SACRA
SOUTH AFRICAN CLINICAL RESEARCH ASSOCIATION

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Integrating clinical trial information for South Africa

South African Clinical Trials Registry (SANCTR), Pan African Clinical Trials Registry (PACTR) and National Health Research Observatory

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Cochrane South Africa

Presented by: Duduzile Ndwandwe
28 September 2018

What is a clinical trial register?

A trials register is a database in which key administrative and scientific information about planned, ongoing and completed trials, with enough information to identify that trial's existence, is stored.

Clinical trial register

Open access, freely available online

Essay

Is Evidence-Based Medicine Relevant to the Developing World?

Systematic reviews have yet to achieve their potential as a resource for practitioners in developing countries

Paul Chinnock*, Nandi Siegfried, Mike Clarke

Although there is still some resistance to the evidence-based medicine movement, evidence-based health care has now become widely accepted and adopted. Systematic reviews of the effectiveness of health care interventions are the engine room of evidence-based health care; much has been written about how these reviews should be conducted and what they can achieve [1,2]. If the case for the use of systematic reviews is good in developed countries—and we think it is—then the case is even stronger in the developing world. Wherever health care is provided and used, it is essential to know which interventions work, which do not work, and which are likely to be harmful. This is especially important in situations where health problems are severe and the scarcity of resources makes it vital that they are not wasted [3].

But are the systematic reviews that have so far been published relevant and of practical use to those who provide health care in "the majority world" (i.e., in developing countries)? In our view, the relevance of systematic reviews to frontline health care workers in developing countries has so far been limited, for a number of reasons.

Reasons Why the Relevance Is Limited

Conditions. Most of the reviews produced to date address health conditions that are priorities in the developed world [4]. Many major health concerns in developing nations have yet to be made the subject of a review, although there are signs that this may be changing [5]. The introductory discussions of most reviews focus on the impact of conditions in the United States and Western Europe.

This may be an indication of the authors' own priorities and experience, or it may be because they have made assumptions about the priorities of journal editors and readers.

Interventions. Health care professionals in developing countries sometimes wonder whether their reliance on older, cheaper, "low-tech" approaches has made their practice quite distinct from that of their colleagues in richer regions [6]. Yet the authors of systematic reviews seem, by and large, to prefer to take on the task of assessing the evidence for more recent (and generally more expensive) technologies. This is not to say that reviewers should avoid high-tech interventions. Again, it is a question of setting priorities, and of recognising the urgent need for more reviews on interventions that are feasible in the majority world.

Health care practitioners in developing countries need the most appropriate evidence to guide their practice
(Photo: World Health Organization/P. Virot)

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Competing Interests: The author's employers are dependent upon the relevance and importance given to systematic reviews.

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"Wherever health care is provided and used, it is essential to know which interventions work, which do not work, and which are likely to be harmful. This is especially important in situations where health problems are severe and the scarcity of resources makes it vital that they are not wasted."

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Clinical trial register

- "... it is usually a body of evidence, consisting of many studies that changes medical practice. When research sponsors or investigators conceal the presence of selected trials, these studies cannot influence the thinking of patients, clinicians, other researchers, and experts who write practice guidelines.

  … If all trials are registered in a public repository at their inception, every trial's existence is part of the public record, and the many stakeholders in clinical trial research can explore the full range of clinical evidence."

ICMJE statement 2004; JAMA, 15 September 2004 – 292 (11)

National Health Research Observatory in South Africa

- Health research observatories are globally recognised proactive institutions that provide appropriate evidence-based information to guide policy-making decisions in a country, thereby improving health care.
- National Health Research Observatory has been established as a comprehensive information and translation system
  - to enable the national co-ordination and integration of research and health information from the country's multiple research platforms

Contribution towards the National Development Plan 2030

Table 1: Contribution of a National Health Research Observatory to the nine priorities of the National Development Plan 2030

National Development Plan priority	Possible contribution of a National Health Research Observatory
Address the social determinants that affect health and diseases	Provide an analysis of social factors that play a key role in determining health status
Strengthen the health system	Identify points of weakness in the health system and their underlying causes and make recommendations for appropriate solutions
Improve the health information system	Collate data from a range of sources; stratify, repackage, translate and disseminate the information in ways that make it accessible for use by different stakeholders
Prevent and reduce the disease burden and promote health	Contribute to the identification of the types and levels of the burden of disease; make recommendations for their prevention, reduction and mitigation
Finance universal health care coverage	Analysis of health care financing; assist in identifying sources, levels and types of healthcare financing available, and identify gaps in universal coverage
Improve human resources in the health sector	Analysis of the full-time equivalents for health sector human resources to reliably determine the quality, qualifications and numbers needed for provision of adequate health care
Review management positions and appointments, and strengthen accountability mechanisms	Analyse data on management functions and infrastructure needs; map out trends in skills availability and thus influence accountability and evidence-based policy- and decision-making
Improve quality by using evidence	Analyse all data received and provide feedback for translation of research into practice; make findings accessible to all stakeholders for improved quality of health care
Meaningful public-private partnerships	Vigilance on events and trends leading to balanced feedback to all sectors will enable development of meaningful partnerships between public and private sector stakeholders to help parties engage in using synergies for mutual benefit

Clinical trial registers can play an important role

What is a clinical trials register?

