

# Clinical Trials Registration in Latin America

Concept paper developed during the  
Clinical Trials Registry Network  
for Latin America and the Caribbean (LAC):  
Consultation and Brainstorming Meeting  
Washington DC 27-28 April 2010.



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## Executive Summary

Clinical Trial Registration is deemed a scientific, ethical, and moral responsibility<sup>1</sup> and is a key component of the objectives of PAHO's Policy on Research for Health aimed at fostering best practices and improved standards for research<sup>2,3,4,5</sup>.

Despite the calls for registering clinical trials in databases that fulfill the WHO criteria for the International Clinical Trial Registry Platform (ICTRP), including PAHO's support stated in its Policy on Research for Health approved by Member States, there are yet no registries that capture these data in English and Spanish<sup>6</sup>. This puts researchers and research sponsors in Latin America at a disadvantage. In this regard, PAHO wants to promote equal access to clinical trial registration<sup>2</sup> and facilitate the development of National Registries that meet WHO's criteria for the ICTRP so that non-English speakers fulfill the requirement of clinical trial registration and allow for an adequate representation in the ICTRP of clinical trials being conducted in the Americas region.

This document outlines the proposal for developing a network of agencies involved in clinical trials registration for Latin America and the Caribbean (LAC) as discussed by the participants in the "Clinical Trials Registry Network for Latin America and the Caribbean: Consultation and Brainstorming Meeting" held in Washington DC on April 27-28 2010 (see list of participants in appendix #\_\_).

During this two-day meeting PAHO/WHO representatives and participants from various countries of the Americas, delegates from registries contributing to ICTRP, and members of the ICTRP Secretariat, undertook the challenge and discussed options for the development of a regional network of registries. Among the options some participants highlighted that some countries may want to have their own registry but this should not preclude having a regional registry that later could be the entry point to the ICTRP; it was also mentioned that many countries may want to dedicate their resources to promoting adherence to registration and work with a

<sup>1</sup> Ghersi D, Pang T. En route to international clinical trial transparency. *Lancet*. 2008;372(9649):1531-2

<sup>2</sup> Panamerican Health Organization. Policy on Research for Health. Washington, D.C.: OPS; 2009 (Document CD49/10). Available at <http://new.paho.org/hq/dmdocuments/PolicyResearchHealthENG.pdf>

<sup>3</sup> Ministerial Summit on Health Research: the Mexico Statement on Health Research. Knowledge for better health: strengthening health systems. Mexico, DF, 16 to 20 November, 2004. [On line]. Available at [http://www.who.int/rpc/summit/agenda/Mexico\\_Statement-English.pdf](http://www.who.int/rpc/summit/agenda/Mexico_Statement-English.pdf)

<sup>4</sup> Bamako Global Ministerial Forum on Research for Health. WHO's role and responsibilities in health research (2009) EB124/12 Add.2.

<sup>5</sup> Pan American Health Organization. Strategic Plan 2008-2012. Official document 328. Available at <http://www.paho.org/english/gov/cd/cd48-od328-e.pdf>

<sup>6</sup> International Clinical Trials Registry Platform (ICTRP). Primary Registries in the WHO Registry Network. Available at:

regional registry; and finally given the volume of clinical trials conducted in many countries and the need for standards in registration it would make sense to join efforts to contribute towards having a regional registry. There was consensus that a regional primary registry and the existence of national registries were complementary options.

To facilitate the discussion and agreement a graphic facilitation method was used. This method consisted in representing graphically the ideas and decisions in three “Game plans”, each focusing on a different plan/strategy selected by the participants:

- Game plan 1.0: The development of a regional database/registry
- Game plan 2.0: Advancing a network of country registries
- Game plan 3.0: Governance for clinical trials registration network in LAC

The main concepts are summarized in the Game plan figures which will be used to develop a Strategic Plan for implementing the clinical trial registration in LAC. The mission of the network will be to support the implementation of clinical trial registration in the LAC region, taking into consideration both the needs of the Member States and the global context in which trial registration and clinical research take place. At the same time, the vision includes four dimensions: 1) to promote trial registration and results reporting and to advocate sound public health policies; 2) to enable the establishment of national and/or regional registries, and an integrated search portal in the records available in the region; 3) to provide leadership and training; and 4) to promote strong partnerships among countries.

A Working Group (Task Team) will facilitate the development of at least one WHO Primary Register that allows data capturing in Spanish, which can be fed into the ICTRP Meta register in English (the working language of the ICTRP). The team will also work in the creation of a Network of Registers with an open platform approach ensuring the network’s governance and development, testing and implementation of the upcoming BIREME’s platform.

PAHO/WHO will provide guidance, leadership, and training to implement this project; resources such as virtual tools to hold meetings; the capability to follow up the registration process across the Region; the promotion of strong partnerships among countries, institutions, organizations and stakeholders. PAHO/WHO have already provided resources and technical support to BIREME for the development of the software required to launch a Spanish language Primary Register for the Region, and Brazil is working on the development of a Primary Register with an interface in Portuguese. Sustainability, however, requires the buy-in from Member States and adequate resourcing.

The initiative will enable the establishment of national registries and an integrated search portal for the records available in the region and will allow giving clinical trials adequate representation in ICTRP's search portal that allows data retrieval by country, and other key variables.

## The Problem

Following the recommendations of the Mexico Ministerial Summit in 2004, the World Health Organization (WHO) set up the International Clinical Trials Registry Platform (ICTRP) “to ensure that a complete view of research is accessible to all those involved in health care decision-making”<sup>3</sup>. Subsequently, standards for the registration of clinical trials in the Platform were developed<sup>7</sup> and endorsed by the International Committee of Medical Journal Editors (ICMJE)<sup>8</sup>. Unfortunately, there are currently no national or Regional Registries meeting the ICTRP standards in the Americas that capture data in Spanish, Portuguese or French. The only data provider to ICTRP is ClinicalTrials.gov, which offers free clinical trial registration in English but is not a Primary Register for WHO-ICTRP.

The lack of a WHO Primary Registry is a barrier to the identification of, and the awareness of, clinical trials being conducted in the Region. Primary Registries in the WHO Registry Network fulfill specific standards and meet requirements about content, quality and validity, accessibility, unique identification, technical capacity and administration. (See the definition of a Primary Register in the glossary).

