Registration
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FOOD AND DRUGS ACT

Regulations Amending the Food and Drug Regulations (Data Protection)

P.C. 2006-1076 October 5, 2006

Her Excellency the Governor General in Council, on the recommendation of the Minister of Health, pursuant to subsection 30(3)[a] of the *Food and Drugs Act*, hereby makes the annexed *Regulations Amending the Food and Drug Regulations (Data Protection)*.

REGULATIONS AMENDING THE FOOD AND DRUG REGULATIONS (DATA PROTECTION)

AMENDMENT

1. Section C.08.004.1 of the *Food and Drug Regulations*[1] is replaced by the following:

C.08.004.1 (1) The following definitions apply in this section.

"innovative drug" means a drug that contains a medicinal ingredient not previously approved in a drug by the Minister and that is not a variation of a previously approved medicinal ingredient such as a salt, ester, enantiomer, solvate or polymorph. (*drogue innovante*)

"pediatric populations" means the following groups: premature babies born before the 37th week of gestation; full-term babies from 0 to 27 days of age; and all children from 28 days to 2 years of age, 2 years plus 1 day to 11 years of age and 11 years plus 1 day to 18 years of age. (*population pédiatrique*)

(2) This section applies to the implementation of Article 1711 of the North American Free Trade Agreement, as defined in the definition "Agreement" in subsection 2(1) of the *North American Free Trade Agreement Implementation Act*, and of paragraph 3 of Article 39 of the Agreement on Trade-related Aspects of Intellectual Property Rights set out in Annex 1C to the World Trade Organization Agreement, as defined in the definition "Agreement" in subsection 2(1) of the *World Trade Organization Agreement Implementation Act*.

(3) If a manufacturer seeks a notice of compliance for a new drug on the basis of a direct or indirect comparison between the new drug and an innovative drug,

(*a*) the manufacturer may not file a new drug submission, a supplement to a new drug submission, an abbreviated new drug submission or a supplement to an abbreviated new drug submission in respect of the new drug before the end of a period of six years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug; and

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[a] S.C. 1994, c. 47, s. 117
[1] C.R.C., c. 870

(*b*) the Minister shall not approve that submission or supplement and shall not issue a notice of compliance in respect of the new drug before the end of a period of eight years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug.

(4) The period specified in paragraph (3)(*b*) is lengthened to eight years and six months if

(*a*) the innovator provides the Minister with the description and results of clinical trials relating to the use of the innovative drug in relevant pediatric populations in its first new drug submission for the innovative drug or in any supplement to that submission that is filed within five years after the issuance of the first notice of compliance for that innovative drug; and

(*b*) before the end of a period of six years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug, the Minister determines that the clinical trials were designed and conducted for the purpose of increasing knowledge of the use of the innovative drug in those pediatric populations and this knowledge would thereby provide a health benefit to members of those populations.

(5) Subsection (3) does not apply if the innovative drug is not being marketed in Canada.

(6) Paragraph (3)(*a*) does not apply to a subsequent manufacturer if the innovator consents to the filing of a new drug submission, a supplement to a new drug submission, an abbreviated new drug submission or a supplement to an abbreviated new drug submission by the subsequent manufacturer before the end of the period of six years specified in that paragraph.

(7) Paragraph (3)(*a*) does not apply to a subsequent manufacturer if the manufacturer files an application for authorization to sell its new drug under section C.07.003.

(8) Paragraph (3)(*b*) does not apply to a subsequent manufacturer if the innovator consents to the issuance of a notice of compliance to the subsequent manufacturer before the end of the period of eight years specified in that paragraph or of eight years and six months specified in subsection (4).

(9) The Minister shall maintain a register of innovative drugs that includes information relating to the matters specified in subsections (3) and (4).

TRANSITIONAL PROVISION

2. Section C.08.004.1 of the *Food and Drug Regulations*, as it read immediately before the coming into force of these Regulations, applies to a drug in respect of which a notice of compliance was issued before June 17, 2006.