- A database in which key administrative and scientific information about planned, ongoing and completed trials, sufficient to identify that trial's existence, is stored.
- The 2004 Ministerial Summit on Health Research called on the WHO to establish:

  "a network of international clinical trial registers to ensure a single point of access and the unambiguous identification of trials."

The Birth of Clinical Trial Registration

August 2004: ICMJE prospective registration a precondition for publication

October 2004: Ministerial Summit on Health Research
"a network of international clinical trial registers to ensure a single point of access and the unambiguous identification of trials"

2005: 58th World Health Assembly call seconded

2005: WHO ICTRP (www.who.int/ictrp) developed out of project started to set norms and standards for clinical trial registration

2007: ICMJE updated their statement endorsing the WHO Primary Registry Network

What is the process to follow to register trials?

Currently two registries available in South Africa:

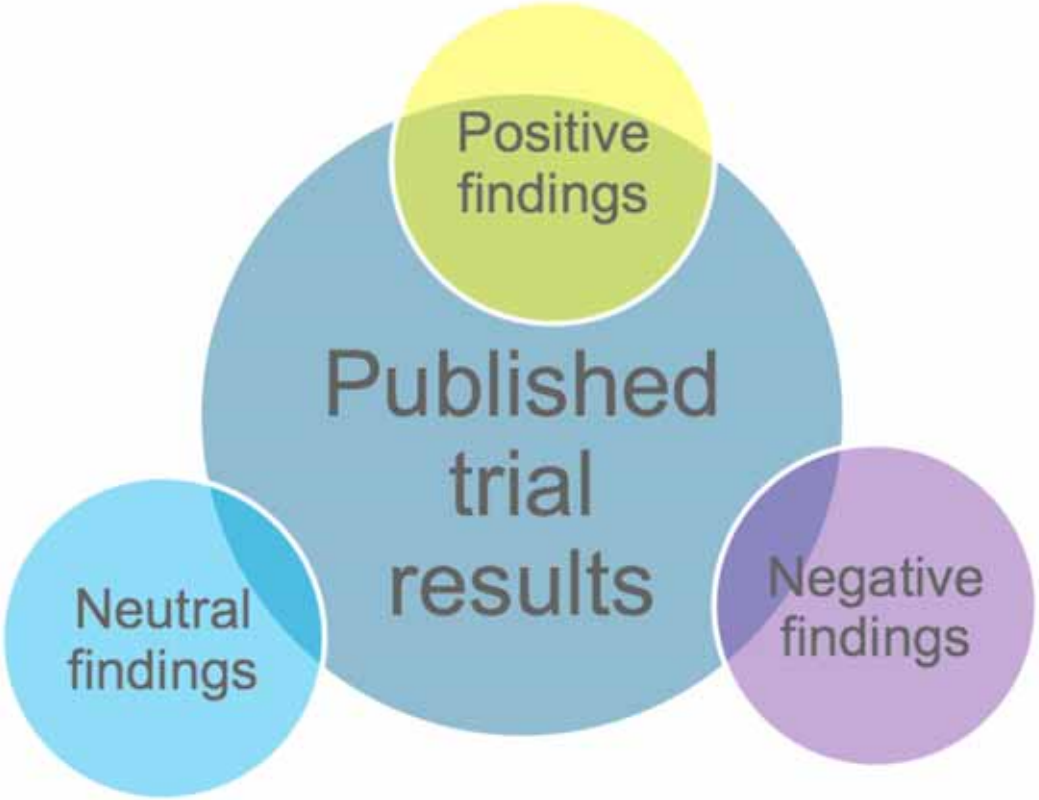
1. South African National Clinical Trials Registry
   - Important to get the NDoH number following ethics approval
   - NDoH number needed prior to recruitment
2. Pan African Clinical Trials Registry
   - To fulfil WHO and ICMJE mandates

Why register a clinical trial?

- Reduction of publication bias/ selective reporting of results
- Fulfill publication mandate
- Allows for transparency thus enhancing public trust
- Reduce duplication of research and the use of limited resources

What is publication bias?

- Publication bias = tendency to publish positive results
- Thus, it's easier to find more results that appear significant, because negative or neutral results are often not published



Publication Bias and Clinical Trial Registration

". . . it is usually a body of evidence, consisting of many studies that change medical practice. When research sponsors or investigators conceal the presence of selected trials, these studies cannot influence the thinking of patients, clinicians, other researchers, and experts who write practice guidelines . . .If all trials are registered in a public repository at their inception, every trial's existence is part of the public record, and the many stakeholders in clinical trial research can explore the full range of clinical evidence."

