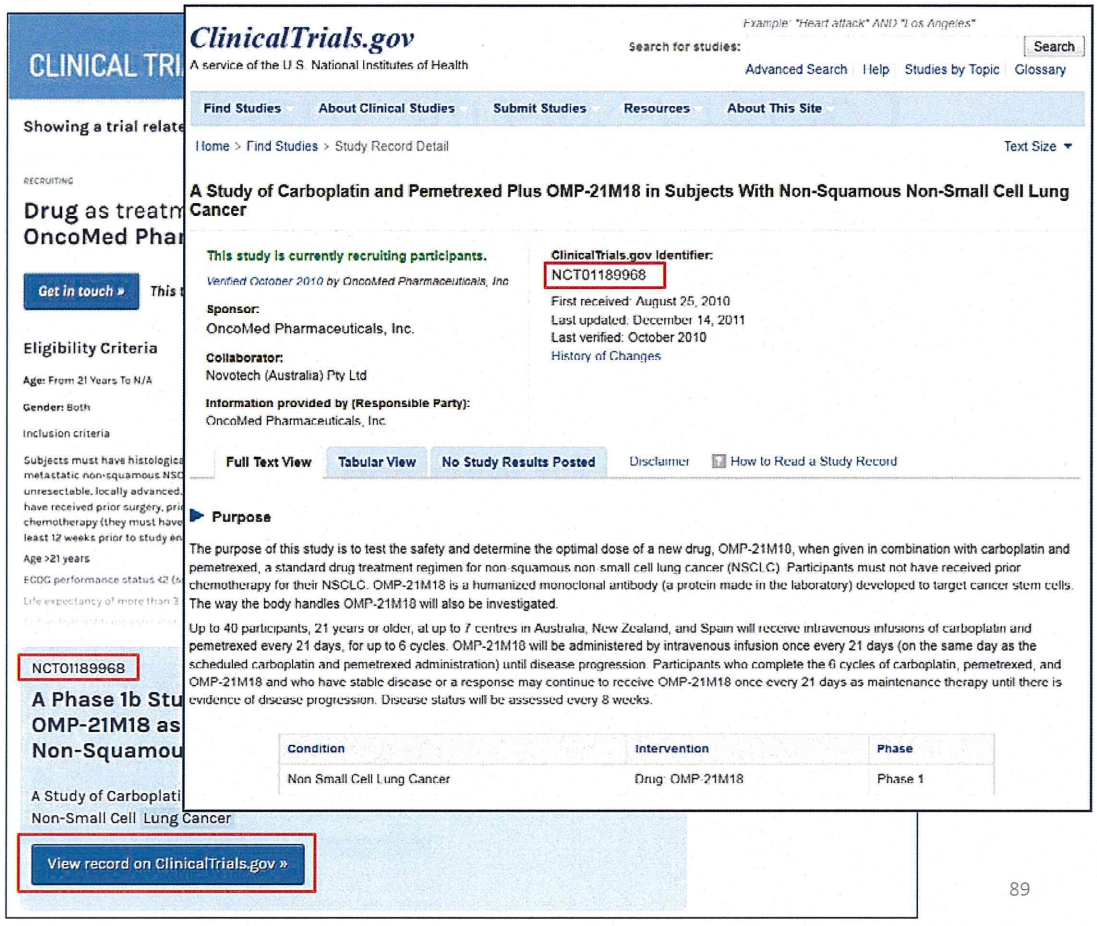


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