Progress and challenges of clinical trials registration in Latin America and the Caribbean's

Ninth Regional Congress on
Health Sciences Information – CRICS9

Ludovic Reveiz
Health Systems Strengthening
Pan American Health Organization

Pan American Health Organization
Regional Office of the World Health Organization

Content

- Introduction
- Progress in the Americas
- Monitoring Trial registration in the Americas
- Result reporting

Pan American Health Organization
Regional Office of the World Health Organization

Prevention

Diagnosis

Treatment

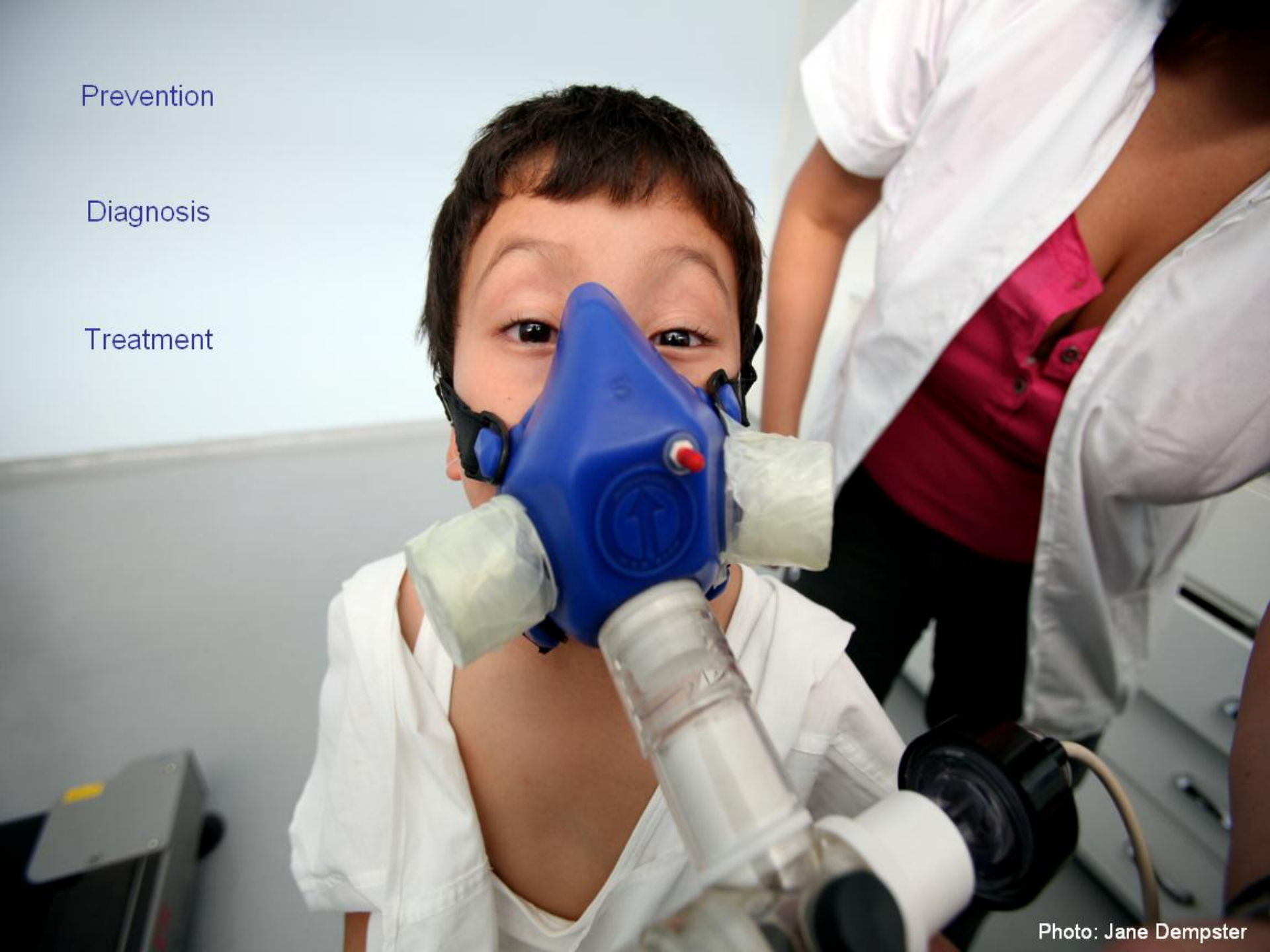


Photo: Jane Dempster

Approved by ethic committees

Introduction

The mission of the WHO International Clinical Trials Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.

Plataforma & red registros

WHO standards

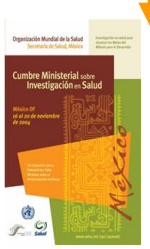
Joint position
EFPIA-
PHRMA-
IFPMA-
JPMA

FDA
Informed
Consent

WHO

FDAAA

1998 2004 2005 2006 2007 2008 2009 2010 2011 2012



Cumbre Ministerial México