This situation causes problems within the field of clinical research, including issues related to:

- Compliance with international guidelines, standards, and norms governing research on human subjects. For example, PAHO’s Policy on Research for Health, WHO’s Strategy on Research for Health, the 7<sup>th</sup> revision of the Declaration of Helsinki, and agreements by regional and global publishers and editors require clinical trial registration<sup>2,3,4,8,9,10</sup>
- Ethics review committees find difficult to comply with their requirement of clinical trial registration before approving clinical trials<sup>11</sup>
- Capacity to effectively and adequately review and oversee clinical trials being conducted in the Region and adequate sharing of information
- Transparency in the ethical review and authorization procedures (describing trials underway or completed, minimizing overlap, reducing duplications and inconsistencies in ethical review standards)

<sup>7</sup> World Health Organization (2006) World Health Organization International Clinical Trials Registry Platform. New standards for registration of human medical research. Geneva: World Health Organization; <http://www.who.int/mediacentre/news/releases/2006/pr25/en/>

<sup>8</sup> Laine C, Horton R, DeAngelis CD, Drazen JM, Frizelle FA, Godlee F, Haug C, Hébert PC et al. Clinical trial registration: looking back and moving ahead. *Lancet*. 2007;369(9577):1909-11.

<sup>9</sup> WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects; Available at <http://www.wma.net/en/30publications/10policies/b3/index.html>

<sup>10</sup> Salvador Declaration on Open Access, 2005. Available at: <http://www.icml9.org/channel.php?lang=en&channel=91&content=439>

<sup>11</sup> Pan American Health Organization. Ethic Review Committee. Standard Operating Procedures for submitting research proposals (2000). Available at: [http://www.paho.org/hq/dmdocuments/2000/ethic\\_review\\_committee\\_standard\\_operating\\_procedures\\_for\\_submitting\\_research\\_proposals.pdf](http://www.paho.org/hq/dmdocuments/2000/ethic_review_committee_standard_operating_procedures_for_submitting_research_proposals.pdf)

- Unreliable communication between policy stakeholders, investigators, patients, funding agencies, sponsors, and other relevant stakeholders which hinders trust and transparency
- Adequate visibility of research produced in the region, highlighting the “focus” of ongoing research

Several countries in the Americas have shown interest in addressing these issues seeking ways for promoting clinical trial registration and some, for example Argentina, Brazil, Chile and Cuba, seem to be willing to implement trial registries that would either feed into a regional Primary Registry, or meet the criteria to become a Primary Registry. Some countries are also making progress in national regulation to improve compliance with clinical trial registration<sup>12,13,14</sup>.

The Research Promotion & Development team of the Pan American Health Organization and the Latin American and Caribbean Center on Health Sciences Information [BIREME (PAHO/WHO)] has been working in coordination with Member States and WHO's ICTRP to develop a clinical trial registry platform for the Americas<sup>15</sup>. This initiative may be especially fruitful for countries that focus their efforts on seeking compliance, or countries where the volume of clinical trials does not offset the resources needed to set up a clinical trial registry and maintain it, or where there is insufficient support to develop a registry.

This document outlines a proposal for developing a network of agencies involved in clinical trials registration in the Americas, as discussed during the "Clinical Trials Registry network for Latin America and the Caribbean (LAC): Consultation and Brainstorming meeting", held in Washington DC on 27-28 April 2010.

**The key elements that justify having clinical trial registries in the Region are:**

- Decisions about health care should be informed by the best relevant synthesis of the evidence.
- National regulations improve compliance with trial registration. Countries would benefit by having a harmonized framework and guidance on clinical trial registration as they make progress in the development of regulations and registries, in line with PAHO's Policy on Research for Health.
- Clinical trial registries and regulations should consider and meet local and national needs, complying with international standards.

<sup>12</sup> Ross JS, Mulvey GK, Hines EM, Nissen SE, Krumholz HM (2009) Trial Publication after Registration in ClinicalTrials.gov: A Cross-Sectional Analysis. PLoS Med 6(9): e1000144.

<sup>13</sup> Zarin, D, Ide N, Tse T. Issues in the Registration of Clinical Trials, JAMA. 2007; 297:2112-2120

<sup>14</sup> <http://www.healthresearchweb.org/common/index.php>

<sup>15</sup> <http://www.healthresearchweb.org/common/index.php>

- Countries will benefit from collaboration and shared solutions that can minimize duplication and improve compatibility.
- Clinical trial registration is increasingly deemed as a good research practice and a moral and ethical imperative.
- Awareness about ongoing clinical trials may reduce unnecessary research, improve research visibility, and streamline the integration of new research into research synthesis.
- Awareness of existing and ongoing research allows better identification of knowledge gaps and areas that need to be further researched.
- Public awareness about ongoing research has been used to promote recruitment and participation.
- Registries can be used to analyze the quality and improvement that can be done on existing research<sup>16</sup>.
- Trial registration facilitates research governance.

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<sup>16</sup> González U, Pinart M, Reveiz L, Rengifo-Pardo M, Tweed J, Macaya A, Alvar J. Designing and reporting clinical trials on treatments for cutaneous leishmaniasis. *Clin Infect Dis*. 2010;51(4):400-10.



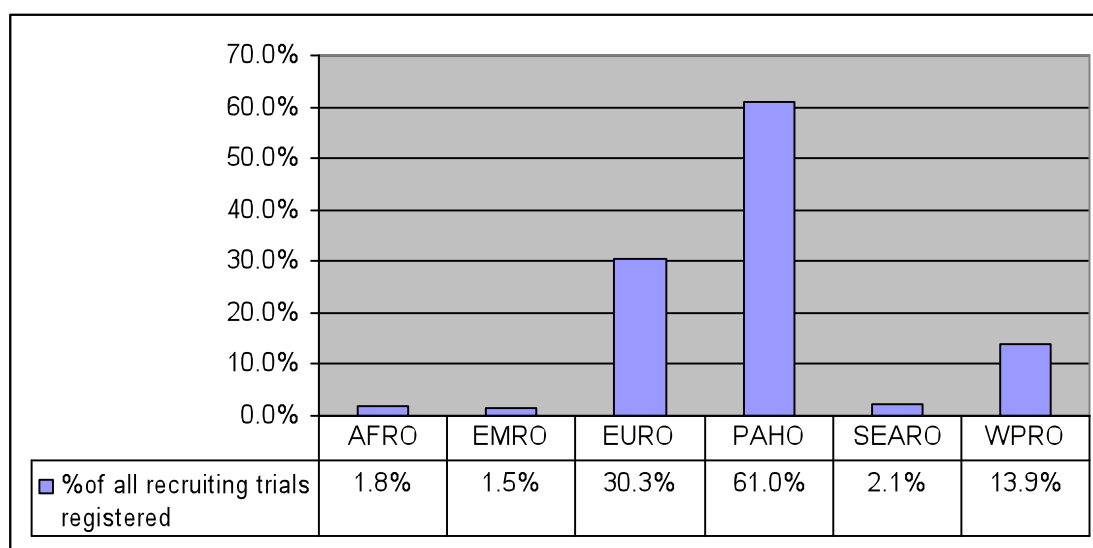
## Background

### About Clinical Trials in the Latin America and Caribbean Region

By December 2010, the number of clinical trial records identifiable in ICTRP's Search Portal was around 123 000; about one third of those clinical trials were recorded as actively recruiting participants.