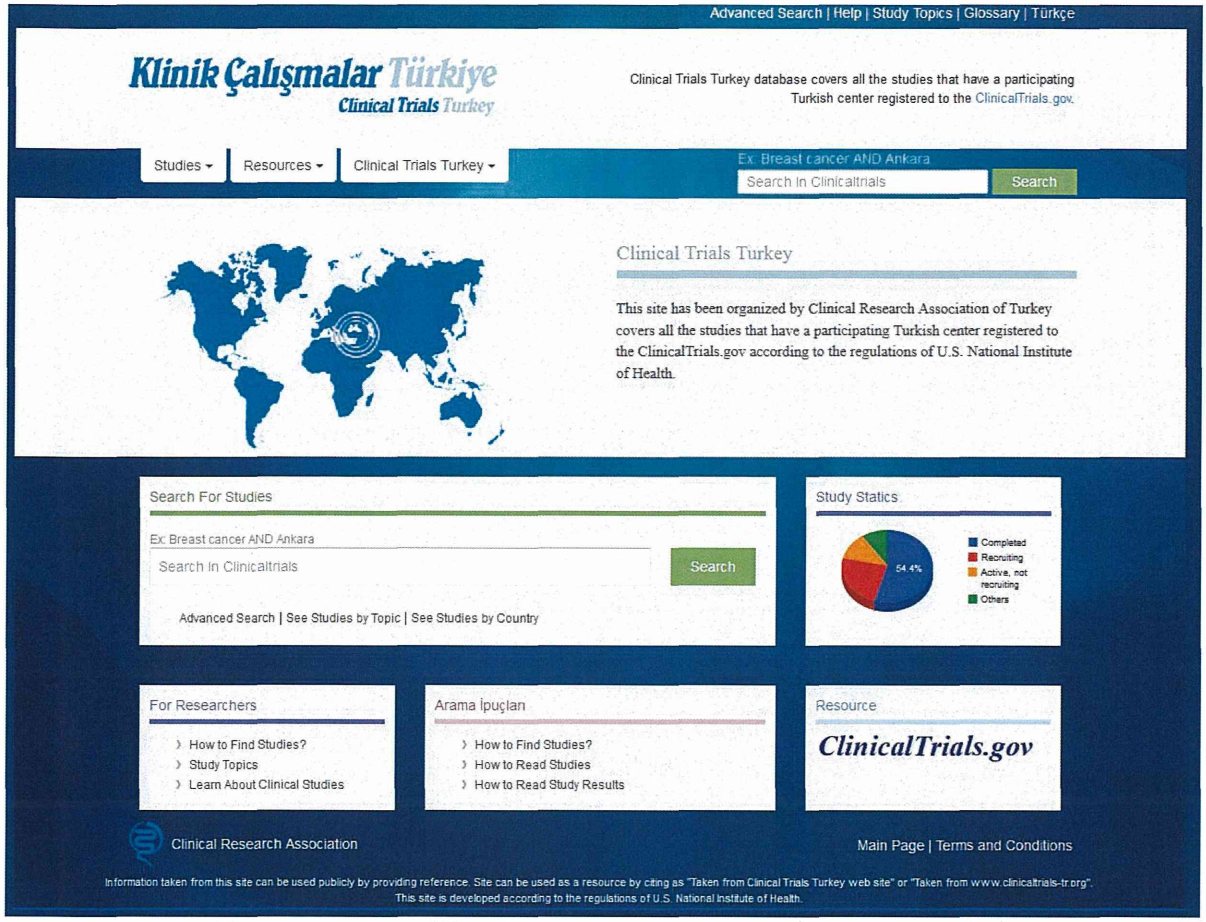
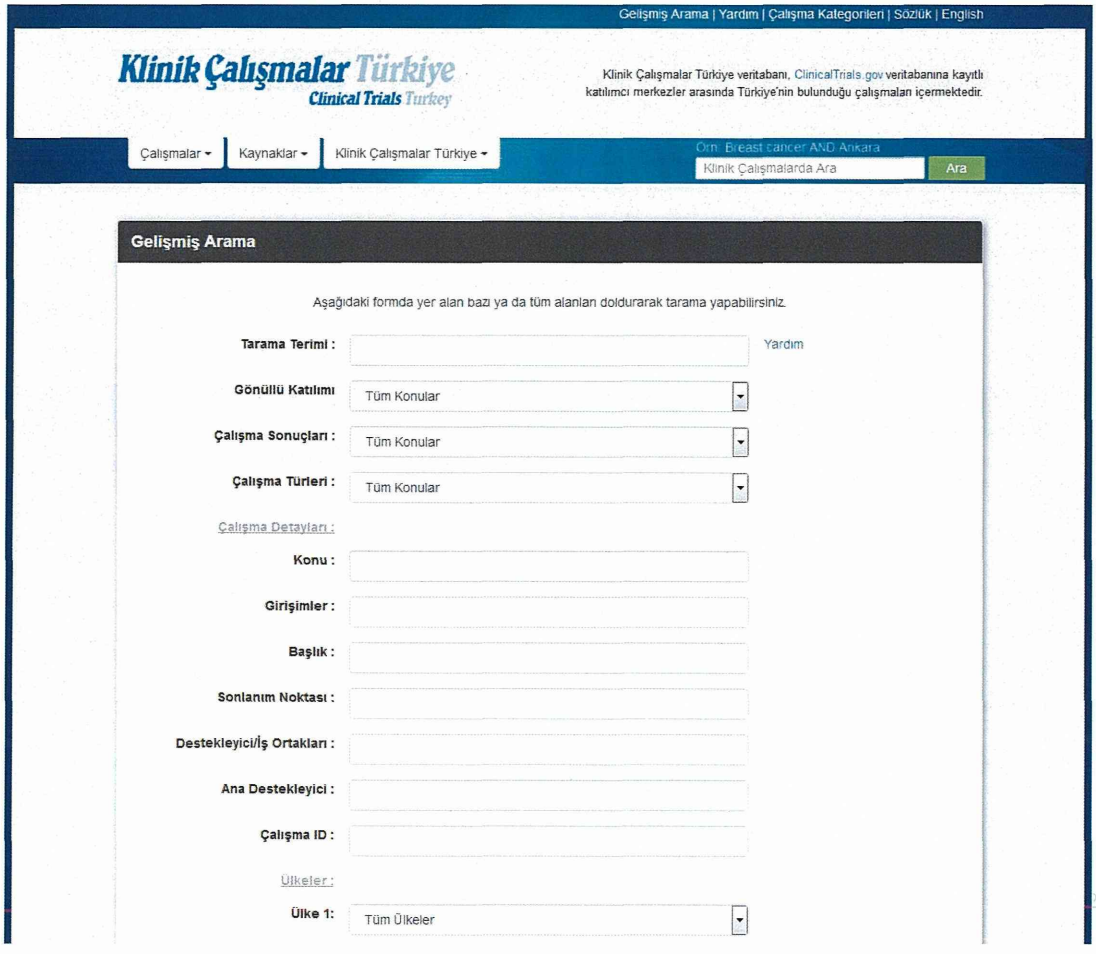
# Country-Specific Trial Portal