ICMJE statement 2004 (JAMA, 15 September 2004 – Vol. 292 No. 11)

Why Register?
Ethics

- Clinical trial registration can assist a researcher to fulfill ethical obligations to his/her participants
- But how?
  - First, what ethical imperatives must a trialist consider?
  - Second, how can a registry assist with this?
    - Ensure transparency and information dissemination (autonomy, do no harm, voluntary informed consent)
    - Enhance public trust in the conduct of clinical research (experiments should serve the public good)
    - Increase participant enrolment in research trials

An Example

In 2004, a lawsuit brought public attention to the issue of publication bias and selective reporting:

- GlaxoSmithKline (GSK; a pharma company) did not report contra-indications of a popular anti-depressant in children (e.g. suicides in young children)
- Efforts to hide data
- Staff were told to "effectively manage the dissemination of data" because it was "commercially unacceptable" to admit that paroxetine did not work in children
- Settlement led to birth of first legislated register: GSK was mandated to publish a registry of its trials

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC421770

Who is responsible for registration?

- A primary Sponsor
  - A primary sponsor does not have to be the primary funder, but takes responsibility for the initiation, management, and/or financing of a clinical trial
- Principal investigator (PI)
  - Overall oversight of the conduct of the study
- A person delegated by the PI to complete registration
  - E.g. Regulatory personnel within a study team

What types of trials should be registered?

For the purposes of registration, the WHO defines a clinical trial as:

"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. . . This definition includes Phase I to Phase IV trials."

When should a trial be registered?

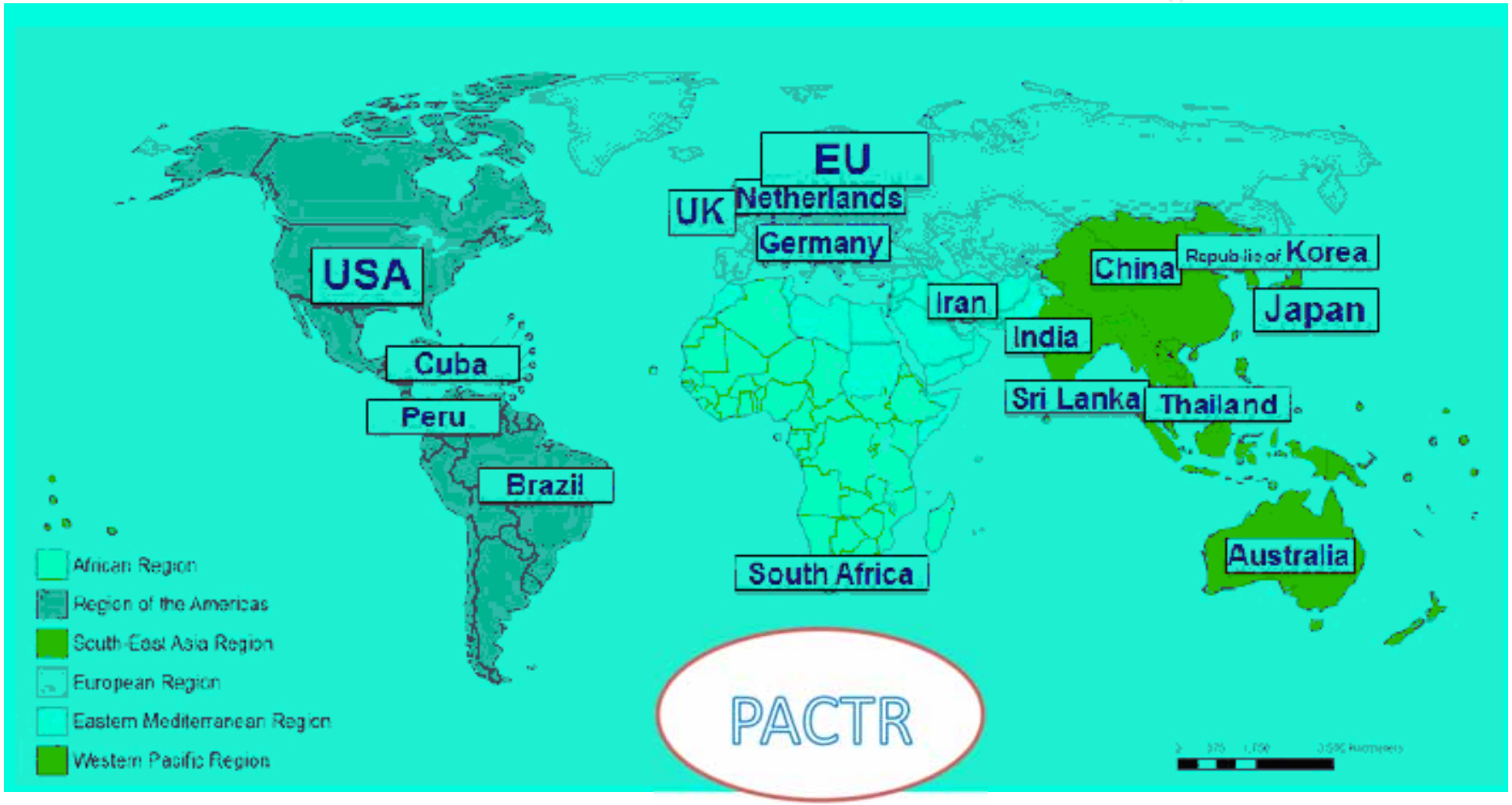
- Before the trial starts (also known as 'prospectively')
  - allows for a trial's outcomes and protocol to be tracked all the way through the course of the trial
  - ensures that objectives cannot be changed throughout the course of the trial
  - captures the intention of the trial from the outset, without allowing for adjustments of results that might not be favourable to the intervention