CIHR Policy

ICMJE

Reglamento

Helsinki declaration

Why is Trial Registration Important?

- There is a need to ensure that decisions about health care are informed by all of the available evidence
- The Declaration of Helsinki states that "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject".
- Describing clinical trials in progress can make it easier to identify gaps in clinical trials research
- Registries checking data as part of the registration process may lead to improvements in the quality of clinical trials by making it possible to identify potential problems (such as problematic randomization methods) early in the research process

What is a clinical trial?

For the purposes of registration, a clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

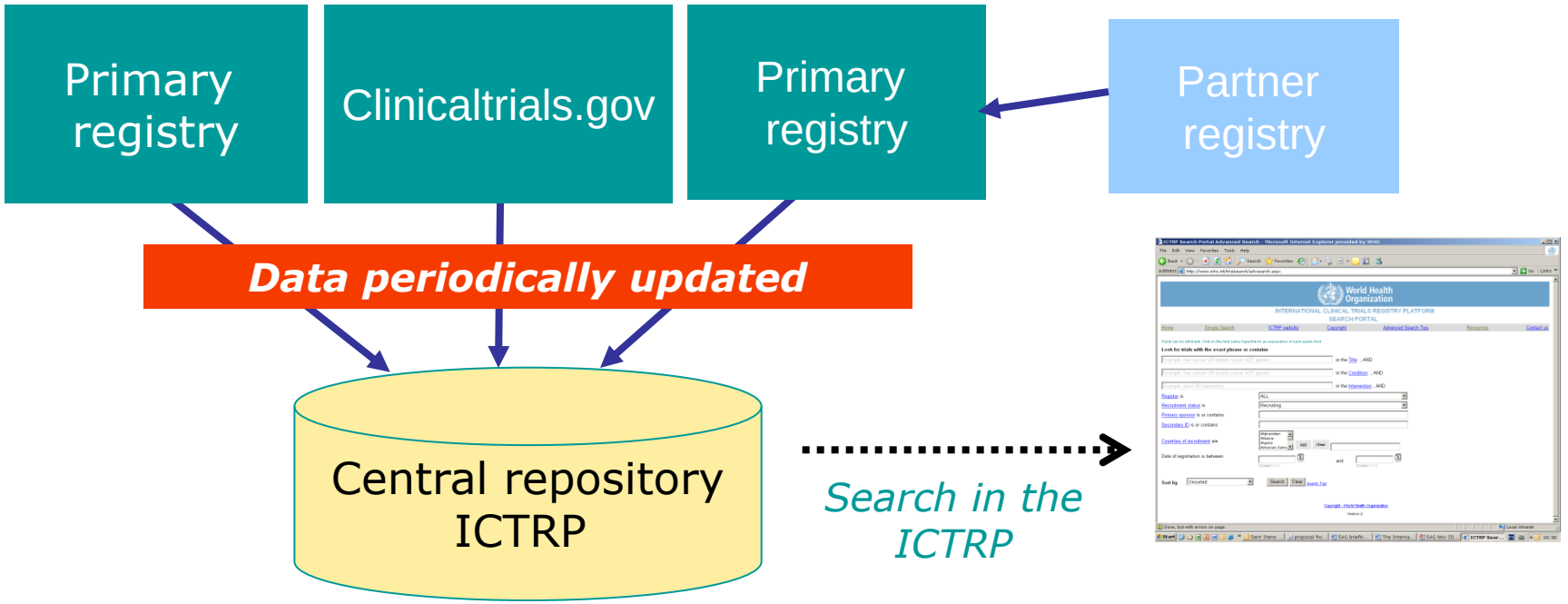
Clinical trials may also be referred to as interventional trials. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc. This definition includes Phase I to Phase IV trials.

