WHO International Clinical Trials Registry Platform

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Outline

- Background
- Registry Platform Governance and Structure
- Registry Platform Overview
  - Trial Registration Data Set
  - Network of Member Registers
  - Universal Trial Reference Number
  - Search Portal
- Summary
Need for Trial Registration and Reporting

- Clinical trials “gold standard” experiment for health interventions
- Extensive media coverage of several cases of selective reporting of results
- Trial registration and full results reporting would help ensure a full unbiased public record on safety and effectiveness
- Restore public trust, avoid drop in participant enrollment
Current Policies

- The International Committee of Medical Journal Editors (ICMJE) now accepts only registered trials for potential publication
- Many Ethics Review Boards (ERBs) requiring registration before ethics approval
- Local and national laws beginning to require trial registration
Need for Standardization, Coordination

- Growing number of registers worldwide
  - different requirements for submission
  - serving different constituencies (country, disease, and/or funder-specific)
  - purposes (recruitment, tracking, analysis)
- Multiple, diverse stakeholders
- Legislative overload
Why World Health Organization?

- Global, neutral, independent body with convening capacity (i.e. World Health Assembly resolutions)
- Authoritative; sets norms and standards in research, policy and practice
- Political legitimacy, accountable to 192 member States
- Contributes to capacity building
- Commitment to achieving world equity in health
Leading up to WHO Registry Platform

- **Oct 03**
  - WHO Director-General highlighted trial registration as example of WHO role in global health research

- **Oct 04** – Rockefeller Foundation meeting, NY
  - WHO to formulate global approach to trial registration

- **Nov 04** – Ministerial Summit, Mexico City, called on WHO to
  - establish network of clinical trial registers
  - ensure unambiguous identification of trials
  - ensure a single point of access
Leading up to WHO Registry Platform

- **April 2005** – Technical Consultation, Geneva
  - Meeting of diverse stakeholders to build consensus policies

- **May 2005** – 58th World Health Assembly
"We are ready to move forward with an international Clinical Trials Registry. This will do much to strengthen the research process and its ability to win public trust"
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Governance and Structure

- WHO EIP/RPC
- Registry Platform Secretariat

International Advisory Board (16 members)
- endorses strategy/direction

Scientific Advisory Group (19 members)
- advises on principles/substantive standards

- Secretariat in RPC

International Advisory Board (IAB)

Chair
- **Sir Richard Sykes**, Rector, Imperial College, UK

Members
- **Alan Bernstein**, President, Canadian Institutes of Health Research, Canada
- **Gail Cassell**, Vice President Scientific Affairs, Eli Lilly, USA
- **Iain Chalmers**, Editor, James Lind Library, UK
- **Heng-Leng Chee**, Asia Research Institute, National University of Singapore
- **Nirmal K. Ganguly**, Director General, Indian Council for Medical Research, India
- **Victoria Hale**, CEO, One World Health, USA
- **Ching-Li Hu**, Director, Shanghai Research Center for Care for Children, China
- **Ana Langer**, EngenderHealth, USA
- **Caroline Loew**, Vice President, Scientific & Regulatory Affairs, PhRMA, USA
- **Pascoal Mocumbi**, European Developing Countries Clinical Trials Partnership, Netherlands
- **Carlos Morel**, Director, Center for Technological Development in Health, Fiocruz, Brazil
- **Kathy Redmond**, European Cancer Patient Coalition (ECPC), Milan, Italy
- **Joerg Reinhardt**, Head of Development, Novartis, Switzerland
- **Hideo Shinozaki**, President, National Institute of Public Health, Japan
- **Hal Sox**, Editor, Annals of Internal Medicine, USA
Scientific Advisory Group (SAG)

Co-Chairs
- Kay Dickersin, Johns Hopkins Bloomberg School of Public Health, MD, USA
- Richard Horton, The Lancet, UK

Members
- Gerd Antes, Deutsches Cochrane Zentrum, Germany
- Chris Chute, Mayo Clinic, USA
- Francis Crawley, European Forum for Good Clinical Practice, Belgium
- Jeffrey Drazen, Editor, New England Journal of Medicine, USA
- Davina Ghersi, University of Sydney, Australia
- Anne Greenwood, Current Science Group, UK
- Karmela Krleza-Jeric, Canadian Institutes of Health Research, Canada
- Rebecca Kush, Clinical Data Interchange Standards Consortium, USA
- David Moher, Children’s Hospital of Eastern Ontario, Canada
- Philip Noguchi, Director Regulatory Affairs, Amgen, USA
- Frank Rockhold, Senior Vice President, GlaxoSmithKline, USA
- Marc Taylor, UK Department of Health, UK
- Toshiro Tango, Director, Technology Assessment, Japan
- Jimmy Volmink, University of Cape Town, South Africa
- Liz Wager, Sideview Consulting, UK
- Janet Wale, Cochrane Consumer Network, Australia
- Deborah Zarin, ClinicalTrials.gov, USA
Strategic Plan

