



ISM Research Ethics Review Policy

Background:

In Canada, the introduction of the Tri-Council Policy Statement in 1998 provided impetus for further initiatives aimed at improving the coherence of REB review across the country. The Tri-Council Policy does not apply to research undertaken outside the context of funded institutions. When dealing with government supported clinical trials, the ICH-GCP apply. If not: no clear guidelines apply, since the TCPS only applies to funded research.

Two categories of concerns can be distinguished in the context of the commercialization of clinical trials.

First, the commercialization of clinical trials has created pressures which may affect the individual behaviour of those involved in medical research. Second, on a more structural level, the safety, health and well-being of research subjects and consumers is threatened by some aspects of the commercialization of medical research. Many private contract research organisations have set up their own internal REB to review in-house studies.

The legal status of the ICH-GCP in Canada is ambiguous, since it is not part of the formal regulations enacted by the government. Guidance documents are intended to provide assistance to industry and health care professionals on how to comply with the regulations. They also can be used by regulatory agents to establish whether good clinical practices are respected in the research that supports an application. As Health Canada states, "Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document may be acceptable provided they are supported by adequate scientific justification." (2)

*The above is excerpted and adapted from: Federal Regulation of REB Review of Clinical Trials: Trudo Lemmens Health Law Review Volume 13
(2) Health Products and Food Branch, "Guidance for Industry, Good Clinical Practice: Consolidated Guide-line ICH Topic*

Regardless of the vagaries of REB review of private research, all ISM research is conducted in accordance with the intended ethics standards established by the Tri-Council.

Issues:

Disclosure of Conflicts
Ethics Review Process

(A) Disclosure of Conflicts:

In all ISM research submissions and in full research papers, we make the following full disclosure of potential conflicts:

Conflict of interest: Dr. Chowdhury Zaman is the Medical Director for ISM and Immune System Management Inc.(ISM) and Dr Ken Lin is the Lab Director for OncomatRx. ISM is the corporate entity that has sponsored this research. There was no government or third party funding of or involvement in this research.

Of course, this potential conflict in itself does not in any way discredit our research. One would need to fully review the methodology, analysis and conclusions of the full research paper to derive any position on “conflict”. It is well recognised that the majority of all new product research in Canada (private & institutional) has some level of potential commercial conflict.

(B) Ethics Review Process

ISM abides by all ethical standards in the conduct of our research (hereinafter “Research”). We subscribe to the principles of the:

- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS)
- The Belmont Report: the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research
- Good Clinical Practice Consolidated Guideline as adopted by ICH and Health Canada
- Council for International Organizations of Medical Sciences International Ethical Guidelines for Biomedical Research Involving Human Subjects
- CMA Code of Ethics

The following details the mechanism of ISM Ethics Review for all research. Because we are involved with private research there are some complexities involved including:

- 1) Applicability of Research Ethics Boards (“REB”) to ISM research & lack of private REBs
- 2) Interpretation of the use of Human Subjects
- 3) ISM internal Ethics Review process

1) REB Origin and Applicability to ISM:

The Tri-Council Policy Statement (TCPS) applies to all research involving humans that is conducted within or by members of research institutions administering funds awarded by any of the three federal granting agencies (Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council, and the Social Sciences and Humanities Research Council). Other Canadian research organizations have also adopted the TCPS. The TCPS requires that all research involving human subjects under the jurisdiction of, or conducted by members of an institution receiving funds from one or more of the three federal granting agencies undergo ethics review by a REB.

Our Research was entirely funded internally. There was no government or institutional funding or involvement.

Since the REB is promulgated by governmental bodies, funding agencies, professional organizations and institutions there are virtually NO private REBs established. This can be confirmed by reviewing the list of REBs as published by:

- (a) National Council on Ethics in Human Research and
- (b) Canadian Association of Research Ethics Boards

In our experience, institutional REBs have no interest or mandate to review research ethics for studies not directly involving their institution. The only non-institutional, commercial contract REB (Ethica) cannot be used by us because of their conflict of interest regarding intellectual property since, Ethica is also a new drug developer.

Hence, we have established our own internal Ethics Review process that is described below.

(2) Applicability of Ethics Review in ISM Research

It is important to understand the context of our research. It is doubtful whether it falls within the mandate of the formal REBs and at most is subject only to “expedited review”.