COMING INTO FORCE

3. These Regulations come into force on the day on which they are registered.

REGULATORY IMPACT ANALYSIS STATEMENT

(This statement is not part of the Regulations.)

Description

The amendments to section C.08.004.1 of the *Food and Drug Regulations* ("Regulations") are intended to provide new drugs with an internationally competitive, guaranteed minimum period of market exclusivity of eight years. An additional six months period of data protection is available for innovative drugs that have been the subject of clinical trials designed and conducted for the purpose of increasing the knowledge of the behaviour of the drug in pediatric populations.

These amended Regulations are based on the proposal that was pre-published in the *Canada Gazette*, Part I, on June 17, 2006. Two minor modifications have been made as a result of the comments received during the consultation period. The first modification was the addition of a provision to allow for an innovative company to consent to the filing of a submission by a subsequent manufacturer. In the second modification, the transitional provision was altered to provide data protection for drug submissions that had not received a notice of compliance before pre-publication on June 17, 2006.

Background

The amendments to section C.08.004.1 of the *Food and Drug Regulations* are intended to clarify and effectively implement Canada's *North American Free Trade Agreement* ("NAFTA") and the *Trade-Related Aspects of Intellectual Property Rights* ("TRIPS") obligations with respect to the protection of undisclosed test or other data necessary to determine the safety and effectiveness of a pharmaceutical or agricultural product which utilizes a new chemical entity. The obligations in TRIPS require that signatories provide protection against the unfair commercial use of the data, whereas NAFTA requires that signatories provide a reasonable period of time during which a subsequent manufacturer is prohibited from relying on the originator's data for product approval. The reasonable period of time is specified as normally not being less than five years from the date on which regulatory approval was granted to the originator of the data. In keeping with the provisions, the government has decided to provide this protection by allowing the innovator, or the originator of the data submitted for regulatory approval, to protect investments made in the development of the product by providing a period of market exclusivity.

Under the current Regulations, the data protection exclusivity period arises when the Minister of Health examines and relies on an innovator's undisclosed data in order to grant a notice of compliance to a generic manufacturer. However, to receive a notice of compliance in Canada, a generic manufacturer need only demonstrate bioequivalence by comparing its generic product to the innovator's product. Therefore, in actual practice, the Minister typically does not examine the data contained in the innovator's submission in order to grant a notice of compliance for a generic product. As a result, data protection does not arise where bioequivalence forms the basis of a generic submission, as affirmed by the Federal Court of Appeal in *Bayer Inc.* v. *Canada (Attorney General)*, 87 C.P.R. (3d) 293.

While the comparison necessary to demonstrate bioequivalence rarely involves an examination of the innovator's data, it does involve reliance on the innovator's product. Therefore, these amendments are being introduced to clarify that the aforementioned reliance will give rise to an exclusivity period.

Amendment to C.08.004.1

The government is introducing an eight-year term of data protection for innovative drugs with a six-year no-filing period within the eight-year term of data protection. As a result, Canada will now provide for a six-year period (within the eight-year term) where a generic manufacturer, seeking to copy an innovative drug, will not be permitted to file a new drug or abbreviated new drug submission with the Minister. This will be followed by a no-marketing period of two years during which the Minister will not grant a notice of compliance to that generic manufacturer. This additional two-year period is generally reflective of the period of time required to approve a drug submission, as well as the time required for a generic manufacturer to meet its obligations under the *Patented Medicines (Notice of Compliance) Regulations* ("PM(NOC) Regulations"). The introduction of these changes will provide an adequate incentive for innovators to invest in research, and to develop and market their products in Canada. It will also bring Canada in-line with a system similar to that of other jurisdictions in respect of the no-filing period.

The introduction of the six-year no-filing period, requires an exception to this provision to allow for the filing of drug submissions within the framework of the Canada's Access to Medicines Regime ("CAMR") also known as *Jean Chrétien Pledge to Africa Act*. Although these drug submissions can be submitted within the no-filing period, the notice of compliance will not be issued until the expiry of the data protection term.