- Clinical Trials Turkey (http://www.clinicaltrials-tr.org/)
- Leverages ClinicalTrials.gov
  - Registered trials with at least one site in Turkey
  - Structured data elements translated to Turkish
  - Trial information displayed in Turkish (where translated) and English
  - Not a trial registry


Advanced Search | Help | Study Topics | Glossary | Türkçe
Klinik Çalışmalar Türkiye
Clinical Trials Turkey
Clinical Trials Turkey database covers all the studies that have a participating Turkish center registered to the ClinicalTrials.gov.
Studies
Resources
Clinical Trials Turkey
Ex: Breast cancer AND Ankara
Search in Clinicaltrials
Search
Clinical Trials Turkey
This site has been organized by Clinical Research Association of Turkey covers all the studies that have a participating Turkish center registered to the ClinicalTrials.gov according to the regulations of U.S. National Institute of Health.
Search For Studies
Ex: Breast cancer AND Ankara
Search in Clinicaltrials
Search
Advanced Search | See Studies by Topic | See Studies by Country
Study Statics
54.4%
Completed
Recruiting
Active, not recruiting
Others
For Researchers
How to Find Studies?
Study Topics
Learn About Clinical Studies
Arama İpuçları
How to Find Studies?
How to Read Studies
How to Read Study Results
Resource
ClinicalTrials.gov
Clinical Research Association
Main Page | Terms and Conditions
Information taken from this site can be used publicly by providing reference. Site can be used as a resource by citing as "Taken from Clinical Trials Turkey web site" or "Taken from www.clinicaltrials-tr.org". This site is developed according to the regulations of U.S. National Institute of Health.


Gelişmiş Arama | Yardım | Çalışma Kategorileri | Sözlük | English
Klinik Çalışmalar Türkiye
Clinical Trials Turkey
Klinik Çalışmalar Türkiye veritabanı, ClinicalTrials.gov veritabanına kayıtlı katılımcı merkezler arasında Türkiye'nin bulunduğu çalışmaları içermektedir.
Çalışmalar
Kaynaklar
Klinik Çalışmalar Türkiye
Örn: Breast cancer AND Ankara
Klinik Çalışmalarda Ara
Ara
Gelişmiş Arama
Aşağıdaki formda yer alan bazı ya da tüm alanları doldurarak tarama yapabilirsiniz.
Tarama Terimi :
Yardım
Gönüllü Katılımı
Tüm Konular
Çalışma Sonuçları :
Tüm Konular
Çalışma Türleri :
Tüm Konular
Çalışma Detayları :
Konu :
Girişimler :
Başlık :
Sonlanım Noktası :
Destekleyici/İş Ortakları :
Ana Destekleyici :
Çalışma ID :
Ülkeler :
Ülke 1:
Tüm Ülkeler

Klinik Çalışmalar Türkiye
Clinical Trials Turkey

Klinik Çalışmalar Türkiye veritabanı, ClinicalTrials.gov veritabanına kayıtlı katılımcı merkezler arasında Türkiye'nin bulunduğu çalışmaları içermektedir.

