The Ottawa Statement, Part One:
Principles for international registration of protocol information and results from human trials of health-related interventions

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A. Objective

The Ottawa Statement aims to establish internationally recognised principles for trial registration (Part 1) as well as their proposed operationalisation (Part 2).[1]

B. Definitions

'Trial' refers to a prospective controlled or uncontrolled research study evaluating the effects of one or more health-related interventions assigned to human participants. For example, a trial may investigate interventions related to one or more of the following: prevention, health promotion, screening, diagnosis, treatment, rehabilitation, or organisation and financing of care.

'Intervention' refers to a deliberate act applied to an individual or group of individuals. Health-related interventions include but are not limited to the use of pharmaceuticals, biological products, surgery, procedures, radiation, devices, education, counselling, behaviour change, complementary health modalities, and management or economic policies.

[1] The operationalisation of these principles is under development and will be presented in a separate

‘Registration’ of a trial involves the assignment of a unique identification number; the recording and public release of protocol information; as well as the recording and public release of trial results.

‘Protocol’ refers to a document written before participant enrolment to describe the objectives, methodology, statistical analyses, organisation, and administrative details of a trial.

‘International’ refers to the applicability of the principles presented in this document to trials conducted in any country or countries worldwide.

‘Sponsor’ is defined as an individual, company, institution, or organisation that takes responsibility for the initiation, management, and/or financing of a trial. The sponsor does not actually conduct the investigation unless the sponsor is an investigator-sponsor.

‘Principal investigator’ is defined as the person responsible for the overall conduct of the trial.

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document as Part 2 of the Ottawa Statement.

C. Rationale for international trial registration

C.1. Ethical rationale

C.1.1. Above all, international trial registration is necessary to fulfill ethical obligations to research participants. When members of the public agree to participate in trials, it is on the understanding that they are contributing to the global body of health-related knowledge. It is thus unethical to conduct human research without ensuring that valid descriptions of the study and its findings are publicly available.

C.1.2. Potential trial participants, care providers, researchers, institutional review boards/independent ethics committees (IRBs/IECs), and sponsors should have access to valid information about trials that have been previously performed.

C.1.3. Potential trial participants, care providers, researchers, IRBs/IECs, and sponsors should have access to valid information about trials that are currently open for enrolment.

C.1.4. The availability of unbiased information about all initiated trials contributes to global open access to knowledge, which constitutes a public good.

C.2. Scientific rationale

Public access to trial protocol information (as approved by the IRB/IEC) and results will help to:

C.2.1. Minimise known risks and potential harm arising from unnecessary exposure to previously tested interventions;

C.2.2. Accelerate research by making knowledge available about prior experiences with interventions;

C.2.3. Identify and deter unnecessary duplication of research and publications;

C.2.4. Identify and deter selective reporting of research (reporting biases);

C.2.5. Provide a means of comparing the original protocol upon which ethics approval was based with the study as it was carried out;

C.2.6. Enhance collaboration among researchers by informing them of ongoing trials.

D. Principles regarding the scope and nature of international trial registration

D.1. Types of trials to be registered

Protocol information (D.4) and results (D.5) from all trials related to health or healthcare – regardless of topic, design, outcomes, or market status of interventions examined – should be registered and publicly available.

D.2. Elements of registration

Registration of each trial comprises three distinct parts: obtaining an internationally unique identification number (D.3), registering the original protocol approved by the IRB/IEC along with subsequent amendments (D.4), and registering the trial results (D.5). A general time-line for registration is shown in the Figure.

D.3. Principles relating to unique identification number (Unique ID)

D.3.1. Assignment of Unique ID

Every trial should have a Unique ID assigned by a single international source prior to participant enrolment. The Unique ID should be verifiable and have built-in error-detecting logic.

D.3.2. Application of Unique ID

The Unique ID should appear on all trial documentation, including the consent form given to participants as well as subsequent presentations and publications.

D.4. Principles relating to protocol registration

D.4.1. Definition of protocol information to be registered

Protocol information in the register should consist of (1) a minimum set of standardised, structured, key items from the protocol approved by the IRB/IEC ("minimum protocol items"); (2) the consent forms approved by the IRB/IEC; and (3) any subsequent protocol amendments. Protocol information from each of these components should be irreversibly recorded and dated at the time of submission to the register (D.4.2). The minimum protocol items registered should be sufficient to enable critical appraisal of trial methodology and statistical analyses. Furthermore, the full protocol as approved by the IRB/IEC, and the data collection forms, should be available in the public domain to enable the interpretation of trial findings.