We estimate, based on these data, that >90% of the registered trials recruiting participants are being conducted in countries categorized as OECD high income, and about 14% in low or lower middle income countries (Figure 1).

Figure 1: Registered trials currently recruiting participants by the WHO region



A search in ICTRP performed by individual country (July 27, 2010) showed a big increase in the number of clinical trials registered in the Americas (Figure 2) as well as an increase in registered trials currently recruiting participants (Figure 3). Note that totaling clinical trials in the region by adding the raw data of trials per country as registered in ICTRP would be inappropriate as this would result in an over-estimation because individual trials may be registered in more than one country (e.g. a multi-centric clinical trial recruiting in Argentina, Brazil, Colombia and Mexico) but count as one in the regional analysis.

Figure 2 and Figure 3 illustrate the totals per country; the total for the Region illustrates the potential overestimation.

Figure 2: Yearly comparison of the total number of clinical trials by country

Country	Records	Trials	2010 (July 26)	2009	2008	2007	2006	2005
Argentina	1186	1060	59	136	215	186	196	159
Bahamas	13	11	1	4	0	1	0	1
Barbados	2	2	0	1	0	0	0	0
Belize	4	4	0	1	3	0	0	0
Bolivia	15	14	2	1	3	2	3	2
Brazil	2231	2108	273	522	474	271	245	190
Canada	7924	7614	542	1222	1347	1030	1090	1393
Chile	648	578	21	98	115	103	105	80
Colombia	435	377	37	69	92	60	57	37
Costa Rica	114	129	5	15	29	16	17	24
Cuba	46	45	7	22	4	7	3	0
Dominican Republic	63	56	3	6	13	7	16	0
Ecuador	60	59	4	5	13	13	10	10
El Salvador	16	15	1	2	1	3	1	3
Guatemala	125	115	11	24	27	10	16	13
Haiti	13	11	0	1	1	0	0	5
Honduras	16	16	1	3	3	1	3	3
Jamaica	18	17	2	5	0	2	3	2
Mexico	1359	1247	91	216	242	213	223	169
Nicaragua	8	8	1	2	1	1	2	1
Panama	92	89	6	12	20	8	17	9
Paraguay	9	8	1	0	0	3	2	0
Peru	568	494	27	90	89	73	71	75
Puerto Rico	1103	1059	42	111	125	100	114	127
Saint Kitts and Nevis	1	1	0	1	0	0	0	0
Trinidad and Tobago	4	4	0	0	0	0	0	3
United States of America	48996	48642	3627	7792	8536	6818	5692	6462
Uruguay	32	30	0	4	5	6	7	4
Venezuela	121	107	7	21	24	16	13	13
<b>Total (+)</b>	<b>65222</b>	<b>63920</b>	<b>4771</b>	<b>10386</b>	<b>11382</b>	<b>8950</b>	<b>7906</b>	<b>8785</b>
<b>Total (from ICTRP)</b>	<b>55395</b>	<b>54898</b>	<b>4567</b>	<b>9198</b>	<b>9795</b>	<b>7694</b>	<b>6473</b>	<b>7452</b>

Figure 3: Yearly registered trials currently recruiting participants by country

Country	Records	Trials	2010 (July 26)	2009	2008	2007	2006	2005	2004 and less
Argentina	306	256	49	86	72	30	13	5	1
Bahamas	5	4	0	4	0	0	0	0	0
Barbados	0	0	0	0	0	0	0	0	0
Belize	0	0	0	0	0	0	0	0	0
Bolivia	4	4	2	0	0	1	0	1	0
Brazil	580	521	97	192	134	61	29	10	-2
Canada	2525	2389	329	686	560	328	236	241	9
Chile	204	168	16	65	46	19	14	3	5
Colombia	165	132	23	46	33	14	12	3	1
Costa Rica	36	27	5	8	7	5	1	1	0
Cuba	21	21	5	14	0	1	1	0	0
Dominican Republic	16	13	2	3	4	3	1	0	0
Ecuador	17	17	3	3	4	4	1	1	1
El Salvador	4	3	1	0	1	1	0	0	0
Guatemala	37	30	8	12	6	4	0	0	0
Haiti	3	3	0	1	1	0	0	0	1
Honduras	3	3	1	1	1	0	0	0	0
Jamaica	9	8	2	3	0	1	0	0	2
Mexico	361	311	49	121	67	42	29	6	-3
Nicaragua	4	4	1	1	0	1	1	0	0
Panama	28	26	4	9	7	2	1	1	2
Paraguay	2	2	1	0	0	1	0	0	0
Peru	194	155	17	62	28	23	10	8	7
Puerto Rico	227	208	31	69	36	22	21	10	19
Saint Kitts and Nevis	0	0	0	0	0	0	0	0	0
Trinidad and Tobago	0	0	0	0	0	0	0	0	0
United States of America	15796	15639	2213	4596	3582	2271	1271	1016	690
Uruguay	8	7	0	3	1	2	1	0	0
Venezuela	39	32	4	15	7	3	1	2	0
<b>Total (+)</b>	<b>20594</b>	<b>19983</b>	<b>2863</b>	<b>6000</b>	<b>4597</b>	<b>2839</b>	<b>1643</b>	<b>1308</b>	<b>733</b>
<b>Total (from ICTRP)</b>	<b>17924</b>	<b>17714</b>	<b>2687</b>	<b>5167</b>	<b>3994</b>	<b>2533</b>	<b>1457</b>	<b>1217</b>	

## Existing Trial Registries in the Region

There is a lack of legislation and policies on trial registration in many LAC countries. Subsequently, few trials registries are currently available for the public.