Innovative Drug

The definition of "innovative drug" specifically prohibits innovators from obtaining additional terms of data protection for variations of medicinal ingredients. The list of variations is not exhaustive, but rather meant to give examples of the types of variations not considered for protection. The exclusion of variations of a previously approved medicinal ingredient from the scope of protection was introduced to avoid the granting of an additional eight years of protection where an innovator seeks approval for a minor change to a drug. For other arguable variations not included in the list, such as metabolites, an assessment will be made as to whether or not approval is being sought primarily on the basis of previously submitted clinical data (i.e. without the support of new and significant clininal data) or not. This position is consistent with both NAFTA and TRIPS which only require the granting of protection for undisclosed data, the origination of which involved a considerable effort.

Combinations of previously approved medicinal ingredients are not eligible for an additional data protection period. Where a combination consists of an innovative drug and another medicinal

ingredient not covered by data protection, a generic manufacturer will not be allowed to file or receive a notice of compliance, as the case may be, in respect of the combination until expiry of the original data protection period of the innovative drug. Where two or more innovative drugs are sold in combination, a generic manufacturer will not be allowed to file or receive a notice of compliance, as the case may be, until expiry of the latest data protection term.

Biologic drugs are included within the scope of innovative drugs. In keeping with the definition, only those biologics that have medicinal ingredients that have not been previously approved and not considered variations will receive protection.

Triggering mechanism

The triggering mechanism is intended to capture generic and second entrant manufacturers that are seeking to rely on direct or indirect comparison between their drug and the innovative drug. As was observed by the Supreme Court of Canada in *Bristol-Myers Squibb Co. v. Canada (Attorney General)*, 2005 SCC 26, such direct or indirect comparisons would exclude submissions in which the submission sponsor does not rely on another manufacturer's safety and efficacy data in seeking approval under the *Food and Drug Regulations*. This is consistent with Article 1711 of NAFTA and paragraph 3, Article 39 of TRIPS, since there would be no unfair commercial use of data or the reliance on such data for the approval of the product. The mechanism is intended to capture both submissions that fall under the abbreviated new drug submission provisions and submissions that are filed under the new drug submission provisions, so long as there is a direct or indirect comparison with the innovative drug.

Pediatric data protection

In addition to the eight-year term of data protection, an additional six months will now be applied if an innovator includes, in its new drug submission, or any supplement to that new drug submission filed within the first five years of the eight-year data protection period, clinical trials which were designed and conducted with the purpose of increasing knowledge about the use of the drug in pediatric populations.

Comments received during the consultation period indicated a need for further clarification regarding the types of pediatric clinical trials required to be eligible for the six-month extension. The purpose of the provision is to encourage sponsors to submit trial data pertaining to the use of the drug in pediatric populations. Therefore, it must be clear that the goal of such studies was to increase knowledge about the behaviour of the drug in pediatric populations that will assist health professionals, parents, caregivers, and patients in making informed choices about drug therapy. This will provide heath benefits for pediatric patients. This goal of increasing knowledge should be reflected in the study hypothesis, objectives, design and conduct. Clinical trial is defined in Division 5 of the Regulations as "an investigation in respect of the 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". For the purposes of the six-month extension provision, the clinical trials must have been conducted in pediatric populations.

Extending market exclusivity in this manner will encourage pediatric research and improve drug information regarding pediatric usage for health professionals, thus providing health benefits to children.

Marketed in Canada

The protection of an innovative drug only applies where the innovative drug has received a notice of compliance and is marketed in Canada. Where the drug is not being marketed in Canada, no protection will be offered. For example, this would prevent the situation where the originally marketed version of a protected innovative drug is withdrawn from the Canadian market by the innovator, but no equivalent generic drug is allowed on the Canadian market until the protection period has expired.

Register of innovative drugs

As a transparency measure, a register of innovative drugs will be created. The register will include the name of the drug, the medicinal ingredient, and the date on which the data protection and, where applicable, pediatric extension will terminate. This register should provide both transparency and predictability for Canadian pharmaceutical companies.