Çalışmalar | Kaynaklar | Klinik Çalışmalar Türkiye

Örn: Breast cancer AND Ankara

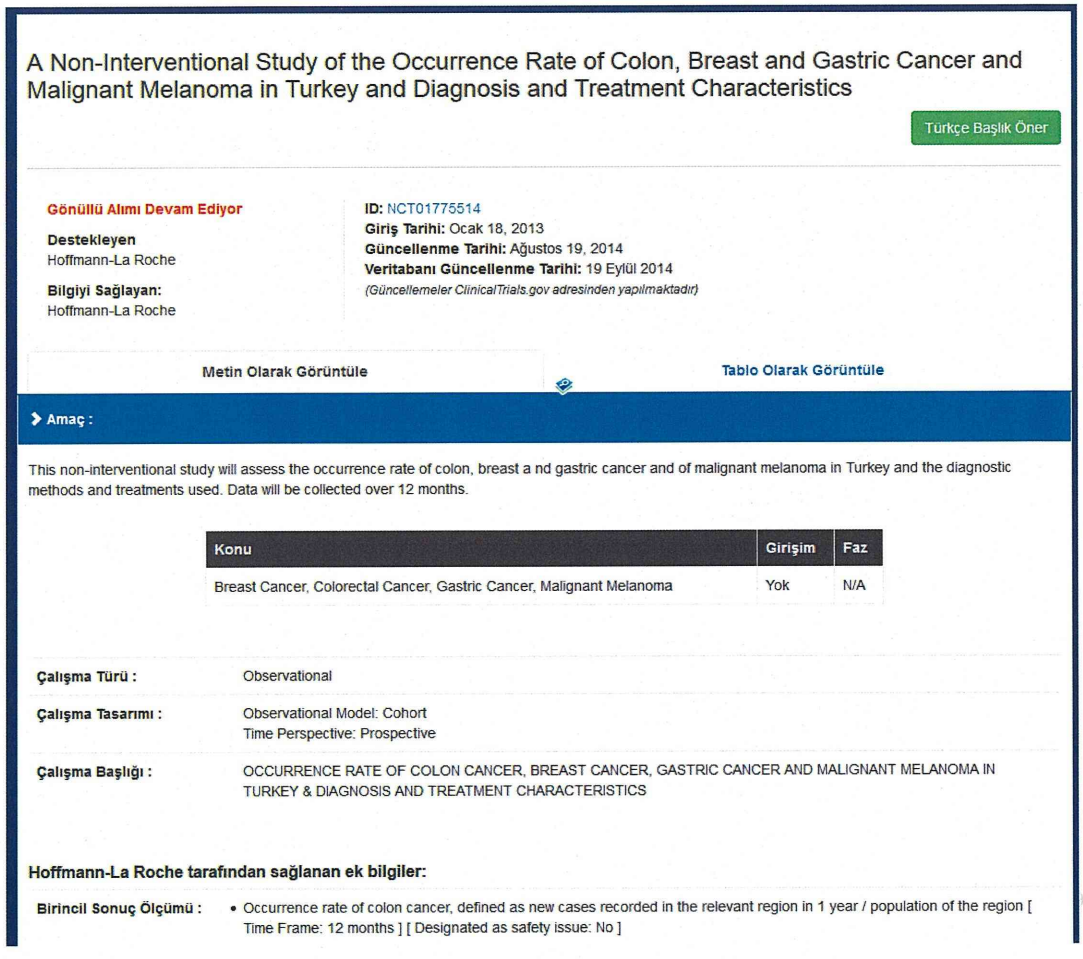
Klinik Çalışmalarda Ara | Ara

**Tarama Kriterleri:** Breast cancer AND Ankara, Açık Çalışmalar
**Bulunan Toplam Sonuç :** 6

**Sonuçlar**

| Sıra | Durum | Çalışma |
|---|---|---|
| 1 | Gönüllü Alımı Devam Ediyor | **A Non-Interventional Study of the Occurrence Rate of Colon, Breast and Gastric Cancer and Malignant Melanoma in Turkey and Diagnosis and Treatment Characteristics**<br>**Konu :** Breast Cancer, Colorectal Cancer, Gastric Cancer, Malignant Melanoma |
| 2 | Gönüllü Alımı Devam Ediyor | **A Safety and Tolerability Study of Assisted- and Self-Administered Subcutaneous Herceptin (Trastuzumab) as Adjuvant Therapy in Patients With Early HER2-Positive Breast Cancer (SafeHer)**<br>**Konu :** Breast Cancer<br>**Girişim :** Drug: trastuzumab [Herceptin] ; Drug: trastuzumab [Herceptin] |
| 3 | Gönüllü Alımı Devam Ediyor | **A Study of Pertuzumab in Combination With Trastuzumab Plus an Aromatase Inhibitor in Patients With Hormone Receptor-Positive, Metastatic HER2-positive Breast Cancer**<br>**Konu :** Breast Cancer<br>**Girişim :** Drug: Aromatase Inhibitor ; Drug: Induction Chemotherapy ; Drug: pertuzumab ; Drug: trastuzumab |
| 4 | Gönüllü Alımı Devam Ediyor | **A Study of Pertuzumab in Combination With Herceptin (Trastuzumab) and A Taxane in First-Line Treatment in Patients With HER2-Positive Advanced Breast Cancer (PERUSE)**<br>**Konu :** Breast Cancer<br>**Girişim :** Drug: pertuzumab ; Drug: taxane ; Drug: trastuzumab [Herceptin] |
| 5 | Gönüllü Alımı Devam Ediyor | **A Study of Patient Satisfaction and Safety With Subcutaneously Administered Herceptin (Trastuzumab) in Patients With HER2-Positive Early Breast Cancer**<br>**Konu :** Breast Cancer<br>**Girişim :** Drug: carboplatin ; Drug: chemotherapy ; Drug: docetaxel ; Drug: paclitaxel ; Drug: trastuzumab [Herceptin] |
| 6 | Henüz Gönüllü Alımı Başlamadı | **Single Versus Double Drains After Mastectomy**<br>**Konu :** Breast Cancer<br>Modified Radical Mastectomy<br>**Girişim :** Procedure: Insertion of a single drain ; Procedure: Insertion of double drains ; Procedure: Ultrasonography after removal of the drains |

1



# A Non-Interventional Study of the Occurrence Rate of Colon, Breast and Gastric Cancer and Malignant Melanoma in Turkey and Diagnosis and Treatment Characteristics

Türkçe Başlık Öner

**Gönüllü Alımı Devam Ediyor**

**Destekleyen**
Hoffmann-La Roche

**Bilgiyi Sağlayan:**
Hoffmann-La Roche

**ID:** NCT01775514
**Giriş Tarihi:** Ocak 18, 2013
**Güncellenme Tarihi:** Ağustos 19, 2014
**Veritabanı Güncellenme Tarihi:** 19 Eylül 2014
*(Güncellemeler ClinicalTrials.gov adresinden yapılmaktadır)*

Metin Olarak Görüntüle | Tablo Olarak Görüntüle

**Amaç :**

This non-interventional study will assess the occurrence rate of colon, breast a nd gastric cancer and of malignant melanoma in Turkey and the diagnostic methods and treatments used. Data will be collected over 12 months.

