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To: Applicants / Sponsors of Clinical Trials

(A) **UPDATES TO THE CLINICAL DRUG TRIAL SAFETY REPORTING REQUIREMENTS – SEPTEMBER 2007**
(B) **ONLINE EXPEDITED SAFETY REPORTING MODULE (ESR) – JANUARY 2008**

The Clinical Trials Unit would like to inform applicants / sponsors of clinical trials on the changes to the safety reporting process and requirements for clinical trials.

Updates To The Clinical Drug Trial Safety Reporting Requirements – September 2007

2 Currently, all adverse drug reactions that are both serious and unexpected arising from ongoing clinical drug trials in Singapore on pre-marketed and marketed products are subjected to expedited reporting and are submitted to HSA. This is based on the Guidance for Industry – Safety Reporting Requirements for Clinical Drug Trials dated September 2004.

3 We are pleased to inform the applicants that with effect from September 2007, a risk-based approach that is stratified by the local registration status will be implemented for the submission of expedited safety reports. The main change proposed relates to clinical trials on locally registered products, whereby only local and overseas adverse drug reactions that are both serious and unexpected and arising from that clinical trial protocol that is studied in Singapore need to be submitted. As these products are already registered in Singapore, we would not require all adverse drug reactions that are both serious and unexpected to be submitted. This is in tandem with our scope to look at the benefit – risk balance for the clinical trial that is currently studied locally in order for signals that are generated to be relevant for the local clinical trial. For unregistered products, a closer monitoring of the safety of the investigational product is required and for this reason, this change in requirement would apply only to registered products. Requirements for submission of active comparator drug reactions are also further spelt out in the revised guidance.

4 An additional revision to the guidance will be to reflect the submission of the treatment allocation code to HSA on the online ESR form if the blind has already been broken for submission to the European Medicines Agency (EMEA) or other national authority(ies). The Guidance for Industry – Safety Reporting Requirements for Clinical Drug Trials has been revised accordingly. Please visit our website for the revised guidance.

Online Expedited Safety Reporting Module (ESR) – January 2008

5 The online PRISM* application system for the various clinical trial modules has been in use since July 2003. The following clinical trial modules for the various submission types are available at http://www.hsa.gov.sg/publish/hsaportal/en/services/prism/clinical_trials.html:

* ***P****harmaceutical* ***R****egulatory and* ***I****nformation* ***S****yste****m***

- Application for Clinical Trial Certificate
- Application for Clinical Trial Materials import permit
- Addition of Clinical Trial Site(s)
- Amendment of Protocol and/or Patient Informed Consent Form
- Change of Principal Investigator
- Extension of Clinical Trial
- Notification of Updated Investigator Brochure
- Submission of Clinical Trial Status Report
- Submission of Clinical Trial Final Study Report - only for completed trials

6 The system has been utilised to a large extent and the majority of applicants are familiar with the various submissions. All clinical trial applications received from 2005 onwards are registered in the system. At present, the only reporting process that is outside of the PRISM system is the expedited reporting of serious adverse events. We would like to integrate this expedited reporting of serious adverse events together with other clinical trial submission modules to provide a systematic and standardized submission process.

7 This integration would enable the current functionalities available in PRISM to be extended to the expedited safety reporting module. In this new submission module, applicants will receive an immediate acknowledgement upon successful submission of the expedited safety reports. Applicants can view and track the drafted/ submitted reports under track@prism and withdraw any duplicate/ inappropriate submissions online. An audit trail is also readily available to display the date of submission of these reports and the report versions that have been submitted through this web-based system. A new mapping function will be also introduced in this module to allow cris administrators to assign local or overseas staff/ partners with a drafter role and map them to a selected protocol in order for him to draft the application before it is submitted. Submission of the application will be completed by staff who have submitter rights to the protocol. Local sponsors of clinical trial applications can apply for a HSA PIN for overseas staff/ partners to draft the applications on their behalf.

8 For ongoing trials that were not submitted online, i.e., the initial application was not submitted via PRISM, please continue to make hard copy submissions.

9 If you need further information or any clarification, please contact myself or Ms Dorothy Toh at Tel: 6866-3442/3 or e-mail your queries to hsa_ct@hsa.gov.sg. Thank you.

Yours sincerely,

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