    . . . reduces publication bias

The World Health Organization & Clinical Trial Registration

- WHO hosts the International Clinical Trials Registry Platform (ICTRP)
- The WHO ICTRP is not a clinical trials registry but a platform that collects data from partner registries
- WHO ICTRP:
  - is a platform facilitating prospective registration of a minimum 24-item data set
  - harmonises and standardises
  - provides a searchable, one-stop portal for registered clinical trials globally

Location of primary registers



The Pan African Clinical Trials Registry *(www.pactr.org)*

1. Launched in September 2009
2. African researchers can register their trials with the only WHO registry in the region
3. African trial data contributes to global data on clinical trials through the ICTRP
4. PACTR provides feasible ways of overcoming obstacles specific to African trialists
5. Registration is free
6. PACTR is easy to search and free to access

PACTR - Strategic objectives

- Ensure research integrity by promoting prospective clinical trial registration.
- Provide a repository for registration of trials in Africa.
- Provide a searchable database of African trials.
- Facilitate investigation of the scope, quality and funding patterns of African trials.
- Enable the identification of research gaps for future studies.

Regional overview

- Facilitates understanding of regional research patterns, i.e. where research is over-done and participants are spread thin vs. places where research has not been conducted.
- Enable the identification of research gaps for future studies.
- Facilitate the investigation of the scope, quality and funding patterns of African trials.

Example

Studies conducted in Africa focusing on infectious & parasitic diseases

A resource for healthcare researchers

- A registry like PACTR can be a resource for:
  - understanding and locating current trial activity
  - determining where research is needed
  - determining if planned research duplicates work already in progress
  - determining appropriate collaborators
  - networking
- The scaling-up of health services can be assisted by the networking opportunities provided by www.pactr.org
- Information translation is more precise and funds are saved through the use of www.pactr.org by ensuring that researchers are not duplicating the efforts of others