D.4.2. Timing of protocol registration

Registration of the minimum protocol items and the consent forms should occur prior to enrolment of trial participants. Amendments to the registered protocol information should be dated and registered as they occur.

D.4.3. Timing of public access to registered protocol information

The public should have cost-free access to the Unique ID, minimum protocol items, and consent forms prior to participant enrolment. Registered amendments should be made publicly available as they occur. The full protocol as approved by the IRB/IEC, and the data collection forms, should be made publicly available as soon as possible and no later than the date of completion of data analysis.

D.5. Principles relating to registration of trial results

D.5.1. Definition of trial results to be registered

At a minimum, results for outcomes and analyses specified in the protocol (as approved by the IRB/IEC), as well as data on harms, should be registered regardless of whether or not they are published. If a trial is terminated prematurely, any available results should be registered along with the reason for termination.

The summary results recorded for each outcome should be sufficient for valid interpretation, and should not enable identification of any individual trial participant to the public.

Full citations to trial publications should be registered as they become available. However, listing of study publications alone does not constitute adequate registration of results.

D.5.2. Timing of registration of trial results

Trial results should be registered once the analyses are completed and verified.

D.5.3. Timing of public access to registered results

Investigators should have sufficient time to publish their findings in a peer-reviewed electronic or print forum before the registered results are released for public, free-of-charge access. Timely public access to results should ultimately be assured regardless of their publication status.

D.6. Organisation and language of registries

The source assigning the Unique ID can exist separately from the register or registers that contain protocol information and trial results. However, all three components (Unique ID, protocol information, trial results) must be cross-referenced.

To facilitate efficient searching, multiple national or regional registers should be linked. Furthermore, registered information must be presented at least in English and also preferably in the major language(s) of the region where the main study

site is located.

E. Responsibilities of involved parties

E.1. Sponsors

The sponsor(s) of the trial has ultimate responsibility for obtaining the Unique ID (D.3) as well as for registering the protocol information (D.4) and results (D.5). The sponsor should also ensure that the full protocol as approved by the IRB/IEC, and the data collection forms, are made publicly available. When there are multiple sponsors, each sponsor is individually responsible for ensuring that these tasks are fulfilled.

E.2. Investigators

The principal investigator has a responsibility to ensure that the sponsor(s) obtains a Unique ID and registers his or her contact information, the protocol information (D.4), and the trial results (D.5). Investigators also have the responsibility to perform analyses in a timely fashion and to submit the findings for publication in a peer-reviewed electronic or print forum.

E.3. Institutional review boards/independent ethics committees

IRBs/IECs have a responsibility to ensure that approved trials have a Unique ID; that minimum protocol items and consent forms, as approved by the board, are registered prior to participant enrolment; and that subsequent protocol

amendments are reported and registered. They are also responsible for ensuring that the Unique ID appears on the consent form. Furthermore, they are responsible for encouraging the publication of trial results in a peer-reviewed electronic or print forum. When a trial receives approval from multiple IRBs/IECs, each board is responsible for ensuring that these tasks are fulfilled.

E.4. Journal editors

Journal editors have a responsibility to promote trial registration by requiring that any trial being considered for publication has a Unique ID, and to include the Unique ID in any resulting publication.

E.5. Policing and sanctions

Trial registration should be a legal requirement, with enforcement of meaningful sanctions against those found to be in violation.