Consent provision

Following comments from stakeholders during the consultation period, a provision was added to allow an innovative company to provide consent to another manufacturer to both file a submission during the six-year "no file" period and to allow for the issuance of the notice of compliance during the entire protection period. This addition was a minor change from the pre-published version to simply correct an oversight.

Transitional provision

The transitional provision has been amended to allow for the protection to extend to drugs that have received notices of compliance following pre-publication in the *Canada Gazette*, Part I, on June 17, 2006. This change is in keeping with the transition period affecting the patent eligibility under the PM(NOC) Regulations.

Amendments to the PM(NOC) Regulations

These amendments are being enacted at the same time as amendments to the PM(NOC) Regulations. Amendments to those regulations are intended to reaffirm the requirements for listing patents on the patent register, thereby restoring the original policy intent of the PM(NOC) Regulations and reducing the number of court cases between innovator and generic manufacturers, which can delay the issuance of a notice of compliance to the latter.

The changes to the PM(NOC) Regulations are also being refined in response to comments received following initial publication. The changes also clarify that the PM(NOC) Regulations apply only to those second-entry submissions in which a direct or indirect comparison or reference is made to the drug for which a patent is listed. The two sets of amended regulations are intended to act as a balanced set of measures, designed to work together to stabilize Canada's intellectual property protection for drugs by ensuring a minimum period of protection and maintaining a reasonable ceiling on the maximum protection available. For further information on the amended PM(NOC) Regulations, refer to the RIAS prepared by Industry Canada and published on the same day as this RIAS.

Alternatives

Terms of protection available internationally:

Currently, the United States offers a five-year term of protection to manufacturers who file a submission for a new active ingredient, with three years of protection available for new uses or other significant changes approved on the basis of new and essential clinical investigations. The United States also offers an additional period of six months of exclusivity for drugs where pediatric studies were conducted and deemed acceptable by the Food and Drug Administration. This additional period attaches to both the new chemical entity exclusivity and patent protection listed in the *Orange Book*.

On November 30, 2005 the European Union began to offer a ten-year period of market protection, which can be extended to eleven years on the basis of the authorization of one or more new therapeutic indications. A generic application can only be submitted after eight years and the product can be approved for marketing after 10 years, or 11 years if, during the first eight years, the innovator obtains an authorisation for one or more new therapeutic indications. The European Commission has proposed new regulations that will enhance protection for drugs with pediatric studies. The draft pediatric regulations provide for a six-months patent extension in the form of an extension to the supplementary protection certificate for eligible medicines, other than orphan medicines. For orphan medicines, an additional two-years of market exclusivity is added to the existing ten-years awarded under the EU orphan regulation. The regulations also provide for ten years of data protection for new pediatric studies on off-patent products.

In determining how best to clarify Canada's NAFTA and TRIPS commitments while also promoting innovation within Canada, these alternative approaches were considered.

Maintain the status quo

The first option considered was to leave the Regulations unchanged. This was found to be an unacceptable option given the need to clarify and effectively implement the NAFTA and the TRIPS agreements while in turn, ensuring the protection offered in Canada was competitive with the protection offered in comparable jurisdictions.

Benefits and Costs

The government believes that these amendments, including changes resulting from stakeholders' comments, will achieve a greater balance between the need for innovative drugs and the need for competition in the marketplace in order to facilitate the accessibility of those drugs.

Introducing a six-year no-filing period within the eight-year term of data protection will allow innovators to enjoy market exclusivity without the threat of any challenges that might be brought against them during that six-year period. During this period, it is anticipated that innovator and generic litigation, and the costs associated with that litigation, would decrease significantly while providing increased predictability, a result which is desirable to stakeholders on both sides of the industry.

The introduction of a register of innovative drugs will ensure that the operation of data protection will be fair and transparent. The definition of "innovative drug" will prevent duplication of data protection terms. Conversely, it will be clearer as to when a generic manufacturer will be subject to data protection. The clarification of which types of studies will qualify an innovator company for the pediatric extension, and the timing upon which such trials must be submitted, will maximize the information received for the benefit of children. Finally, the goals of CAMR will not be hindered by the implementation of these amendments.