International Clinical Trials Registry platform (ICTRP)

- The minimum information that must be registered is specified in the WHO Trial Registration Data Set

- A Primary Registry in the WHO Registry Network is a clinical trial registry with at least a national remit that meets WHO Registry Criteria for content, quality and validity, accessibility, unique identification, technical capacity and governance and administration

ICTRP model



October 2012: more than 175.140 clinical trials; 15 primary registries and clinicaltrials.gov

Pan American Health Organization
Regional Office of the World Health Organization

INTERNATIONAL CLINICAL TRIALS REGISTRY PLATFORM

SEARCH PORTAL

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

Back to Results

Main

Note: This record shows only the 20 elements of the WHO Trial Registration Data Set. To view changes that have been made to the source record, or for additional information about this trial, click on the URL below to go to the source record in the primary register.

Register:	ClinicalTrials.gov
Last refreshed on:	17 March 2009
Main ID:	NCT00862004
Date of registration:	13/03/2009
Primary sponsor:	The First Affiliated Hospital of Guangzhou Medical College
Public title:	Video-Assisted Thoracoscopic Surgery (VATS) Major Pulmonary Resection With Systematic Node Dissection (SND) for Stage IIIA Non-Small Cell Lung Cancer
Scientific title:	Feasibility of VATS(Video-Assisted Thoracoscopic Surgery) Major Pulmonary Resection With SND for Clinical Stage IIIA Non-Small Cell Lung Cancer
Date of first enrolment:	December 2008
Target sample size:	30
Recruitment status:	Recruiting
URL:	http://clinicaltrials.gov/show/NCT00862004
Study type:	Interventional
Study design:	Non-Randomized, Open Label, Safety Study, Single Group Assignment, Treatment, Uncontrolled

Countries of recruitment

China

Contacts

Name:	Jianxing He, MD, FACS	**Name:**	Jianxing He, MD, FACS	**Name:**	Daoyuan Wang, MD
Address:		**Address:**		**Address:**	

Pan American Health Organization

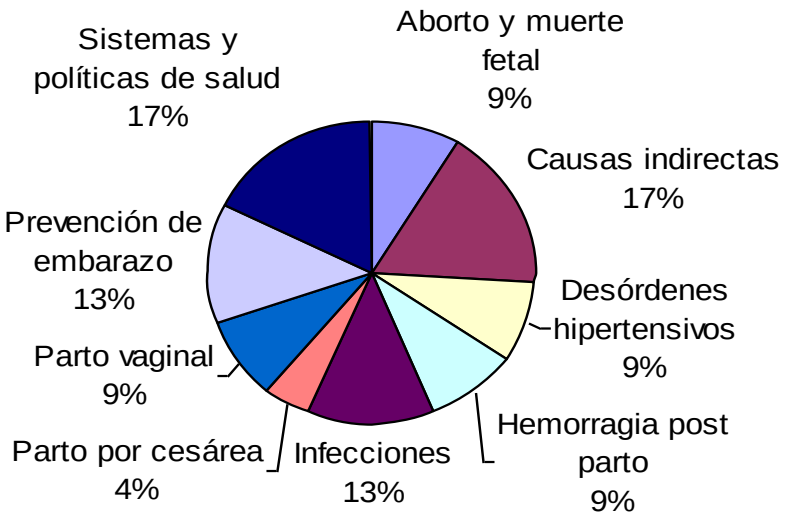
Regional Office of the World Health Organization