| Konu | Girişim | Faz |
|---|---|---|
| Breast Cancer, Colorectal Cancer, Gastric Cancer, Malignant Melanoma | Yok | N/A |

| | |
|---|---|
| **Çalışma Türü :** | Observational |
| **Çalışma Tasarımı :** | Observational Model: Cohort<br>Time Perspective: Prospective |
| **Çalışma Başlığı :** | OCCURRENCE RATE OF COLON CANCER, BREAST CANCER, GASTRIC CANCER AND MALIGNANT MELANOMA IN TURKEY & DIAGNOSIS AND TREATMENT CHARACTERISTICS |

**Hoffmann-La Roche tarafından sağlanan ek bilgiler:**

**Birincil Sonuç Ölçümü :**
- Occurrence rate of colon cancer, defined as new cases recorded in the relevant region in 1 year / population of the region [ Time Frame: 12 months ] [ Designated as safety issue: No ]

# Japan and ClinicalTrials.gov

As of January 25, 2016

- 3,950 Studies in ClinicalTrials.gov
  - Submitted by 456 data providers
- 319 PRS Organizations from Japan
  - (Does not include most multinationals)

95

# Some Organizations from Japan

- Translational Research Informatics Center, Kobe, Hyogo, Japan
- Japan Clinical Oncology Group
- Kyorin University
- Kyoto University, Graduate School of Medicine
- Kumamoto University
- Hiroshima University
- Tokyo University
- Osaka University
- Chiba University
- Kansai Hepatobiliary Oncology Group

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# PRS Implementation Details

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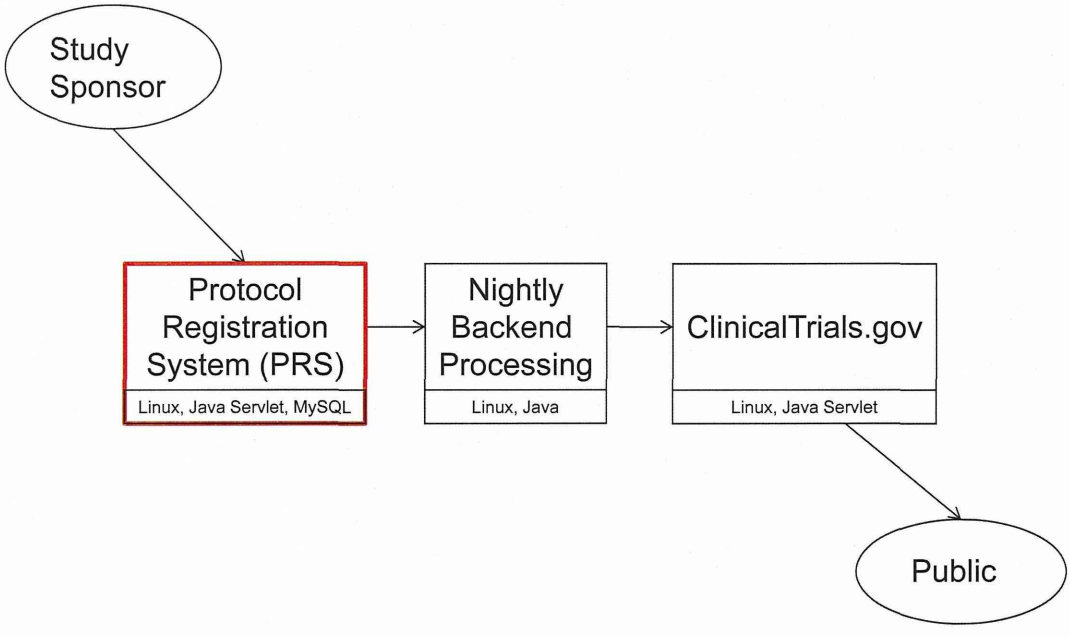
# Highest Level Overview

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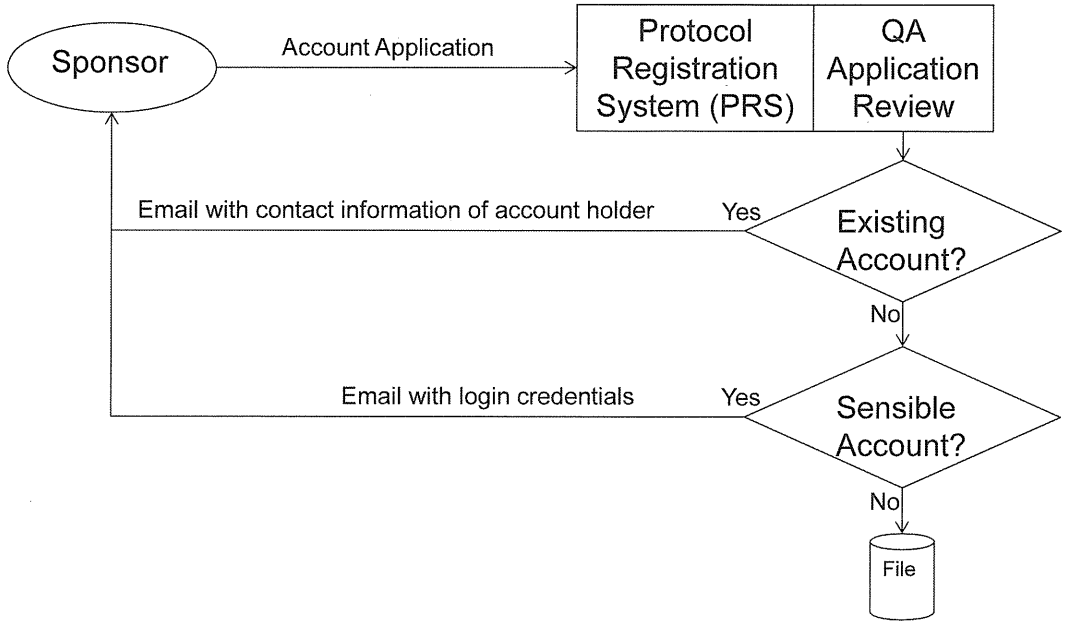
# Protocol Registration System