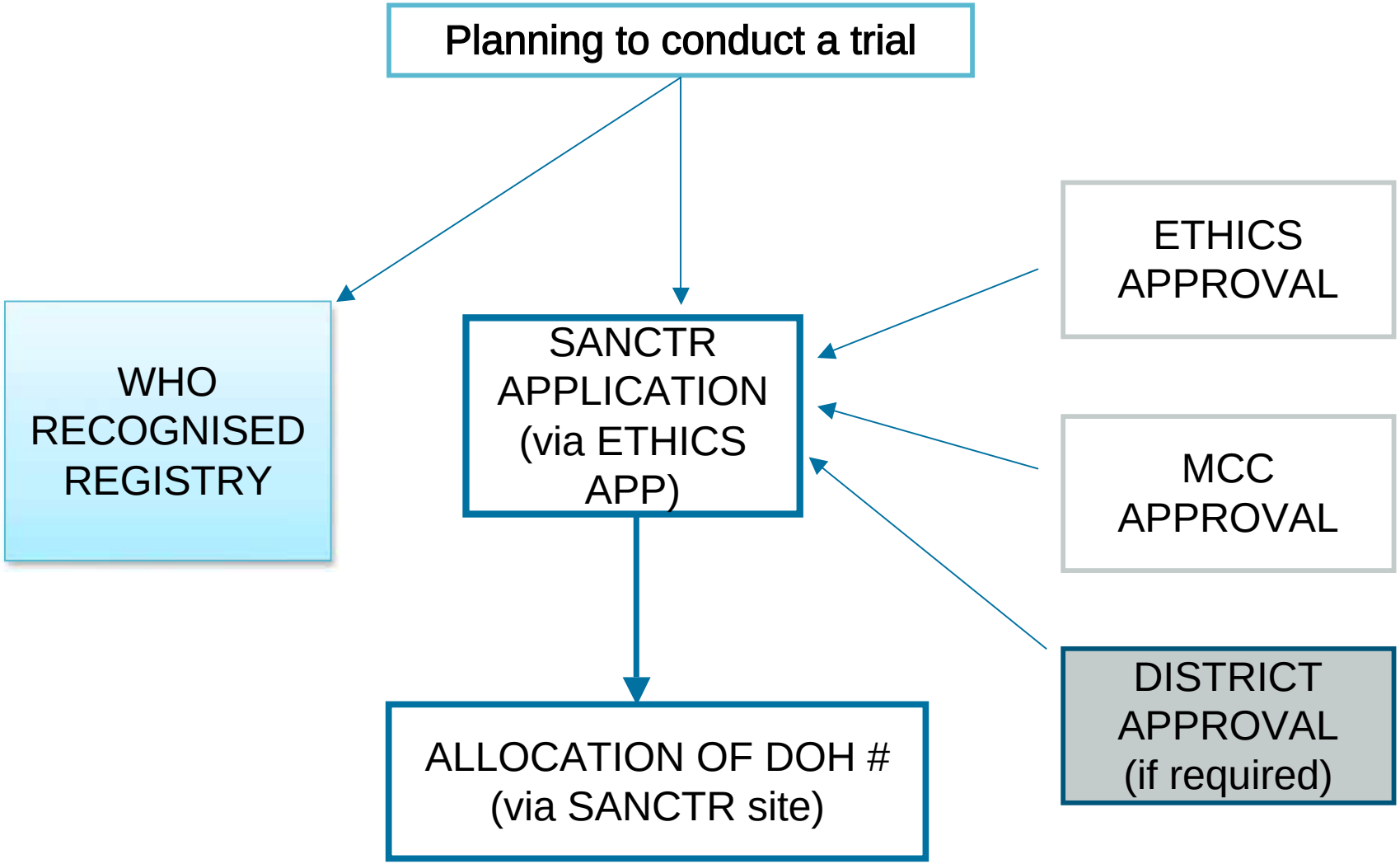
Linking SANCTR & PACTR

- Department of Health has requested SAMRC to support trial registration in SA and manage SANCTR
  - Ensure that SANCTR collects the WHO required data fields
  - Develop a formal partnering with a WHO recognised primary register (PACTR)
  - Minimise trialists burden to register twice in South Africa
  - New SANCTR team will verify each submission for collection of accurate data elements
  - Requires database redevelopment
  - SANCTR to be user friendly and searchable

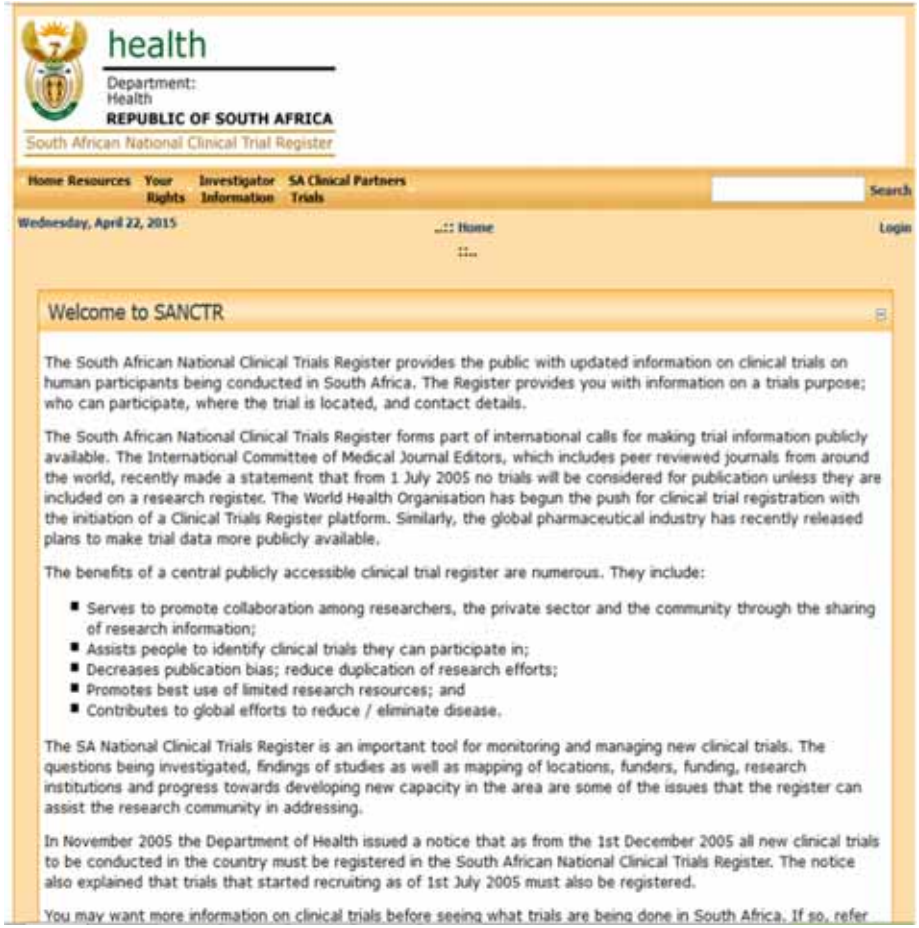
Progress: SANCTR integration with PACTR

- SANCTR was developed by Wits Health Consortium (WHC)
- SAMRC approached by the DoH in 2015 to redevelop the database
- SAMRC houses PACTR which conforms to the WHO data requirements and has technical and administrative skills
- SANCTR is in a process of being redeveloped. The redevelopment process includes the following activities:
  - Data migration of the data from WHC to a new database
  - Understanding the ideal flow for trial registration in SANCTR
  - Stakeholder consultation underway to ensure that SANCTR meets needs for SA while conforming to the international standards

What we understand the current process flow to be



Access to current SANCTR database



health

Department:
Health
REPUBLIC OF SOUTH AFRICA

South African National Clinical Trial Register

Home Resources Your Rights Investigator Information SA Clinical Partners Trials Search

Wednesday, April 22, 2015 ..:: Home ::.. Login

Welcome to SANCTR

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides you with information on a trials purpose; who can participate, where the trial is located, and contact details.