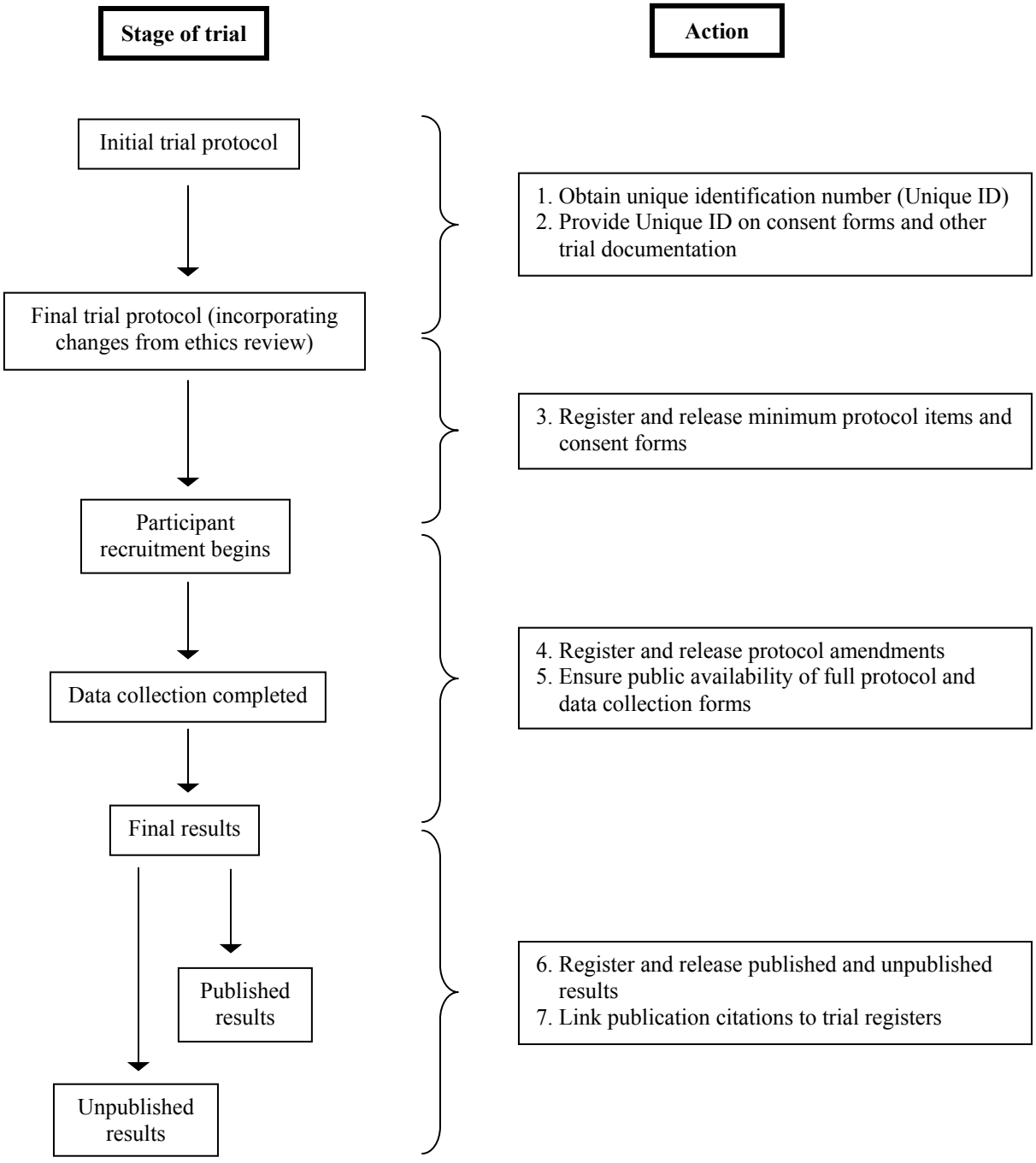

Figure. General time-line for process of trial registration

THE OTTAWA GROUP

The members of the Ottawa Group listed below have formally endorsed Part 1 of the Ottawa Statement:

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Various organisations that endorsed the Ottawa Statement are listed alphabetically below, along with the individual who signed on their behalf (in parentheses).

1. Current Trials Ltd - **www.controlled-trials.com/isrctn** (Anne Greenwood)

2. European Clinical Research Infrastructure Network www.ecrin.org, (Christian Gluud)

As of January 2005, ECRIN covers six European countries representing 112 centres conducting 1500 clinical studies. Each national network and the European Forum for Good Clinical Practice are represented in ECRIN as follows:

a) Danish Clinical Research Infrastructures Network (Christian Gluud)

b) French Clinical Research Centre's Network (Jacques Demotes-Mainard)

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c) French Clinical Trial Unit Network (Jean-Pierre Pignon)

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h) Swedish Clinical Research Infrastructures Network (Pierre Lafolie)

i) European Forum for Good Clinical Practice (Francis P. Crawley)

3. Research-based Education and Quality Improvement - ReBEQI

(Andy Oxman)

ReBEQI (www. rebeqi.org) is a European Union funded project that brings together seven of Europe's leading quality improvement research groups with around 25 active researchers. Its objectives include the prospective registration of quality improvement trials and promoting publication of protocols. The centres and co-ordinators of the project are as follows:

a) Santé Publique et Informatique Médicale (SPIM), Faculté de Médecine Broussais - Hôtel Dieu, Paris, France (Pierre Durieux)

b) Unit of Clinical Governance, Agenzia Sanitaria Regionale (Regional Health Care Agency) of Emilia-Romagna, Bologna, Italy (Roberto Grilli)

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5. **Dutch Cochrane Centre** (Rob Scholten)

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7. **Cochrane Consumer Network, Perth Australia** (Janet Wale)

8. **The Cochrane Collaboration, www.cochrane.org** (Jim Neilson)

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