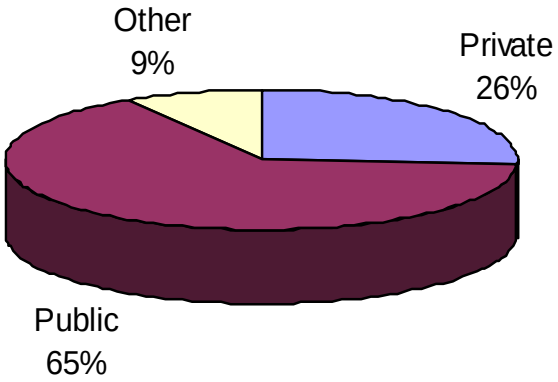
Examples

Assessment of clinical trials registered from LAC in 2010 related with maternal mortality and neglected diseases/ HIV/ Malaria

Maternal mortality

- 950 clinical trials
- 23 (2.4%) related with maternal mortality
- 65% from Brazil
- 13% multinational



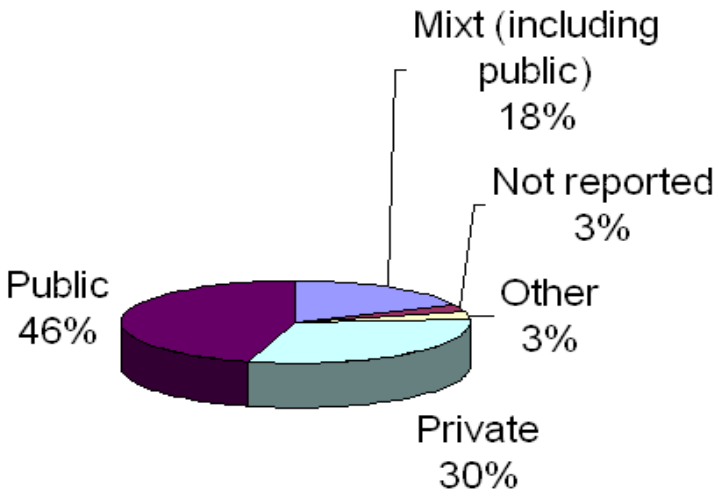


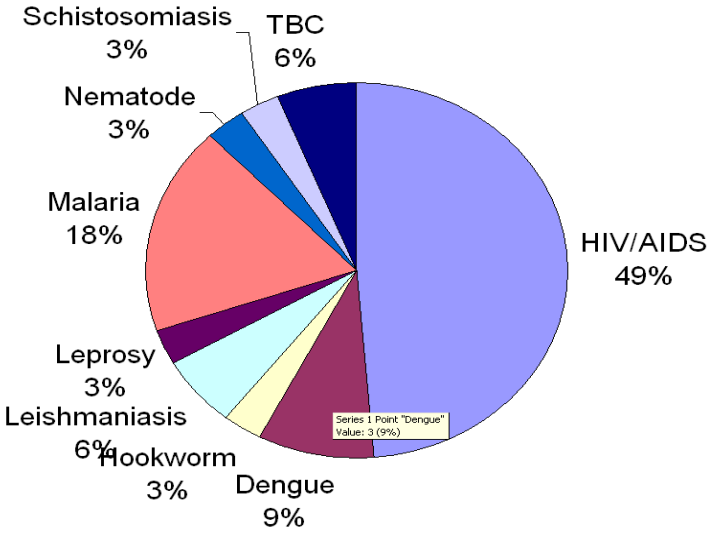
Pan American Health Organization
Regional Office of the World Health Organization