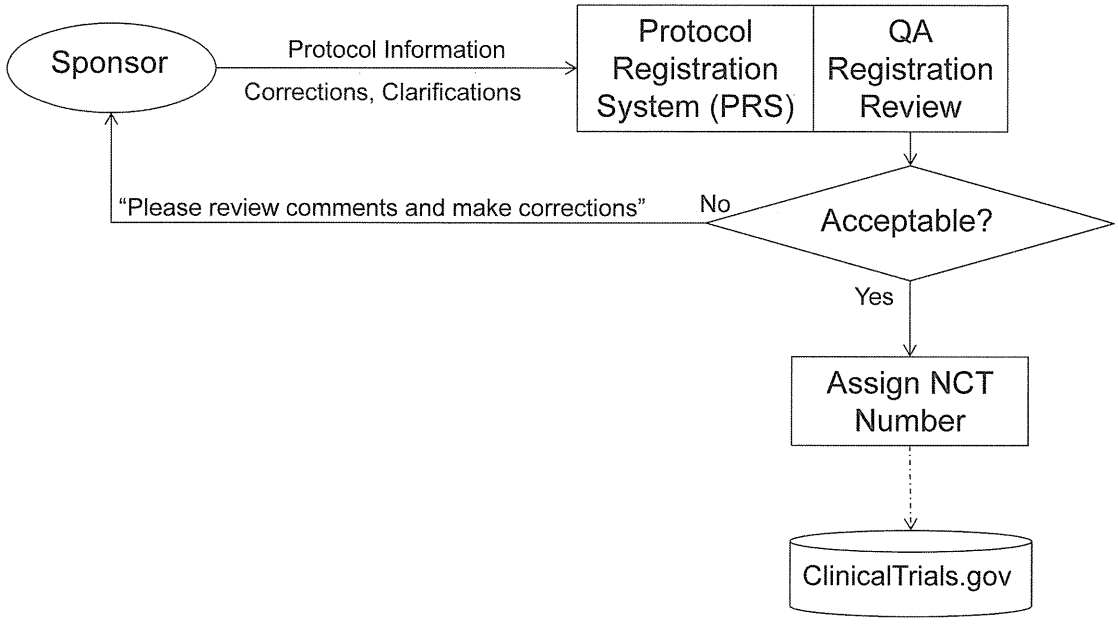
## Step 1 – Getting an account




QA = Quality Assurance staff

# Protocol Registration System

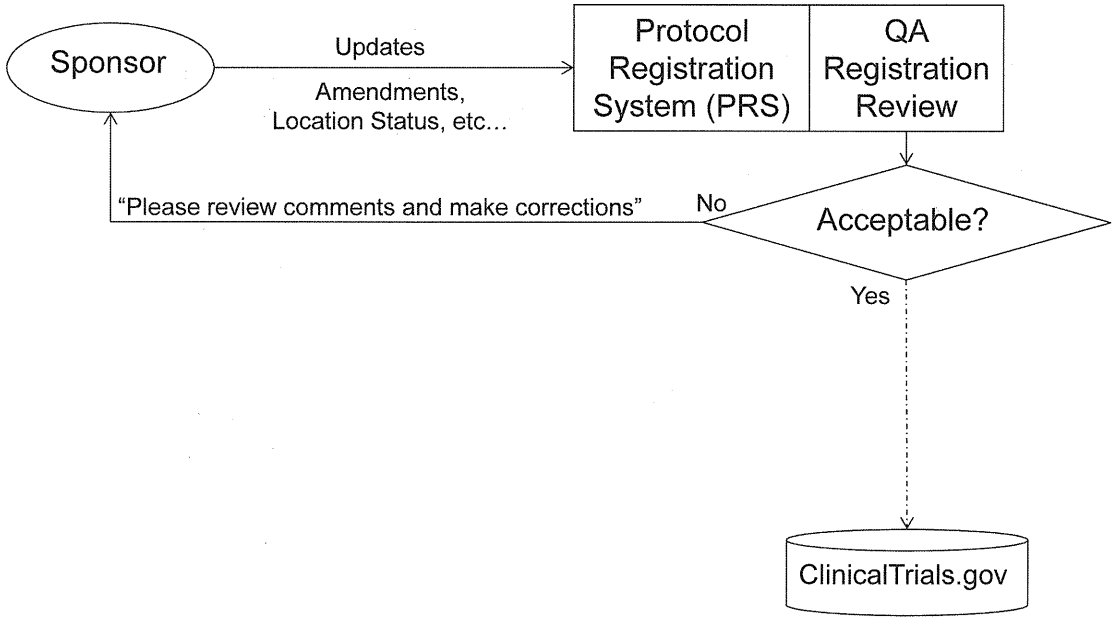
## Step 2 – Providing Study Registration