1. ClinicalTrials.gov: Based in the US, funded by the US federal government, and ICMJE-approved. English language only and open to registration of clinical trials from outside the US ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)).
2. Registro Cubano (RPCEC): Based in Cuba. Applied to become a WHO Primary Registry and would allow registration in Spanish and English (<http://registroclinico.sld.cu/>).
3. Registro Brasileiro de Ensaios Clínicos ([www.ensaiosclinicos.gov.br](http://www.ensaiosclinicos.gov.br)). Established by Brazilian law, this registry was developed using the software was developed by BIREME, with the technical assistance from the PAHO Research Promotion and Development team. It is active since December 2010, hosted by Fundação Oswaldo Cruz (Fiocruz).
4. "Registro de Ensayos Clínicos de Peru": Operated by the Ministry of Health in Peru, established by law (<http://www.ins.gob.pe/registroec/tramitesyserviciosSolicitud.asp?ftp=1&t=0>).
5. Base de Consultas acerca de los Estudios en Farmacología Clínica ([http://www.anmat.gov.ar/aplicaciones\\_net/applications/consultas/ensayos\\_clinicos/principal.asp](http://www.anmat.gov.ar/aplicaciones_net/applications/consultas/ensayos_clinicos/principal.asp)).
6. Registro Latinoamericano de Ensayos Clínicos en Curso ("LatinRec"): Based in Colombia, is geared towards the registration of clinical trials from Latin America in Spanish and English, and has applied to become a WHO Primary Registry ([www.latinrec.net](http://www.latinrec.net)).

Some studies have evaluated barriers and limitations that exist for investigators and sponsors in the use of existing international registries<sup>17,18</sup>. Moreover a pilot survey conducted in Argentina in 2010 showed that the foremost factor hampering registration was a lack of knowledge. Although 75% of the 27 interviewees were familiar with clinicaltrials.gov, most had limited knowledge and experience with other existing international registries and the ICTRP<sup>18</sup>. Another study found that, although around two thirds of participants supported registration of all 20 WHO Data Set items, one third of participants expressed the lack of sufficient knowledge as the primary reason for not registering trials<sup>17</sup>. A gap between

<sup>17</sup> Reveiz L, Krljeza-Jerić K, Chan AW, de Aguiar S. Do trialists endorse clinical trial registration? Survey of a Pubmed sample. *Trials*. 2007 Oct 23;8:30.

<sup>18</sup> White L. Barriers and Limitations to Clinical Trial Registration: Building a Culture of Clinical Trial Transparency in Argentina. Report for Pan American Health Organization: Area of Technology, Health Care, and Research (THR/RP) in conjunction with El

sponsors and researchers was also identified; the responsibility for registration sometimes lies in a limbo<sup>18</sup>.

## Methods used in the Consultation and Brainstorming Meeting

Based on the experience that PAHO/WHO accumulated providing technical support and cooperation to networks of health institutions that deliver scientific and technical information, a two-day meeting was convened with the objective of developing a cooperative network of interoperable national and regional clinical trial registries. The meeting gathered representatives from PAHO/WHO and WHO's ICTRP, participants from different countries of the Americas, and delegates from ICTRP data providers. Together the participants took the challenge and put forth ideas and discussed options for the development of a regional registry network. A graphic facilitation method that helped people organize their thoughts and communicate effectively through a visual approach was used.

The Meeting's specific goals were:

1. To share the state of development of the ICTRP and the participation of Member States
2. To develop a strategy for achieving clinical trial registration in LAC, including:
  - a. A strategy for developing a cooperative network of regional and national registries, including a primary registry to serve the region of the Americas
  - b. Fostering the development of common and interoperable software platforms that would improve compatibility, reduce duplication, and enable the localization of interfaces
  - c. Sharing experiences about the development of clinical trial registries from inside and outside the Region, and from settings with economies similar to those in the Americas
  - d. Identifying key partners and potential advisors to assist in the implementation of the network and regional registry
3. To explore collaboration opportunities to expand the network to other regions and to promote collaboration between countries and regions

## Concepts Resulting from the Meeting

Three “Game plan” topics were defined and subgroups of the meeting participant’s divided for each of them

- Game plan 1.0: The development of a regional database/registry
- Game plan 2.0: Implementing a network of country registries
- Game plan 3.0: Governance for clinical trials registration network in LAC

Game plans 1.0 and 2.0 included the following sections:

- Team/resources;
- Success factor;
- Stages/tasks (Year 1, 2);
- Challenges and target.

Game plan 3.0 included the following sections:

- Models to consider; core support/membership; key milestones;
- Guiding principles;
- Network of advocates for registration transparency;
- Target and advisory boards.

In addition, all participants took part in a shared Vision Themes session.

The concepts are summarized in the proposed Strategic Plan to be developed for the implementation of clinical trial registration. These concepts were also used to propose a mission, vision, and the key elements of a network.

## The Strategic Plan

The meeting offered the basis to develop a Strategic Plan that will enable the network to pursue its mission. The guiding principles in the strategy are:

- To allow for flexible models of communication and information sharing with defined standards
- To allow for different models of data flow. For example, some countries will have regulatory and ethical review processes occurring simultaneously, and other have such processes occurring under a serial approach
- To allocate responsibilities to each Partner Registry/registry to maintain data integrity and to establish processes for the implementation of Registries
- To promote compliance through national legislation

- To implement reliable and efficient data exchange protocols

The initiative will enable establishing national registries as well as an integrated search portal for the records available in the region. The countries that do not have or do not wish to have their own system could adopt the model proposed by BIREME to implement their national registry.

## **The Network of Agencies Involved in Clinical Trial Registration in LAC**

### **The Mission**

The mission of the network is to support the implementation of clinical trial registration in the Americas, giving priority to non-English speaking countries taking into consideration both - the needs of the member states and the global context in which trial registration and clinical research takes place. It was noted that most ICTRP Data providers and Primary Registers offer clinical trial registration in English only.

