

SUBSEQUENT ENTRY BIOLOGICS IN CANADA: NEW GUIDANCE

Ian Goodman
Shapiro Cohen



In March 2010, Health Canada released a document entitled *Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics (SEBs)*. While this document does not have the force of law, its purpose is to assist sponsors of SEBs to obtain authorisation by meeting the regulatory requirements of Canada's Food and Drugs Act and regulations.

Biologic drugs are derived using metabolic processes in living organisms. They tend to be more structurally complex than drugs manufactured by chemical processes. The document defines a 'biologic drug' as a drug listed in Schedule D of the Food and Drugs Act. Schedule D includes substances such as blood and blood derivatives; drugs obtained by recombinant DNA procedures; monoclonal antibodies, their conjugates and derivatives; and various hormones. SEBs are biologic drugs that enter the market subsequent to a previously authorised, similar biologic drug. SEBs are referred to as 'similar biological medicinal products' in the European Union and 'follow-on protein products' in the United States.

In Canada, a new drug submission must be filed to obtain authorisation for an SEB. In seeking authorisation to sell an SEB, a sponsor of the SEB relies in part on the information that was submitted in relation to the reference biologic drug and submits a reduced clinical and non-clinical package. In other words, the new guidance provides a somewhat abbreviated submission package for SEBs, by accepting a reduced non-clinical data package. The new drug submission should contain a full chemistry and manufacturing data package (also required for approval of new biologic drugs) and data on the similarity between the SEB and the reference biologic drug. The reference biologic drug must be a biologic drug authorised for use based on complete, high-quality non-clinical and clinical data packages. The reference biologic drug should not be an SEB. Preferably, the reference drug will be authorised for sale and available in Canada. However, if certain requirements as outlined in the new guidance document are met, a non-Canadian reference biologic drug may be used.

In determining the similarity of the SEB to the reference biologic drug, the new guidance provides a number of criteria for comparison, including physicochemical properties, biological activity, immunochemical properties, purity, specifications and stability.

Under this SEB submission process, a sponsor can claim one or more of the clinical indications that were authorised for the reference biologic drug in Canada. In cases where a sponsor seeks a clinical indication for an SEB that is not also an indication of the reference biologic drug, full clinical data are required.

Prior to authorisation, the new guidance requires a risk management plan to be filed with Health Canada. The plan should outline how the sponsor

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intends to monitor and detect safety concerns. Once a notice of compliance has been issued authorising the marketing of the SEB in Canada, there are a number of post-approval requirements, including the reporting of adverse drug reactions, filing of periodic safety update reports and labelling requirements. Labels must include the indications for which the SEB is approved and a statement that the product is an SEB. However, there should be no claims for the bioequivalence or clinical equivalence between the SEB and the reference biologic drug.

In view of the new guidance, Health Canada has further released updates relating to data protection under C.08.004.1 of the Food and Drugs Regulations and Patented Medicines (Notice of Compliance) Regulations.

Ian Goodman is a lawyer at Shapiro Cohen. He can be contacted at: igoodman@shapirocohen.com