- Near-term funding
  - Internal startup funds
  - External support
    - Department of Health, UK
    - Wellcome Trust
  - Awaiting responses on foundation grant, other requests

- Considering various models of partnership going forward
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Which Trials Must Register

- All interventional trials
  - all health interventions (drugs, devices, procedures, behavioural treatments, care process changes, etc)
- All hypothesis-testing trials
  - Marketed and not-yet-approved products
  - Primary and secondary indications
- Strongly encourage registration of exploratory trials
- If in doubt, register
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Trial Registration Data Set (1)

1. Primary Register and Trial ID# (e.g., ISRCTN #)
2. Date of Registration in Primary Register
3. Secondary ID#s (e.g., study #, ERB #)
4. Funding Source(s)
5. Primary Sponsor
6. Secondary Sponsor(s)
7. Responsible Contact Person
8. Research Contact Person
9. Public Title
10. Scientific Title
Trial Registration Data Set (2)

11. Research Ethics Review
12. Disease or Condition Studied
13. Intervention(s)
14. Inclusion & Exclusion Criteria
15. Study Type
16. Date of First Enrollment
17. Target Sample Size
18. Recruitment Status at time of registration
19. Primary Outcome(s)
20. Secondary Outcome(s)
Threats to Competitive Advantage?

- "Public registration gives the scientific idea away to competitors and threatens our success"
  - Pharmaceutical and biotech industry
  - Investigators from developing countries

- Pharmaceutical industry position, "lockbox" (IFPMA, Sep 05)
  - For trials of their choosing, will disclose these items only after product is approved for indication studied
    - scientific title
    - target sample size
    - interventions
    - primary and secondary outcomes
Balancing Against Transparency

- Selective disclosure threatens integrity of the clinical research system
  - Scientific integrity
    - Need all trials fully registered and disclosed at outset to ensure full, unbiased disclosure of results
  - Ethical integrity
    - Participants enroll expecting to contribute to public knowledge, not to have results hidden
    - Public disclosure helps avoid unnecessary duplication, harm to participants
- Working on a mutually acceptable compromise
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A Standard for Registers

- Ideally, want single definition for what is an internationally acceptable register
  - for medical journal (ICMJE) acceptability
  - for use in local, national, and international legislation
Key Register Acceptability Criteria

- Collect full Trial Registration Data Set
- Participate in global trial duplication checking (e.g., request Universal Trial Reference Number)
- Adopt common technical standard for exchanging data
- Be searchable by public at no charge
- Must not have conflicts of interest over which trials or trial information to register
Register Network Membership

- Registers meeting criteria for will
  - become Members of the Network of Registers
  - qualify for ICMJE acceptance
- Trial investigators to register in one and preferably only one Member Register
  - fewest number of registers necessary to meet local regulations
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Universal Trial Reference Number

- Trials might be registered in more than one register, leading to confusion
  - For patients wanting to enroll in trials
  - For scientists who may overcount results
- Need to clearly identify duplicate registrations
  - WHO planning to assign UTRNs
    - globally unique number to cross-reference same trial across registers worldwide
    - Only Member Registers can apply for a UTRN
- Some resistance to a "new number"
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Open Access One-Stop Search Portal

- WHO Search Portal to search registers worldwide
  - All Member Registers
  - Link to registers for full information and results
- WHO may code conditions, interventions, primary and secondary outcomes fields in MeSH
  - Improve search performance over registers’ free text entries
- Provides neutral “public face” of trial registration worldwide
  - (re)build public trust and confidence
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Value Added of Registry Platform

- Only neutral body well-placed to define standards
  - Registration Data Set (and "lockbox")
  - Results reporting standards
- Single international definition and network of high-quality registers
  - Simplifies, coordinates where to register
  - Global accountability, sharing of best practices
- Duplication checking and unique trial identification (UTRN)
  - Enhances global integrity and information quality
- One-stop search portal of registers worldwide
  - "Public face," transparency, restore trust/confidence
Approximate Project Timeline

Q4 2005
- Finalize Trial Registration Data Set

Q1 2006
- Establish Network of Member Registers

Q2 2006
- Establish duplication checking and UTRN assignment
- Launch Registry Platform Search Portal
Conclusion

- Clinical trials transparency and public trust is a global issue
- WHO taking lead on policy and technical platform for coordinated trial registration and reporting worldwide
- Overriding principle is to promote scientific and ethical integrity in clinical trial research
- Invite comments and consultation as Registry Platform develops
WHO Registry Platform Team

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http://www.who.int/ictrp