HIV/SIDA, malaria, tuberculosis, dengue, lepra, leishmamiasis y otras enfermedades desatendidas

- 950 clinical trials
- 33 (3.5%) EC
- 46% from Brazil
- 21% multinational

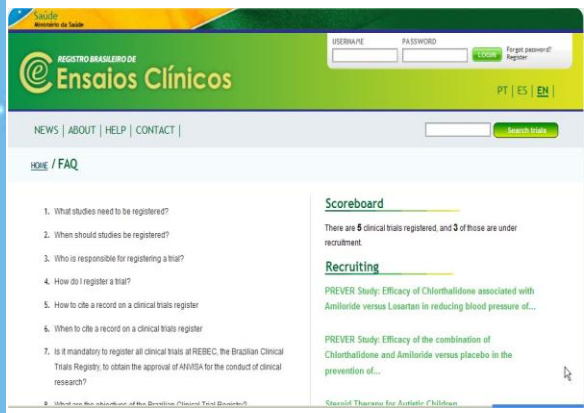
(private)





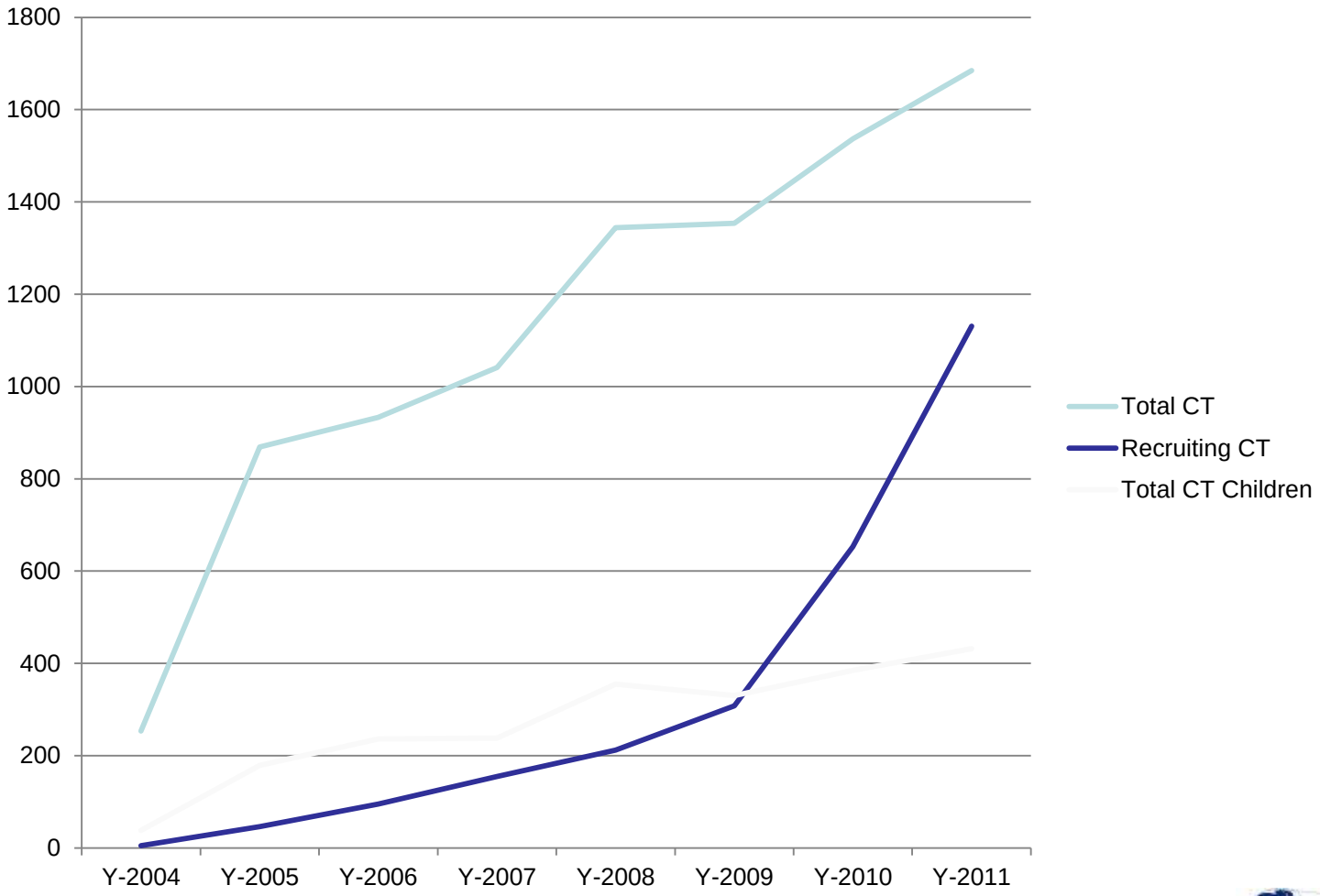
Pan American Health Organization
Regional Office of the World Health Organization