### **The Vision**

The vision of the Network is to provide a functional collaborative regional network of organizations and stakeholders involved in clinical trial registration in the Americas. The vision includes 4 dimensions, which are aligned with PAHO's Policy on Research for Health:

1. Promote trial registration, reporting of outcome, and advocate for sound public health policies
2. Enable establishing national and/or regional registries and an integrated search portal of the records available in the region
3. Provide leadership, capacity building, training, and standards
4. Foster strong partnerships and collaboration between countries and registries

### **Aims**

The network will pursue its mission by:

- Promoting and enabling the registration of all trials in the Americas into databases that feed WHO's ICTRP, recognizing that this requires addressing regulatory, economic, financial, political, and organizational challenges
- Organizing knowledge; fostering communication on trial registration through workshops, conferences, newsletters and a website
- Submitting and publishing projects, concepts, experiences and strategies for implementation of trial registration

- Making trial registration responsive to local and regional needs and priorities, and compliant with international standards
- Making data capturing and dissemination available in Spanish, Portuguese, and French, in addition to English
- Promoting efficiencies, improving standards (e.g. terminology translation, harmonization and indexing), minimizing duplication and reducing overall costs
- Seeking collaboration, solidarity and sharing of relevant lessons learned
- Promoting compliance with international ethical and regulatory guidelines, norms and standards, and addressing local needs in benefit of clinical trial participants and validity of generated data; promoting best practices for clinical trial registries
- Promoting collaboration and communication among the ethics committees and regulatory authorities of the countries in the region
- Working in close cooperation with key stakeholders for clinical trial registration, such as clinical trial sponsors, researchers and research institutions, health care consumers and international organizations, among others
- Linking to internal and external partners, such as BIREME and the National/Regional registries, to facilitate the implementation of the databases developed and hosted by BIREME

## **Steps to Set up the Working Group Network:**

### **Establishing Network Governance**

As agreed by participants, the next step would be to develop a working group that would explore how to establish and govern a primary registry in the region and interact with other registries within a network approach. Among others, The Network should develop guiding principles, a mission statement; identify key aspects for governance, ensure solid communication, sharing experiences on clinical trials within and between regions. The composition of the working group should be established amongst key stakeholders. The Working Group can meet virtually via the Elluminate system. Virtual meetings could be open to all members of the national/regional registries representative of the WHO Registry Network, and all members of the national/regional registries can review and comment upon the documents produced by the Working Group.

## Implementation of the Open Trials software developed by BIREME in LAC

Between 2008 and 2009 a group composed by DECIT (Science, Technology and Innovation Department from the MoH), ANVISA (Sanitary Surveillance NRA) and FIOCRUZ (a Foundation that belongs to the MoH), started working with BIREME and PAHO to develop a database that would contain the clinical trials. The open-source software ("Open Trials") chosen will allow potential users to meet requirements and comply with ICTRP standards and best practices. The project was jointly funded by the Ministry of Health of Brazil, Fiocruz and PAHO. The Brazilian registry of clinical trials will implement Open Trials. Other countries may choose to use the same software to establish and host their own National Registries, or use BIREME's hosting facilities as well as adapting and using the open platform. The platform will be launched in November 2010.

Countries planning or developing national registries will be encouraged to use the Open Trials software.

### Software features

- Multi-lingual

- User interface and content can be translated to any language or set of languages
- Clinical Trial registry operators can edit help text, vocabularies etc. at any time

- Multi-platform

- Runs on any modern computer (Windows, MacOSX, Linux, FreeBSD...)

- Modular

- Functionality is split into reusable modules

- Program is written in Python, a modern, easy-to-learn programming language and leverages Django, a modern, easy to learn Web development toolkit; it also uses relational database storage, which is compatible with Oracle, PostgreSQL and MySQL.

### Designed for Wide Deployment

- Multi-lingual user interface, help system and repository
- Multi-platform language and toolkit
- Mainstream database technology
- Technical documentation in English
- Source code in English
- Standard Open Source procedures and best practices

### Open Source Software



Open Source Software is licensed with a copyright license compliant with the Open Source Definition (OSD)

- Software is distributed with its source code in a human readable format
- Software is developed in an open and collaborative way by groups of developers

## **Identifying key National/Regional Stakeholders**

The "Clinical Trials Registry network for Latin America and The Caribbean: Consultation and Brainstorming meeting" was the first step to bring together representatives from PAHO/WHO, participants from various countries of the Americas, delegates from registries contributing to ICTRP, and members of the ICTRP Secretariat.

Support from Country offices will be required to identify and contact further key stakeholders in each country. Particularly, national regulatory agencies will be contacted and encouraged to participate in the process of regulating the clinical trial registration and in the implementation of clinical trial registries or the adherence to regional registries.

## **Establishing at least one Regional Primary Register in LAC**

There are currently no registries that can capture clinical trials in French, Portuguese or Spanish. Furthermore, LAC is the only region lacking from a regional clinical trial registry that meets WHO standards. There is a need to establish a regional Primary Register in LAC and the Brazilian trial registry with the support of BIREME, and PAHO has the potential to become a Primary registry not restricted to trials in Brazil. In addition, BIREME could be utilized by countries without plans for a national registry.

## PAHO/WHO Technical Cooperation

The role of PAHO includes the following key elements:

1. Leadership and training to move this project forward
2. PAHO has resources, tools for virtual meetings, and the capability to follow up the registration process across the Region, and can propose options seeking support and buy-in from stakeholders
3. Promote strong partnerships between countries, institutions, organizations and stakeholders
4. Funding management
5. Capacity building - an awareness campaign targeting local investigators, sponsors, ethic committees, and the public
6. Helping local and national scientific journals to adopt and/or implement ICMJE standards, in coordination with BIREME

## Conclusion

The Network of Agencies Involved in Clinical Trials Registration will facilitate the implementation of clinical trial registration in the LAC region, taking into consideration both the needs of the Member States and the global context in which trial registration and clinical research take place. A Working Group will assist the development of at least one WHO Primary Register that allows data capturing in Spanish (feeding to ICTRP in English - the working language of the ICTRP meta-register), the creation of a Network of Registers with an open platform approach, ensure the network governance and the development, testing and implementation of the upcoming BIREME's platform.

The initiative will enable establishing national registries and an integrated search portal for the records available in the Region and will allow giving clinical trials adequate representation in ICTRP's search portal that allows retrieving data by country, and other key variables.

## About Clinical Trial Registration

The registration of all interventional trials is considered to be a scientific, ethical and moral responsibility. In August 2004 the International Committee of Medical Journal Editors (ICMJE) announced that, as of September 13<sup>th</sup> 2005, they would no longer publish manuscripts reporting the results of clinical trials unless a minimum amount of information about those trials had been registered in a publicly accessible clinical trials registry<sup>19</sup>. This policy was informed by a large body of evidence demonstrating the existence of publication bias and selective reporting, and its impact on the ability of healthcare providers and consumers to making informed healthcare decisions. In a number of high profile cases, the trial's sponsors were found to have withheld negative trial outcomes from the public, regulatory agencies and others<sup>20</sup>. These cases gained significant negative media attention and the demand for transparency increased. More recently, in 2008 the Declaration of Helsinki was revised, it now states that "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject"<sup>9</sup>. Clinical trial registration is also a key component of PAHO's Policy on Research for Health<sup>2</sup>. Clinical trial registration provides visibility to research, access to the evidence, governance on research, networking among research groups and researchers, and avoidance of duplication of research.