The South African National Clinical Trials Register forms part of international calls for making trial information publicly available. The International Committee of Medical Journal Editors, which includes peer reviewed journals from around the world, recently made a statement that from 1 July 2005 no trials will be considered for publication unless they are included on a research register. The World Health Organisation has begun the push for clinical trial registration with the initiation of a Clinical Trials Register platform. Similarly, the global pharmaceutical industry has recently released plans to make trial data more publicly available.

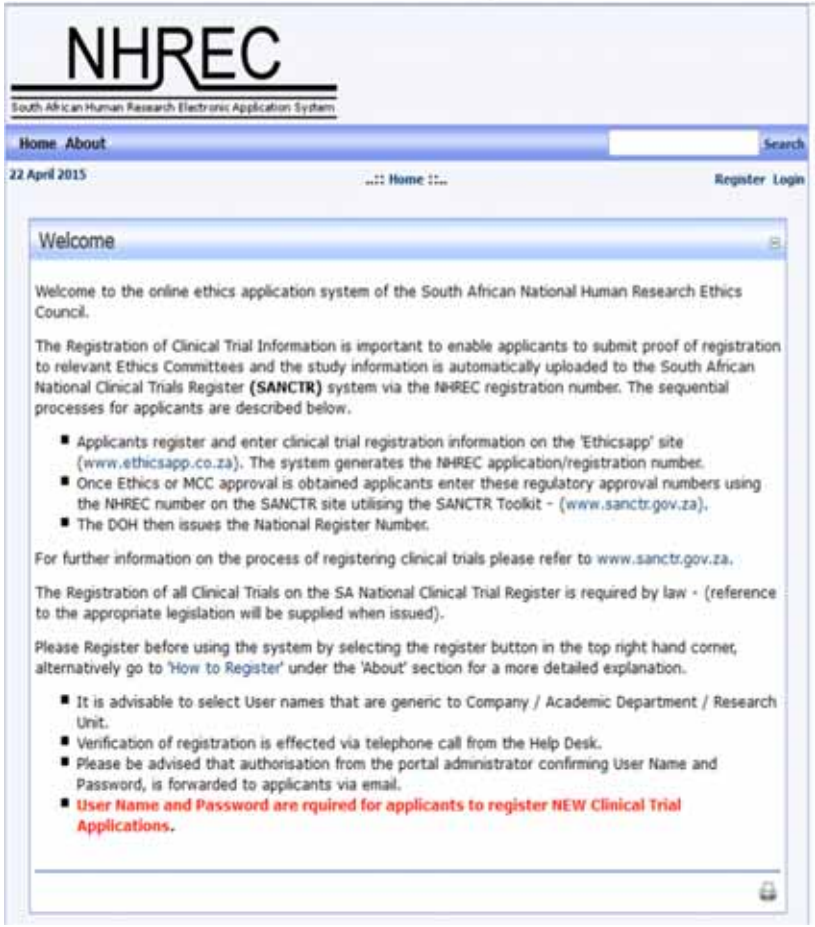
The benefits of a central publicly accessible clinical trial register are numerous. They include:

- Serves to promote collaboration among researchers, the private sector and the community through the sharing of research information;
- Assists people to identify clinical trials they can participate in;
- Decreases publication bias; reduce duplication of research efforts;
- Promotes best use of limited research resources; and
- Contributes to global efforts to reduce / eliminate disease.

The SA National Clinical Trials Register is an important tool for monitoring and managing new clinical trials. The questions being investigated, findings of studies as well as mapping of locations, funders, funding, research institutions and progress towards developing new capacity in the area are some of the issues that the register can assist the research community in addressing.

In November 2005 the Department of Health issued a notice that as from the 1st December 2005 all new clinical trials to be conducted in the country must be registered in the South African National Clinical Trials Register. The notice also explained that trials that started recruiting as of 1st July 2005 must also be registered.

You may want more information on clinical trials before seeing what trials are being done in South Africa. If so, refer



NHREC

South African Human Research Electronic Application System

Home About Search

22 April 2015 ..:: Home ::.. Register Login

Welcome

Welcome to the online ethics application system of the South African National Human Research Ethics Council.