Progress in the Américas



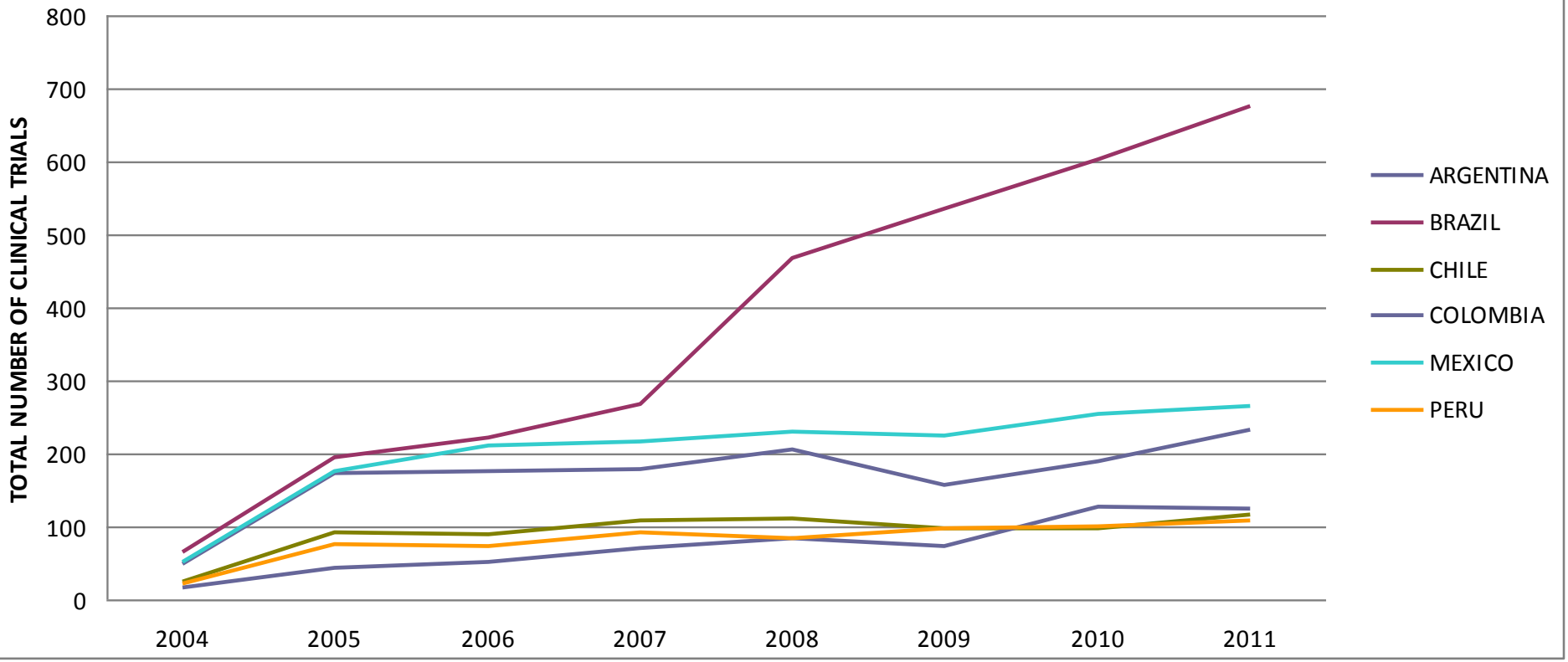
Pan American Health Organization
Regional Office of the World Health Organization