(a) Un-identified Secondary Data

In the research, ISM ensures that only un-identifying, secondary data regarding the Research subjects is used. There is no direct personal information about subjects provided to research analysts by any means. All subject’s personal information is contained in a non-identified database of information that originated from clinical processes at the Immune System Management Inc. (ISM). There is no further transfer of patient information between researchers and ISM regarding this Research.

(b) No Direct Human Subject Contact

It is also important to distinguish between the data analysis research and the clinical patient activities (ISM) where the data originated. The distinction between research and clinical practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard clinical practice are often called "experimental" when the terms "experimental" and "research" are not at all the same.

For the most part, the term "clinical practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals. This is the case for the ISM clinical practice. It administers Health Canada accepted nutraceuticals. While not required by Health Canada, the ISM clinical practice is done under the supervision of a licensed medical doctor, registered pharmacist and registered nurse. *“The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research”*, has recognized that the fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Therefore, the clinical practices of ISM do not fall within the concept of research, since they are only involved with the clinical application of known, tested and approved natural nutraceuticals.

By contrast, the term "research" designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to general knowledge. Therefore, it is the researcher’s responsibility to follow ethical research principles.

(c) Compliance with CMA Code of Ethics

All ISM patients sign a consent form to treatment and diagnostic evaluation of their information. As mentioned above, since the ISM clinical practice does not involve “research”, there is no further need at the clinic level to obtain further informed consent from patients.

(3) ISM’s Ethical Research Review Approach

Due to the lack of independent REBs available to ISM, we have established our own internal Ethics Review procedures to ensure compliance with the objectives of the TCPS.

Despite the likelihood that our Research is not subject to detailed review by an REB, prior to commencing the Research we nonetheless complied with all facets of the TCPS including:

- a) ISM Ethics Review infrastructure
- b) Free and informed consent
- b) Privacy and confidentiality
- c) Conflict of interest

d) Minimal Risk

Appropriate measures have been taken to protect the privacy of the individuals, to ensure the confidentiality of the data, to minimize harm to subjects and ensure that individuals to whom the data refer have not objected to secondary use.

The following discusses the ISM Ethics Review of the Research at issue:

(a) Membership of the ISM “REB”

As a small company, we have tried as much as possible to maintain an independent Ethics Review. All research is discussed and reviewed with a minimum of:

- medical doctor
- pharmacist
- legal counsel
- biochemist with knowledge of ethical research matters
- business and community associates

(b) Free and Informed Consent

All data used by ISM researchers is un-identifying. There is no ability to correlate or link with any other source of identifying information such as patient charts or direct contact with the patient. All information is catalogued by random number association.

There is no transfer of personal information other than generic age, gender and survival status.

Subject consent is NOT required for the use of data since:

- it is anonymous data that is NOT linked to other sources of data and
- subjects are not being contacted for any research-related purpose and
- it is impossible to identify the individuals whose records exist within the Research database.

(c) Privacy and Confidentiality

As discussed above, all information is un-identifying hence, subjects are not identified in any way in any Research report and/or document generated through the Research activity (e.g., no names, initials, or unique identifiers).

Our secondary use of pooled data cannot be traced to the original research participants. Confidentiality safeguards in place include:

- ensuring each research subject is only identifiable as a random code number
- only that number is used on all data about the subject
- the use of locked rooms and filing cabinets for storage of data
- strictly limited secure access to data to authorized research personnel only
- fire-walls on all electronically stored data

Anonymity: Data is presented only in aggregate form hence, there is no potential to link specific responses to individuals.

(d) Conflict of Interest

See discussion in (A) above.

(e) Minimal Risk

At a clinical level (not subject to Ethics Review as discussed above), there is NO risk to the patients since all diagnostics and therapeutics comply completely with Health Canada guidelines and Natural Health Products Directorate regulations. All ISM patient procedures

are also inherent in the treatment that the patient undergoes as a part of his or her current everyday life and hence, pose no potential harm.

At the Research level, all data is anonymous and there is no direct contact with subjects and no ability to identify individual or groups of subjects hence, there is NO social, emotional or physical risk to the subject.

Should you have any questions regarding the ethical context of ISM Research, please contact:

ISM
Suite 2, 99 Fifth Avenue
Ottawa, ON K1S 5K4
www.ISM.com
613 239 0220