The Registration of Clinical Trial Information is important to enable applicants to submit proof of registration to relevant Ethics Committees and the study information is automatically uploaded to the South African National Clinical Trials Register **(SANCTR)** system via the NHREC registration number. The sequential processes for applicants are described below.

- Applicants register and enter clinical trial registration information on the 'Ethicsapp' site (www.ethicsapp.co.za). The system generates the NHREC application/registration number.
- Once Ethics or MCC approval is obtained applicants enter these regulatory approval numbers using the NHREC number on the SANCTR site utilising the SANCTR Toolkit - (www.sanctr.gov.za).
- The DOH then issues the National Register Number.

For further information on the process of registering clinical trials please refer to www.sanctr.gov.za.

The Registration of all Clinical Trials on the SA National Clinical Trial Register is required by law - (reference to the appropriate legislation will be supplied when issued).

Please Register before using the system by selecting the register button in the top right hand corner, alternatively go to 'How to Register' under the 'About' section for a more detailed explanation.

- It is advisable to select User names that are generic to Company / Academic Department / Research Unit.
- Verification of registration is effected via telephone call from the Help Desk.
- Please be advised that authorisation from the portal administrator confirming User Name and Password, is forwarded to applicants via email.
- **User Name and Password are rquired for applicants to register NEW Clinical Trial Applications.**

Purpose for redevelopment of SANCTR

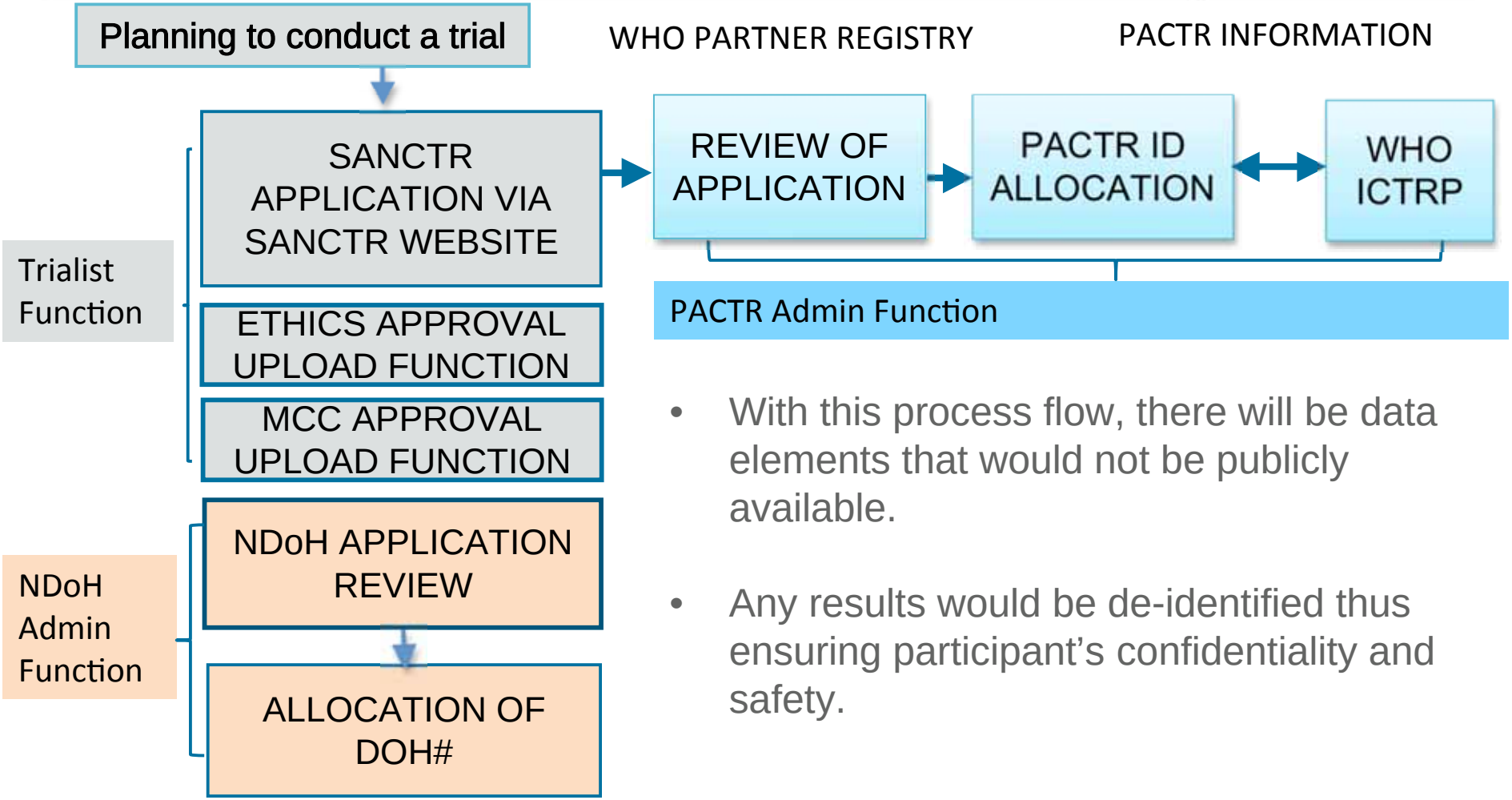
Ensure SANCTR database conforms to WHO requirements