Number of Clinical trials from LAC



Pan American Health Organization
Regional Office of the World Health Organization

TOTAL NUMBER OF REGISTERED CLINICAL TRIALS IN LATIN AMERICA FROM 2004-2011



Pan American Health Organization
Regional Office of the World Health Organization

Monitoring trial registration 2011

*Objective**: To determine to what extent LAC biomedical journals have endorse and implement clinical trial registration and reporting guidelines

Methods:

- We identified randomized controlled trials published in 2011 from journals indexed in LILACS;
- From the online author instructions we extracted information regarding endorsement of trial registration
- We check for compliance (Trial registration in the ICTRP and mention of using CONSORT) in published RCT of those journals

*Reveiz L. Endorsement of the clinical trial registration initiative and reporting guidelines by biomedical journals.Unpublished data.

Pan American Health Organization
Regional Office of the World Health Organization

Monitoring trial registration 2011

Results

- 477 controlled trials were identified by the search. A random sample of 240 were assessed and finally 101 RCT published in 56 journals (10 countries) were included
- Prospective trial registration was explicitly required by 20/56 journals (36%)
- Trial registration was reported in the abstract of 9 RCT (9%) and in 20% of manuscripts. Overall, prospective registration was done in 7 RCT (7%).
- 11/56 journals (20%) had at least one RCT reporting trial registration

Monitoring trial registration 2010

*Objective**: To determine the prevalence of trial registration in randomized controlled trials (RCTs) from LAC researchers and assess methodological characteristics

Methods:

- We identified and assessed randomized controlled trials published in 2010 from LAC authors in PUBMED/LILACS;
- Data were independently extracted by two authors
- We also check in the International Clinical Trials Registry platform (ICTRP)

Reveiz L et al. Trial registration in Latin America and the Caribbean's: study of randomized trials published in 2010
Reveiz L et al. Characteristics of randomized trials published in Latin America and the Caribbean according to funding source

Pan American Health Organization
Regional Office of the World Health Organization

Monitoring trial registration 2010

Results

Trial registration

- 526 RCTs from 19 countries were finally included (70% Brazil).
- 17% (89/526) of RCTs were registered in the ICTRP
- Only 4.0% were prospectively registered.
- 16% RCT were published in LAC journals; only 15% of them were registered
- Overall, registered RCTs were multinational, had larger sample size and longer follow-up, and reported more frequently information on funding, conflict of interests, and ethic issues
- 21% of publicly funded RCTs were registered compared to 36% of non-publicly funded RCTs (private, NGOs).

Informed consent

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 50

[Docket No. FDA–2009–N–0592]

RIN No. 0910–AG32

Informed Consent Elements

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the current informed consent regulations to require that informed consent documents and processes for applicable drug (including biological products) and device clinical trials include a specific statement that clinical trial information will be entered into a databank. The databank referred to in this final rule is the clinical trial registry databank maintained by the National Institutes of Health/National Library of Medicine (NIH/NLM) which was created by statute. The submission of clinical trial information to this data bank also is required by statute. This amendment to the informed consent regulations is required by the Food and Drug Administration Amendments Act of 2007 (FDAAA) and is designed to promote transparency of clinical research to participants and patients.

DATES: *Effective date:* This rule is effective March 7, 2011.