On September 2007, the Food and Drug Administration's Amendments Act of 2007 (FDAAA or US Public Law 110-85) was passed. This law requires mandatory registration and reporting of outcomes for certain clinical trials of drugs, biologics, and devices based in US and funded by the US federal government<sup>21</sup>.

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<sup>19</sup> DeAngelis C, Drazen JM, Frizelle FA, Haud C, Hoey J, Horton R, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. *N Engl J Med*. 2004;351:1250-1.

<sup>20</sup> Sterne JAC, Egger M, Moher D. Chapter 10: Addressing reporting biases. In Cochrane Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.1 [updated September 2008]. The Cochrane Collaboration, 2008. Available from [www.cochrane-handbook.org](http://www.cochrane-handbook.org).

<sup>21</sup> Food and Drug Administration Amendments Act (FDAAA) of 2007. Available at <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/SignificantAmendmentstotheFDC>

## About the ICTRP

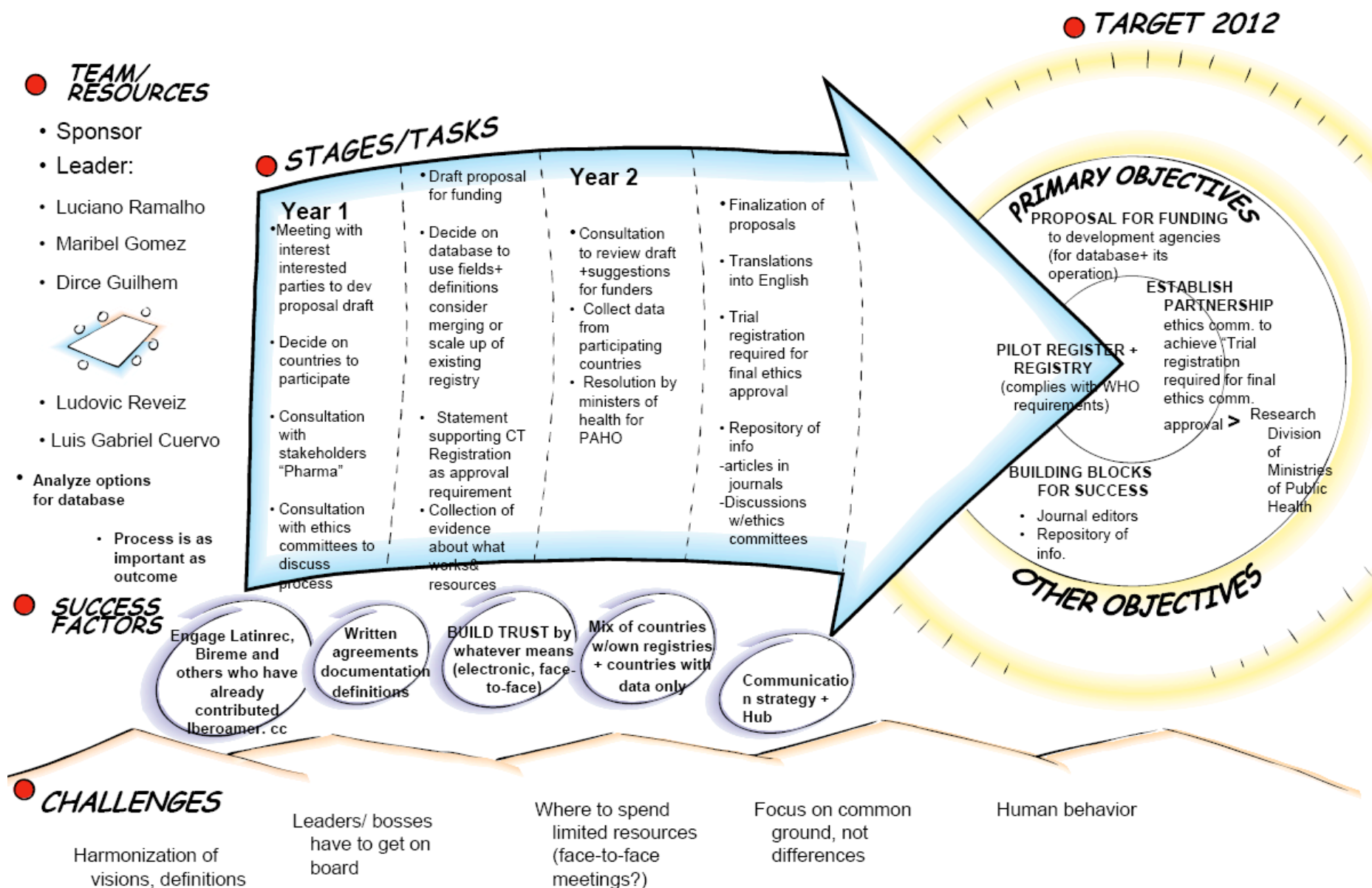
During the Ministerial Summit on Health Research<sup>3</sup> in November 2004, a call for action was issued by "All major stakeholders, facilitated by WHO secretariat, to establish a platform linking a network of international clinical trials registers to ensure a single point of access and the unambiguous identification of trials." The call was spread during the 58<sup>th</sup> World Health Assembly (WHA 58.34) of May 25<sup>th</sup> 2005<sup>22</sup>. to "The global scientific community, international partners, the private sector, the civil society, and other relevant stakeholders" seeking to "establish a voluntary platform to link clinical trials registers in order to ensure a single point of access and unambiguous identification of trials, with a layout that would improve access to information by patients, families, patient groups and others"<sup>6</sup>.

Subsequently, the World Health Organization launched on May 4<sup>th</sup> 2007<sup>6</sup> the WHO Clinical Trials Search Portal: International Clinical Trials Registry Platform (ICTRP), which currently has 2 key elements: "the Network of Collaborating Trial Registries" (the Registry Network) and the Clinical Trials Search Portal. The Registry Network provides a forum for the exchange of information across registries, and the Clinical Trials Search Portal provides a single point of access for the identification of trials. Data searchable on the portal is provided by registries that meet WHO criteria for quality and content.

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<sup>22</sup> World Health Organization. World Health Assembly, Resolution WHA 58.34 Geneva: WHO; 2005

# Database+Registry for region GAMEPLAN 1.0



# Network of National Registries GAMEPLAN 2.0

ADVISORY AND  
RESEARCH National  
Institutes of Research

## TEAM/RESOURCES

Steering committee  
where member  
nations are rep.