QA = Quality Assurance staff

# Protocol Registration System

## Step 3 – Providing Periodic Updates

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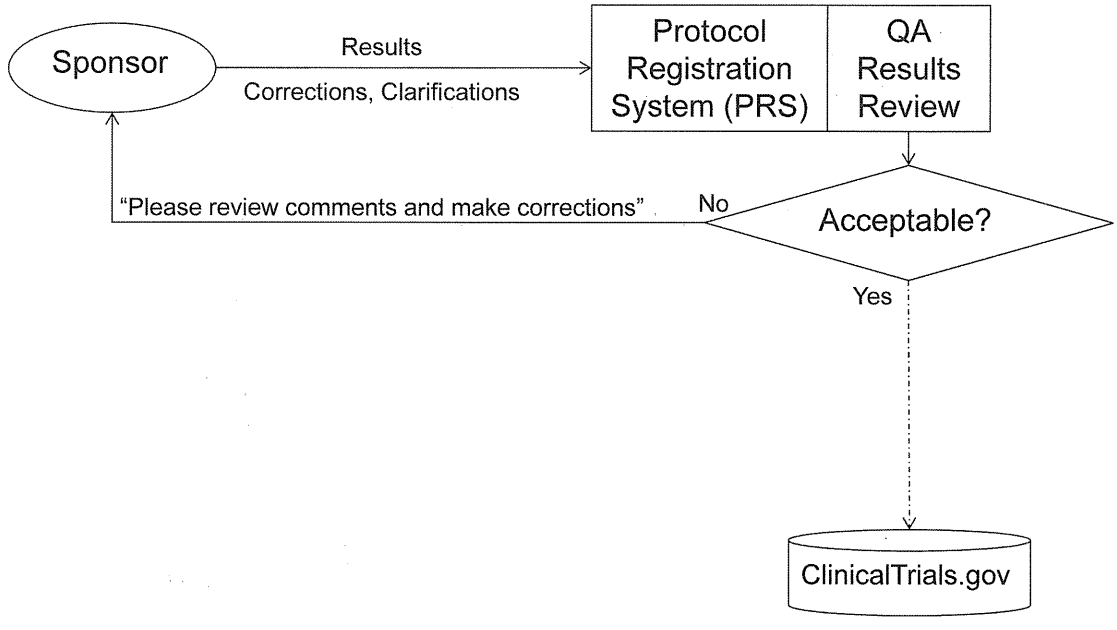
QA = Quality Assurance staff

# Protocol Registration System

## Step 4 – Providing Results

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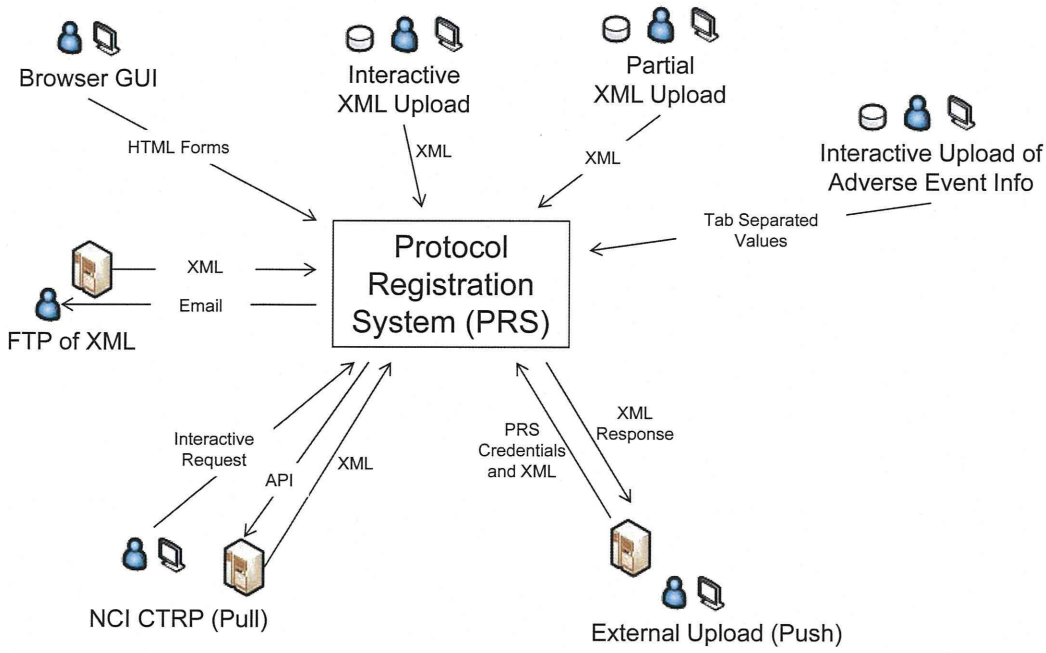
QA = Quality Assurance staff

