



## RESEARCHED MEDICINES INDUSTRY ASSOCIATION SUBMISSION ON

### THE ETHICS OF INTERVENTION STUDIES - DISCUSSION DOCUMENT AND DRAFT ETHICAL GUIDELINES FOR INTERVENTION STUDIES, JUNE 2008

#### PREAMBLE

The Researched Medicines Industry Association of New Zealand (RMI) is the professional and trade organisation of New Zealand's research-based pharmaceutical industry. Its member companies are engaged in the research, development, manufacture and marketing of prescription medicines and the ongoing improvement of medical and scientific knowledge about their products.

RMI member companies conduct clinical trials in New Zealand and the RMI publishes the "Guidelines on Clinical Trials Compensation for Injury Resulting from Participation in an Industry-Sponsored Trial". The RMI strongly supports the conduct of clinical trials which are both scientifically and ethically sound.

The RMI's comments on the NEAC Discussion Document and Draft Ethical Guidelines for Intervention Studies is provided below.

#### COMPENSATION FOR INJURY

1. The Discussion Document notes (p 43) that "The RMI *Guidelines* are written principally for medicines, not medical devices. Cover arrangements for participants injured in B trials of medical devices are unclear."

The RMI Guidelines are written in the context of trials for "medicinal products" as the RMI represents the research-based pharmaceutical industry in New Zealand, not the medical devices industry, and the Guidelines were produced by the association for use by RMI member companies.

2. The Discussion Document further notes (p 43) that "the RMI Guidelines relate only to phase II and III trials and consequently appear not to cover phase I trials.....This exclusion has the potential to leave participants in phase I B trials with neither ACC-equivalent not RMI -equivalent cover."

The RMI is currently reviewing the RMI Guidelines on Clinical Trials Compensation with regard to the inclusion of phase I trials.

3. The Discussion Document states (p 44) that one of the issues of the existing New Zealand guidance is that “there are a number of situations in which participants may not be entitled to any compensation for injury, such as where there is:
  - medical negligence in B trials
  - ‘significant’ departure from the study protocol by either the investigator or the participant in B trials.

In these situations the participant’s only method of receiving compensation may be through pursuit of a tort law action.”

Section 3.4 of the RMI Guidelines states that compensation may be abated where there is negligence or a significant departure from the protocol.

Adherence to the trial protocol is a key mandate of good clinical practice and is closely monitored by sponsors of trials in New Zealand. It is key to compliance with International Conference on Harmonisation - Good Clinical Practice (ICH-GCP) guidelines and provides assurance that not only is the safety of trial participants protected but also the veracity of the data generated by the trial and, therefore, that prescribing information for future patients is also protected.

Given the experimental nature of clinical trials, it is particularly important that patients get proper, professional medical care. To the extent standards are not maintained, patients are put at increased risk.

Pharmaceutical companies are unable to change the conditions of their global insurance to cover investigators who are negligent and/or do not adhere to the protocol.

The RMI considers that all health practitioners involved in intervention studies should be required to have professional indemnity insurance to avoid participants having to take legal action in cases where there is negligence or a significant departure from the protocol resulting in injury.

4. Paragraph 8.1 of the NEAC Guidelines state that “investigators, study sponsors and ethics committees have responsibilities to ensure that compensation for injury is available to all participants in intervention studies, to at least the level of cover provided by the Accident Compensation Corporation (ACC) for those who have comparable injuries outside a clinical trial”.

The RMI is currently considering whether an amendment should be made to the RMI Guidelines to specify a minimum level of compensation in cases of injury other than those situations for which there are exclusion or abatement criteria specified in the RMI Guidelines.

5. Paragraph 8.5 of the Draft Guidelines states compensation should not be excluded or abated because the adverse reaction causing injury was foreseeable or predictable. The RMI's position, outlined in the RMI Guidelines Section 4.2, is as follows:

“4.2 Compensation may be abated, or in certain circumstances excluded, in the light of the following factors (on which will depend the level of risk the patient can reasonably be expected to accept):

4.2.1 the seriousness of the disease being treated, the degree of probability that adverse reactions will occur and any warnings given;

4.2.2 the risks and benefits of established treatments relative to those of the trial medicine known or suspected.

This reflects the fact that flexibility is required given the particular patient's circumstances. As an extreme example, there may be a patient suffering from a serious or life-threatening disease who is warned of a certain defined risk or adverse reaction. Participation in the trial is then based on an expectation that the benefit/risk ratio associated with participation may be better than that associated with alternative treatment. It is reasonable, therefore, that the patient accepts the high risk and should not expect compensation for the occurrence of the adverse reaction about which he or she was told.”

#### **REGISTERING TRIAL PROTOCOLS - DRAFT GUIDELINES 5.33-5.36**

When international trial registers are used they may not comply exactly with required data items listed: For example the US trial register <http://clinicaltrials.gov/> does not include a list of investigators or the study statistics. Would studies registered on such a list then be required to re-register on a separate NZ list in order to fulfill the NZ requirements completely?

#### **PHASE I TRIALS - DRAFT GUIDELINES 5.41**

The guidelines state that early clinical studies of novel biologic or chemical agents with potential to cause harm should be conducted only under certain conditions. It could be argued that all agents have the potential to cause harm. Therefore, further definition of "potential to cause harm" would be necessary in order for these guidelines to be followed appropriately.

It is relatively common in New Zealand for phase I units to be located near a public hospital. However, it is uncommon for the public hospital resuscitation team to provide personnel to cover resuscitation events at a private phase I unit. Phase I units should have their own resuscitation equipment and have staff skilled at using this equipment.

## **FREE AND INFORMED CONSENT - DRAFT GUIDELINES**

The guidelines state (6.9) that information provided should be tailored to the individual. The RMI agrees that verbal information should be tailored to meet the needs of the individual participant. Written information should be tailored to the study and must receive ethics committee approval. It would be impossible to tailor written information for each individual.

## **STOPPING A STUDY - DRAFT GUIDELINES 6.51 - 6.56**

The RMI believes that the trial sponsor should have the right to stop or suspend a study for any reasons they consider relevant including reasons relating to commercial interest or public relations as in 6.5.5. Study participants should be, and are, informed at the time of consenting to participate that they may be asked to leave the study for any reason. Consideration to ongoing treatment access should be considered prior to study start and made clear to patients in the information prior to study consent.

## **DISCLOSURE OF INFORMATION OBTAINED BY INTERVENTION STUDIES - DRAFT GUIDELINES 7.9**

Section 7.9 states that “restrictions on publications of study results or dissemination of findings are also inappropriate, so investigators should not normally enter into contracts that limit, or apply time restrictions to, publication”.

However, the RMI notes that in large global studies it is inappropriate for individual investigators to publish or disseminate local data as a subset given that the data would be incomplete.

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