- Lucia Ruggiero
- Josue Laguardia
- Carolina O'Donnell
- Ileana Herrera
- Luis Gabriel Cuervo
- Juana Tobos

One person from each registry

PAHO takes on  
leadership

## STAGES/TASKS

May-Sept '10	Oct-Feb '11	Mar-July '11	Aug-Dec '11
<ul style="list-style-type: none"> <li>• Countries decide what type of membership in network. I.E.               <ul style="list-style-type: none"> <li>-Own Registry</li> <li>-Buy in on regional req.</li> <li>-Partnership with other regional req.</li> </ul> </li> <li>• Strategic information dissemination plan established</li> <li>• Select/Invite advisory board</li> <li>• Network governance/ One person from each registry represented</li> <li>• Training Materials created</li> </ul>	<ul style="list-style-type: none"> <li>• Finished Platform for registry software</li> <li>• Use PAHO portal to link all tools for communication</li> <li>• Publication in journals Using registry launch as opportunity to spread word of importance of reg's.</li> </ul>	<ul style="list-style-type: none"> <li>• Platform Testing</li> <li>• Agreement on Standards</li> <li>• Invite journal editors to meetings (virtual)</li> <li>• A meeting/round table @ conferences presentation on experiences</li> </ul>	<ul style="list-style-type: none"> <li>• Achievements Report</li> <li>• 4 meetings over 2 years to bring together epidemiologists, policy members to discuss advancement XXX?</li> </ul>

**TARGET 2012**

## PRIMARY OBJECTIVES

**ACTIVE MEMBERS**  
Brazil, Argentina, Chile, Costa Rica and Cuba. All countries in region participate.

**PLATFORM FUNCTIONING**  
Data reliable and available

**LEGISLATION REVIEWED + Understood**

**GUIDELINES**  
• Developed in 3 languages  
• Solution to translation issues

**INFORMATION ADVOCACY**  
Words spread about need for registry

Action Plan for barriers

## OTHER OBJECTIVES

Standards defined in previous stage

Registry able to generate data for specific pathologies/diseases

## SUCCESS FACTORS

Meeting/ mix of tools

Passionate team to push agenda

Maintain relevance in region

Virtual Meeting every 3 months

Easy to use +Participate

## CHALLENGES

Languages

Resources

Political will/ motivation

# Governance for Clinical Trial Registration Network in LAC

## GAMEPLAN 3.0

### Working Group >

Jordi                      Maria  
Marisol                  Davina

### Models to Consider >

Iberoamerican Cochrane  
PANDH??  
People who care about CT  
Someone pushes for  
Something to happen >CHAMPION

### Core Support



### Membership

PAHO                  EXEC Representative  
  
Stake Holders in region  
Advisory Board\_  
Clear responsibilities (e.g. journal editors)

What must we do to get started?

### Key Milestones>

### Guiding Principles

### Network of Advocates for registration + Transparency

- Network fill the gap countries can't do alone
- Meet international requirements
- Sharing enthusiasm
- Meet local needs e.g. translation
- Raise awareness

### TARGET

- Effective governance
- Equitable representation
- Valuable Network

**Mission:** To ensure all trials recruiting people in Latin America are publicly registered.

Draft  
+Approve  
mission  
statement

### Leadership Passion

Select establish  
Secretariat  
champion!

Gather  
needs of  
countries

Annual  
Meeting?

Establish  
Advisory  
Board

CHAMPIONS!



### Advisory Board (Skills, Competencies needed) or Governance

- (Sponsor) who pays for trials (Funder)
- Researchers

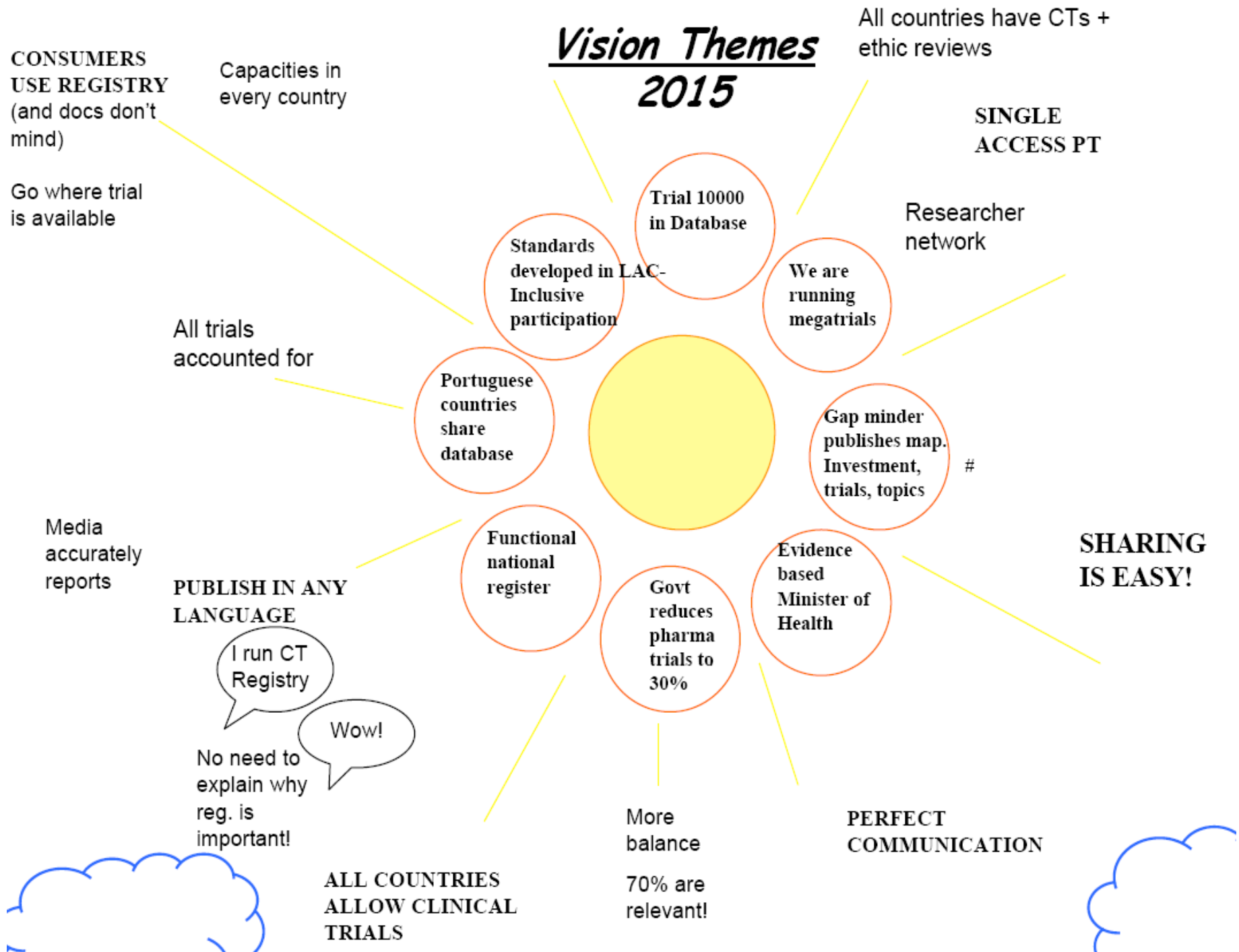
- Pharma
- People who want to publish
- Others don't know its needed