# Protocol Registration System

## Methods of Interaction

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# PRS Basics

- Structured data elements:
  - Some required* and others optional
  - Pull-down menus and text
- Business rules
  - STOP ERROR Study cannot be released; must be addressed
  - ⚠ WARNING Should be addressed
  - NOTE Helpful hints; may or may not apply
- We must accommodate all study designs
  - No exceptions to business rules
  - If one study in 1000 has X<Y, then we allow X<Y.
- PRS supports a basic work flow

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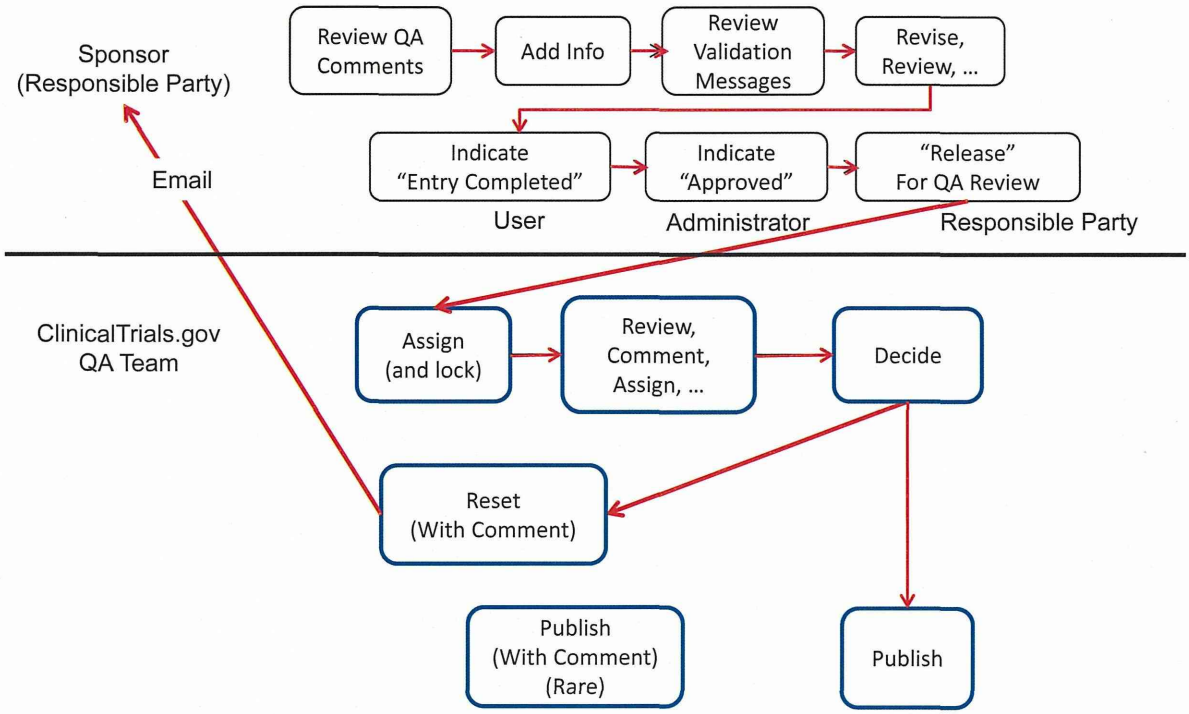
# Protocol Registration System

## Internal Work Flow

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# Structured Information

What we want:

**Type 1 diabetes**

What we get:

**Peoples who had diabeties as teenagers**

We have studies from around the world, some users with weak English skills, and data feeds from other systems.

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# Structured Information

What we want in Collaborators field:

**Merck**
**Bill & Melinda Gates Foundation**

What we get:

**Merk Incorporated,**
**a grant from the Gates Foundation,**
**New Delhi Office**

We don't know ground truth of the study.
We don't have copies of study documents.
Our comments might be ignored.
Our email pleas might be ignored.

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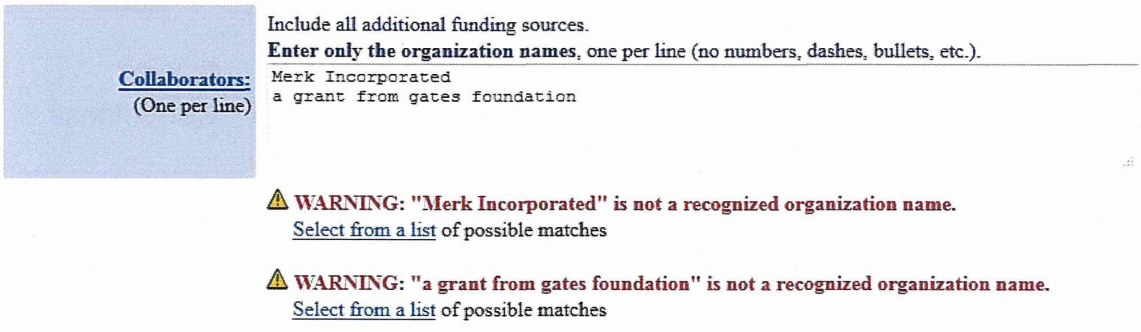
# Structured Information




We try, but lacking a bigger stick,
at some point we have to take what we are given.
(And then try to make the best of it!)

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