
Drug/Medical Device Combination Products

1. PURPOSE

The purpose of this policy is to ensure timely access to drug/medical device combination products by establishing a single window approach and more efficient submission processing system, while ensuring that combination products marketed in Canada are safe, effective, and of high quality.

2. BACKGROUND

At present, sponsors of drug/medical device combination products must satisfy the requirements of two sets of regulations. The drug component of a combination product must comply with the *Food and Drug Regulations* and the device component must comply with the *Medical Devices Regulations*.

The Therapeutic Products Directorate (TPD) and the Biologics Genetic Therapies Directorate (BGTD) are aware of the regulatory burden that this creates for sponsors and the disincentive it presents to marketing combination products in Canada. The Directorates believe that the risks associated with a combination product can be managed appropriately under one set of regulations. This approach would harmonize regulatory requirements with both the United States and European Union and would assist in the development of mutual recognition agreements with those jurisdictions.

With the announcement of this policy, drug/device combination product classification decisions will consider the principal mechanism of action by which the claimed effect or purpose of the product is achieved. The entire product will then be regulated under either the *Food and Drug Regulations* or the *Medical Devices Regulations*.

Ultimately, it will be necessary to amend the *Food and Drugs Act* and/or the *Food and Drug Regulations* and/or the *Medical Device Regulations* to provide an appropriate regulatory framework for new and emerging therapeutic products that are difficult to define under current frameworks, including combination products. Therefore, this policy provides an interim mechanism to address a gap in the current regulatory schemes for drugs and medical devices.

3. SCOPE

This policy applies to combination products as defined in the definitions section of this policy.

This policy does not apply to combinations of drugs and medical devices where the drug component and the device component can be used separately (e.g. products sold together in procedure packages and trays). The *Food and Drug Regulations* shall apply to the drug component of such a product and the *Medical Devices Regulations* shall apply to the device component.

This policy will not be applied retrospectively to products already classified as drugs or devices; however the Directorates reserve the right to reclassify products where the continuing classification status results in unfair or unreasonable application of fees or other regulatory requirements.

4. DEFINITIONS

Combination product is a therapeutic product that combines a drug component and a device component (which by themselves would be classified as a drug or a device), such that the distinctive nature of the drug component and device component is integrated in a singular product.

Immunological is understood as an action in or on the body by stimulation and/or mobilisation of cells and/or products involved in a specific immune reaction.

Metabolic is understood as an action which involves an alteration of the normal chemical processes participating in, and available for, normal body function. The fact that a product is itself metabolized does not imply that it achieves its principal intended action by metabolic means.

Pharmacological is understood as an interaction between the molecules of the substance in question and a cellular constituent, usually referred to as a receptor, which either results in a direct response, or which blocks the response to another agent and, for the purposes of this policy, includes anti-infective activity.

Therapeutic Products Classification Committee is a committee appointed by the Director General of TPD to develop, maintain, evaluate and recommend for approval policies, procedures and guidelines concerning the classification and review of therapeutic products as drugs, devices or combination products; to assess submissions for combination products referred to it and determine an appropriate classification and review mechanism for the submission.

5. POLICY STATEMENT

It is the policy of the Directorates that:

1. A combination product will be subject to either the *Medical Devices Regulations* or the *Food and Drug Regulations* according to the principal mechanism of action by which the claimed effect or purpose is achieved.
2. Where the principal mechanism of action by which the claimed effect or purpose is achieved by pharmacological, immunological, or metabolic means, the combination product will be subject to the *Food and Drug Regulations*, unless that action occurs *in vitro*, without reintroducing a modified cellular substance to the patient, in which case the product will be subject to the *Medical Devices Regulations*.

3. Where the principal mechanism of action by which the claimed effect or purpose is **not** achieved by pharmacological, immunological, or metabolic means, but may be assisted in that effect or purpose by pharmacological, immunological, or metabolic means, the combination product will be subject to the *Medical Devices Regulations*.
4. Although a combination product will be subject to either the *Food and Drug Regulations* or the *Medical Devices Regulations*, both the principal and ancillary components shall meet acceptable standards of safety, efficacy and quality.

6. POLICY REQUIREMENTS

1. The sponsor of a combination product may make a presentation to TPD or BGTD (as appropriate) for the purpose of classifying the product. The presentation may be in advance of the sponsor making a submission to support sale of the product in Canada or to support investigational testing of the product in Canada.
2. The sponsor of a submission for a combination product not previously classified may present a written request for a classification decision to the relevant Bureau Director in advance of the submission filing providing the following information:
 1. name of the product and identification of the device/drug components,
 1. a synopsis of relevant data describing the mechanism of action of each component and the principal mechanism of action of the product, including composition, study design, measurements of efficacy in terms of structural, pharmacologic, metabolic, immunologic and ADME¹ studies conducted, toxicity studies, etc.
3. A Screening Deficiency Notice will be issued by the receiving Bureau if a submission requiring a classification decision has not been supported by a classification request and synopsis.
4. On receipt of a submission for a combination product, the classification of the product will be confirmed by using the three criteria identified in the Policy Statement. The receiving Bureau shall consult with other Bureaux affected for this purpose and, where a decision cannot be reached or where there is no consensus among the Bureaux as to the classification, the submission will be referred to the Therapeutic Products Classification Committee (TPCC) for a final decision within 30 days of receipt.
5. The TPCC will classify the submission and notify the sponsor of the decision within 30 days of accepting the submission from the receiving Bureau.

¹ Absorption, Distribution, Metabolism and Elimination

6. The TPCC may request the sponsor to provide additional information with respect to the submission and may invite the sponsor to make a presentation to assist in its deliberations.
7. If the sponsor wishes to request a Reconsideration of the decision of the TPCC, a written Letter of Intent should be sent to the Director General within 30 days of receiving the notification of the decision of the TPCC. The Request for Reconsideration will proceed in accordance with the procedure outlined in the Health Canada Guidance: *Reconsideration of Final Decisions Issued for Human Drug Submissions*.
8. The sponsor is required to attest in the application or submission for a licence, Notice of Compliance, or drug identification number, as the case may be, that the ancillary component of the combination product meets acceptable standards of safety, efficacy and quality.
9. The review of submissions for combination products will be undertaken according to the expertise required to assess the risk/benefit profile of the product. The review may be undertaken by one Bureau or a team of reviewers representing more than one Bureau.
10. Additional information to support the safety, efficacy or quality of either component of the combination product may be requested during the review period.
11. Where a joint review of a combination product is conducted and the product is considered to be in compliance with the relevant Regulations, the Notice of Compliance will be signed by the Director General.
12. Submissions for combination products classified as drugs and regulated under the *Food and Drug Regulations* will be subject to any fees payable for drugs under the regulations enacted for that purpose.
13. Submissions for combination products classified as devices and regulated under the *Medical Devices Regulations* will be subject to any fees payable for devices under regulations enacted for that purpose.
14. TPD will maintain a list of products that the TPCC considers subject to the *Food and Drug Regulations* or the *Medical Devices Regulations* for the guidance of sponsors and Directorate staff.
15. A classification decision made for the purposes of investigational testing may change during the review phase of a submission on the basis of new information contained in the submission.

7. EFFECTIVE DATE

This revised Policy is effective as of March 1, 2006 and replaces the previous Policy dated May 13, 1999.