Consultation with various stakeholders that play an important role in shaping the redevelopment of SANCTR registry is important

Meet regulatory requirements to conduct a clinical trial in the country

Reduce administrative burden for trialist

Proposed integration of SANCTR to PACTR

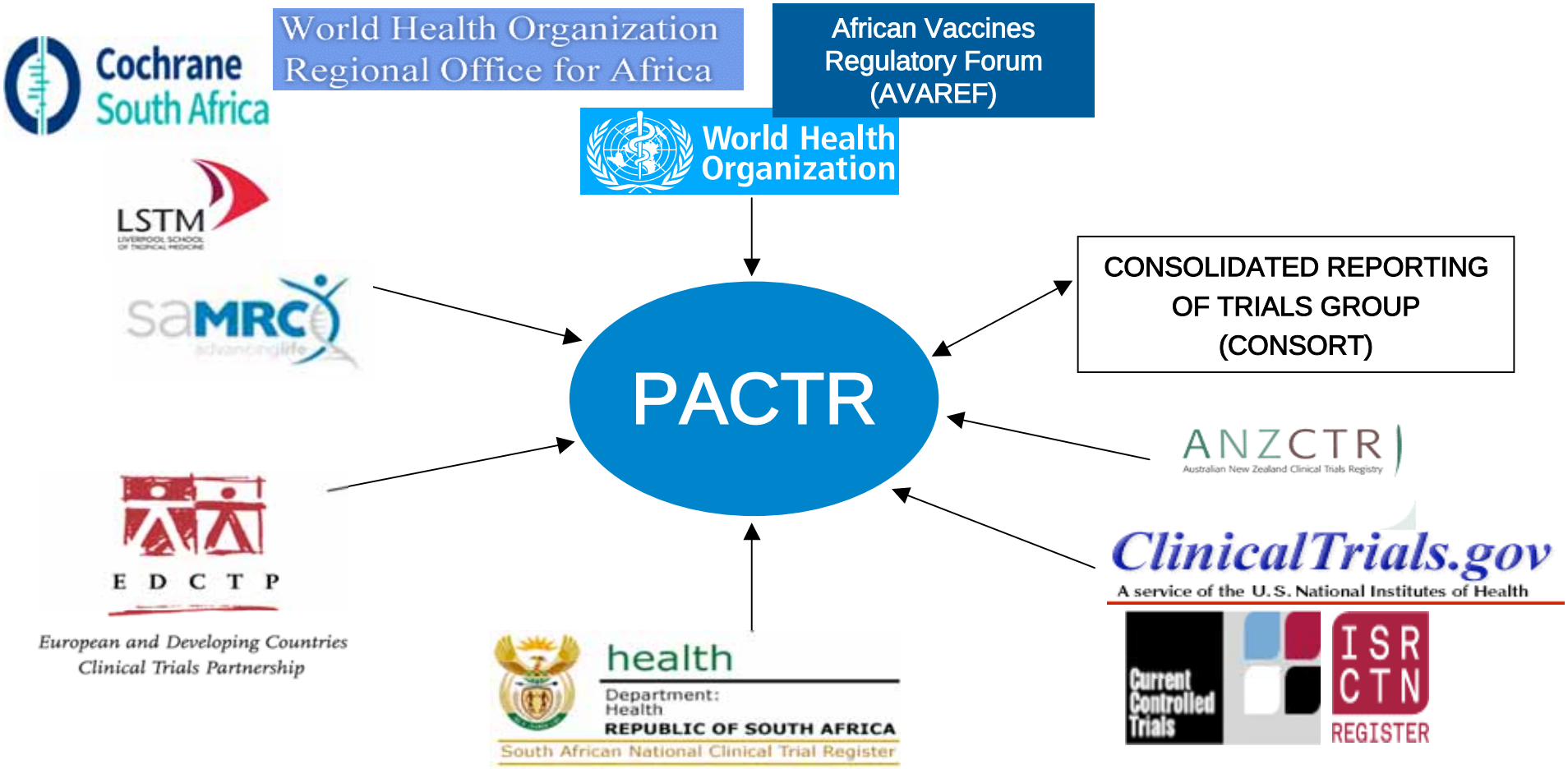


- With this process flow, there will be data elements that would not be publicly available.
- Any results would be de-identified thus ensuring participant's confidentiality and safety.

Integration with National Health Research Observatory

- SANCTR provides a platform for improved health information systems
- With the proposed flow we would ensure that SANCTR conforms to the WHO standards as well as the requirement to the country
- **SANCTR has a potential to be further developed to provide a one-stop shop for all health research information in one portal**
- Thus reducing the multiple platforms that collects clinical research conducted in the country
- For this, we need consultation and innovative ideas

Acknowledgements



Thank you……