### Who knows Registration?

- Journals of region
- Ethics Committees
- Regulators

- Legislator

# *Vision Themes* **2015**





## Milestones

- Immediate (first 3 months)
- Short term (3-6 months)
- Medium term (6-24 months)
- Long term (24 months - 5 years)

	Activities	Timeline	Responsibilities	Remarks
1.1	Establish the Working Group	Immediate		
1.2	Working Group agrees on processes to follow (meeting intervals, dissemination of minutes, etc.)	Immediate		
1.4	Prepare concept paper	Immediate		
1.5	Disclose concept paper to the Working Group	Immediate		
2.2	First draft of strategic plan	Short term		
2.5	Prepare manuscript for publication (recognizing need: based on concept paper)	Short term		
2.6	Disclose manuscript to the Working Group	Short term		
2.8	Submit manuscript	Medium term		
2.9	Finalize strategic plan	Short term		
3.2	Agree on pilot projects	Medium term		
3.3	Approach potential funding agencies	Medium term		
4.1	Conduct needs assessment for LACCTR	Medium term		
4.2	Develop plan for LACCTR database development based on results of needs assessment	Medium term		

## List of Participants

PAHO HQ Participants	Organization	Country
Carolina O'Donnell	Ministerio de Salud de la Nación	Argentina
Dirce Guilhem	FLACEIS	Brazil
Josué Laguardia	REBRAC, Researcher Instituto de Comunicacao e Informacao Cientifica e Tecnologica en Saude	Brazil
Trudo Lemmens	ACHR	Canada, Toronto
Jordi Pardo	ICCN	Canada
Gabriel Rada	EVIPNet Support Group	Chile, Santiago
Marisol Navarrete	Ministerio de Salud	Chile, Santiago
Juana Tobos	Invima	Colombia
Ludovic Reveiz	Latinrec	Colombia, Bogotá
Maribel Gómez	ICTRP	Costa Rica
Ileana Herrera	PAHO	Costa Rica, San José
María Amparo Pascual	Ministerio de Salud	Cuba
Kay Dickersin	Cochrane/ICTRP	USA, Baltimore
Juliana Villabona	PAHO	USA, WDC
Luis Gabriel Cuervo	PAHO	USA, WDC
Sergio Muñoz	PAHO	USA, WDC
Jose Luis Castro	PAHO/HSS MT	USA, WDC
Ana Lucia Ruggiero	PAHO	USA, WDC
Marcelo D'Agostino	PAHO	USA, WDC
Luciano Ramalho	BIREME	Brazil, Sao Paulo
Davina Gherzi	WHO/HQ	Switzerland, Geneva
Ghassan Karam	WHO/HQ	Switzerland, Geneva
Amber Abrams	PACTR	South Africa, Cape Town
Deborah Zarin	NIH - Clinical Trials	USA, WDC
Kayla Kirsch	FACILITATOR	

## Acronyms

Acronym	Term	Remarks
LACCTR	Latin America and The Caribbean Clinical Trial Registry	
CIOMS	Council for International Organizations of Medical Sciences	

DoH	Declaration of Helsinki	
REC	Research Ethics Committee	May also be referred to as EC (Ethics Committee), REC (Research Ethics Committee) or similarly
EMA	European Medicines Agency	
FDA	Food and Drug Administration	
GCP	Good Clinical Practice	
ICH	International Conference on Harmonization	
ICMJE	International Committee of Medical Journal Editors	
ICTRP	International Clinical Trial Registry Platform	<a href="http://www.who.int/ictip">http://www.who.int/ictip</a>
IRB	Institutional Review Board	
MoH	Ministry of Health	
NRA	National Regulatory Authority	
PACTR	Pan African Clinical Trial Registry	
PAHO	Pan American Health Organization	
WHO	World Health Organization	

## Glossary

### Best Practice for Clinical Trial Registries

Best Practice for Clinical Trial Registries documents the minimum standards expected of clinical trials registries in relation to all aspects of their work. They include, but are not restricted to, minimum standards for:

- Minimizing (unplanned) duplicate registration of single trials
- Validation
- Compliance
- Comprehensiveness
- Databases
- Data sharing

## 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, radiology procedures, devices, behavioral treatments, process-of-care changes, preventive care, etc. This definition includes [Phase I to Phase IV trials](#).

## Clinical Trial Register

The formal record of an internationally agreed minimum amount of information about a clinical trial ([trial registration data set](#)). This record is usually stored in and managed using a database.

## Clinical Trial Registry

The entity that houses the clinical trial register. It is responsible for ensuring the completeness and accuracy of the information the register contains, and that the registered information is used to make informed health care decisions.

## Partner Registries

Partner Registries meet the same criteria as Primary Registries in the WHO Registry Network (i.e. for content, quality and validity, etc) except they do not need to:

- Have a national or regional remit or the support of government
- Be managed by a not-for-profit agency
- Be open to all prospective registrants

For example, they may be limited to trials about a particular condition or intervention

As of October 1<sup>st</sup> 2008, all Partner Registries must also be affiliated with either a Primary Registry in the WHO Registry Network or an ICMJE approved registry.

It is the responsibility of Primary Registries in the WHO Registry Network to ensure that their Partner Registries meet [WHO Registry Criteria](#).

## Primary Registries in the WHO Registry Network

Primary Registries in the WHO Registry Network meet [specific criteria](#) for content, quality and validity, accessibility, unique identification, technical capacity and administration. Primary Registries meet the ICMJE requirements.