TO THE EDITOR: The ICMJE supports a solution to the selective reporting of clinical studies. Although efforts have been made to encourage investigators to register their trials, registration is still voluntary. Several major barriers to the development of a comprehensive registry of clinical trials have been described.[1] Research involving human subjects poses complex ethical issues. As stated by the ICMJE, patients who volunteer to participate in clinical trials deserve to know that their contribution to the improvement of human health will be available to inform health care decisions. Therefore, prospective trial registration is an ethical obligation and should be a legally required component of written informed consent.

*Reveiz L, et al. Clinical trial registration. N Engl J Med. 2005;352(2):198-9.

Pan American Health Organization

Regional Office of the World Health Organization

Mapping ethic review committees

Pan American Health Organization
Regional Office of the World Health Organization

Result reporting

“The ClinicalTrials.gov results database was launched in September 2008 to implement Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801), which requires the submission of "basic results" for certain clinical trials, generally not later than one year after the Completion Date”

Full Text View | Tabular View | **Study Results** | Disclaimer | How to Read a Study Record

Results First Received: April 2, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Meconium Aspiration
Interventions:	Drug: Lucinactant Other: Standard Care

Baseline Characteristics

Hide Baseline Characteristics

Reporting Groups

	Description
Lucinactant	Lucinactant via bronchoaveolar lavage
Standard Care	Standard Care included the use of oxygen, CMV, sedation, paralysis, vasopressors, and/or alkalinizatior

Baseline Measures

	Lucinactant	Standard Care	Total
Number of Participants [units: participants]	38	31	69
Age [units: participants]			
<=18 years	38	31	69
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Gender [units: participants]			
Female	16	15	31
Male	22	16	38
Region of Enrollment [units: participants]			
United States	38	31	69
Gestational Age [units: weeks] Mean ± Standard Deviation	40.0 ± 1.30	39.7 ± 1.09	39.9 ± 1.21

▸ **More Information**

Hide More Information

ertain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

- ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.
- ☑ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.
- ☐ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

imitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

Early termination led to a small number of subjects analyzed. Results should be interpreted with caution.

lesults Point of Contact:

lame/Title: Dr. Robert Segal
)rganization: Discovery Laboratories, Inc.
hone: 215-488-9300
-mail: rsegal@discoverylabs.com

lo publications provided

lesponsible Party:	Discovery Laboratories
:linicalTrials.gov Identifier:	NCT00004500 History of Changes
)ther Study ID Numbers:	KL4-MAS-03, FD-R-001938
itudy First Received:	October 18, 1999
lesults First Received:	April 2, 2012
ast Updated:	May 1, 2012

1. Primary: Number of Days Receiving Mechanical Ventilation (MV) [Time Frame: 28 days]

Hide Outcome Measure 1

Measure Type	Primary
Measure Title	Number of Days Receiving Mechanical Ventilation (MV)
Measure Description	A patient is not receiving MV if he/she is removed from the mechanical ventilator for ≥ 24 hours. If a patient subsequently requires intubation and MV, the additional time will count as days receiving MV.
Time Frame	28 days
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Data from the initial Phase 1/2 trial were used to estimate the number of subjects required for testing the null hypothesis of no difference between treatment groups. A sample size of 100 subjects per group is required to test the hypothesis at a significance level of 0.05 with a power of 80%.

All enrolled infants were analyzed (intent-to-treat).

Reporting Groups

	Description
Lucinactant	Lucinactant via bronchoaveolar lavage
Standard Care	Standard Care included the use of oxygen, CMV, sedation, paralysis, vasopressors, and/or alkalinization

Measured Values

	Lucinactant	Standard Care
Number of Participants Analyzed [units: participants]	38	31
Number of Days Receiving Mechanical Ventilation (MV) [units: days] Mean ± Standard Deviation	10.2 ± 9.96	8.1 ± 8.52

No statistical analysis provided for Number of Days Receiving Mechanical Ventilation (MV)

Thanks

Ludovic Reveiz

reveizl@paho.org

Pan American Health Organization

Regional Office of the World Health Organization