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March 21, 2003

To: Schedule C Drug Stakeholders

Subject: Regulatory Requirements Governing Investigations with Schedule C Drugs (Radiopharmaceuticals, Kits and Generators)

As a follow-up to earlier communications and consultations on Positron-Emitting Radiopharmaceuticals (PERs), we would like to reinforce that hospitals or academic centres that sell new drugs for such uses onsite or otherwise that amount to a clinical trial[1], must in all cases comply with Part C, Division 5 of the Food and Drug Regulations (Drugs for Clinical Trials Involving Human Subjects.)

At a meeting with the Consultative Working Group (CWG) on PERs held December 5-6, 2002, the CWG put forward the recommendation to Health Canada that "clinical studies conducted within a single institution, not designated for the commercialization of a new drug, sponsored and directed by a physician, falls within the practice of medicine and pharmacy". After extensive analysis, Health Canada has determined there are no compelling arguments to support the view that investigations/studies with Schedule C drugs, even when conducted within a single institution and not designated for the commercialization of a new drug, should be treated differently from other investigations with unapproved drugs. The primary intent of Division 5 of the Food and Drug Regulations is to protect the safety of all human subjects. We would also like to reassert that the production of PERs is a manufacturing activity and is not considered compounding.

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Division 5 of the Food and Drug Regulations, which came into force on September 1, 2001, defines a clinical trial as: *an investigation in respect of a drug for use in humans that involves human subjects and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug, or ascertain the safety or efficacy of the drug.*(reference C.05.001).

We would like to reconfirm that compliance with Division 5 of the Food and Drug Regulations, including the submission of a Clinical Trial Application (CTA), is required for all uses of Schedule C drugs (including PERs) for the purposes of clinical trials involving human subjects, including but not limited to: investigations with radiopharmaceuticals not approved by Health Canada; investigations with radiopharmaceuticals approved by Health Canada but not approved for that use (e.g. indication or population, etc.); confirming animal data for novel drugs; characterizing the in vivo profile of a radiolabeled form of a new drug. Division 5 applies to the sale[2] or importation of pharmaceuticals, radiopharmaceuticals (Schedule C) and biological drugs(Schedule D) used for the purposes of clinical trials involving human.

These Regulations describe the responsibilities of sponsors, including those for researchers/qualified investigators when acting as sponsors, when applying to Health Canada to obtain an authorization for proceeding with a clinical trial. The Regulations apply to drugs for clinical trials involving human subjects, including trials which are not supported by commercial sponsors. This includes phase I, II and III clinical trials.

Ensuring that clinical trials are conducted in accordance with the regulatory requirements of Division 5 is the shared responsibility of all stakeholders. The Biologics and Genetics Therapies Directorate is the main contact for monitoring the use of Schedule C drugs and queries pertaining to CTA requirements for these drugs should be directed to this Directorate.

Health Canada will continue to work with stakeholders to facilitate compliance with the CTA requirements. You may wish to note that Health Canada officials will deliver a presentation on clinical trial applications at the annual meeting of the Canadian Society of Nuclear Medicine in May 2003. A list of information/publications related to Clinical Trail Applications is provided in Annex A.

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[2] Sale includes offer for sale, expose for sale, have in possession for sale and distribute, whether or not the distribution is made for consideration.

For questions related to clinical trials with biologics or radiopharmaceuticals, please contact Dr. Agnes Klein, Manager, Clinical Evaluation Division, Biologics and Radiopharmaceuticals Evaluation Centre, Biologics and Genetic Therapies Directorate at (613) 954-5706. For questions related to compliance monitoring activities of clinical trials, please contact Mr. Jean Saint-Pierre, Good Clinical Practices Coordinator, Health Products and Food Branch Inspectorate at (613) 952-8173.

Yours sincerely,

Original signed by Dr. Alan Mortimer for
Julia Hill
Acting Director General

cc: Mr. Jean Lambert, Director General, HPFB Inspectorate; Research Ethics Boards: *members of the National Council on Ethics in Human Research (NCEHR), members of the Canadian Association of Research Ethics Board (CAREB), Ethics Committee of the Canadian Medical Association, Private Research Ethics Boards*; Canadian Institutes of Health Research; Natural Sciences and Engineering Research Council

Annex A

The following is a list of information available related to clinical trial applications:

Food and Drugs Regulations. Regulations Amending the Food and Drug Regulations (schedule 1024 – Drugs for Clinical trials Involving Human Subjects). Canada Gazette Part II:
http://www.hc-sc.gc.ca/hpfb-dgpsa/inspectorate/food_drug_reg_amend_1024_gcp_e.pdf

Good Clinical Practice: Consolidated Guideline, International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use - Topic E6:
http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/guides/ich/efficacy/goodclin_e.pdf

Guidance for Clinical Trial Sponsors - Clinical Trial Application, developed by the Therapeutic Products Directorate (TPD) and the Biologics and Genetic Therapies Directorate (BGTD):
http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/consult/draft_guidance/cta-guidance_e.pdf

HC-SC 3011: Drug Application for: Human, Veterinary, or Disinfectant Drugs and Clinical Trial Applications/Attestation:
http://www.hc-sc.gc.ca/hpb-dgps/therapeut/htmleng/forms.html

Health Products and Food Branch Compliance and Enforcement Policy:
http://www.hc-sc.gc.ca/hpfb-dgpsa/inspectorate/compliance_enf_policy_e.pdf

Inspection Strategy for Clinical Trials:
http://www.hc-sc.gc.ca/hpfb-dgpsa/inspectorate/insp_strat_clin_tria_e.pdf

Quality Information Summary-Radiopharmaceuticals (QIS-R) and Certified Product Information Document- Radiopharmaceuticals (CPID-R) Templates:
http://www.hc-sc.gc.ca/hpb-dgps/therapeut/htmleng/bgtd.html