The net effect of the amendments to the data protection provisions in these Regulations, concurrent with amendments to the PM(NOC) Regulations, will be to provide a balanced, stable regime that encourages innovation while at the same time ensuring Canadians have access to affordable medicines. In addition to maintain predictability, the amendments also include a grandfathering provision, which provides that innovator submissions which have received from Health Canada a notice of compliance prior to June 17, 2006, remain subject to the data protection provision as it was interpreted and applied prior to that date.

Consultation

Pre-publication in the *Canada Gazette*, Part I, on June 17, 2006, was followed by a 30-day consultation period, during which time stakeholders were given the opportunity to provide comments on the proposed amendments to the *Food and Drug Regulations (Data Protection)*. Health Canada received representations from approximately 43 sources including innovator and generic manufacturers and their trade associations, biopharmaceutical manufacturers and their trade associations, members of parliament, universities, international pharmaceutical trade associations, provincial and territorial Ministers of Health, law firms and consumer groups. All of the stakeholder commentary was taken into consideration by the government. The amendments reflect the concerns and suggestions received from the various stakeholders. The following is a summary of the comments received from the stakeholders during the 30-day consultation period.

Proponents for the generic drug industry contended that Canada's existing data protection provisions are in accordance with NAFTA and TRIPS and that the proposed changes exceed Canada's commitments under international trade agreements and will result in the delay of generic drug products entering the Canadian marketplace leading to increasing health care costs for Canadian citizens. More specifically, the generic drug industry raised objections to the 8-year term and indicated that the proposed regulations for data protection would impose a moratorium on generic approval for a period that is three years longer than is required under NAFTA and in other jurisdictions, including the United States and Mexico. In the alternative, the generic drug industry recommended that, if there is to be a ban on competition, the starting date should be the date either of first approval in Canada or in another jurisdiction. Some proponents indicated that data protection should apply only if the product is launched in Canada within 90 days from receipt of the Notice of Compliance. In addition, the generic drug industry contended that the definition of "innovative drug" should be amended to expressly exclude metabolites and pro-drugs as many active metabolites are not covered by the words salt, esters, enantiomers, solvates or polymorphs. Further, the generic drug industry objected to the additional six-month pediatric exclusivity period as, in their opinion, it will not encourage pediatric research or pediatric trials in Canada, but will prolong the brands' monopolies.

Proponents for the innovative drug industry supported the eight-year term of data protection but urged the government to adopt a data protection period consistent with that of the European Union. The innovative drug industry requested that the scope of data protection be expanded to include product variations that have different safety and efficacy profiles from the original product, such as metabolites, enantiomers, salts and esters. In addition, they requested that the term of data protection be extended for new indications for previously approved compounds and on the switch of a product from prescription to non-prescription status. They also noted that the current language inadequately reflects the intent of providing protection to the original medicinal ingredient, and all products incorporating that medicinal ingredient, including combination products, different formulations and polymorphs. Further, the innovative drug industry, specifically the biopharmaceutical manufacturers, raised the concern that the term "variation" may be broadly interpreted to exclude innovative products, such as biologics, because it is unclear whether a different product developed by a subsequent innovator for a similar, but not identical, ingredient is considered a "variation" of the first product.

The innovative drug industry further objected to the marketing requirement for the application of data protection and contended that it is contrary to Canada's obligations under NAFTA and TRIPS. In the alternative, they noted that, if the marketing requirement remains, greater clarity on what "marketing" means and how it will be applied is necessary. They also noted that there

is a lack of clarity as to some of the wording in the provisions regarding pediatric extension. They indicated that the pediatric extension could be inadvertently undermined by wording regarding "supplements", requiring a "health benefit" and the ministerial approval for protection in a timely manner. Furthermore, the innovative industry indicated that the new regulations should include a provision permitting an innovator to consent to early filing of a submission by a subsequent manufacturer in addition to the provision permitting an innovator to consent to the early issuance of a Notice of Compliance. Finally, the innovative drug industry urged the Government to consider granting data protection to all products that receive Notices of Compliance after the date of pre-publication of the *Canada Gazette*, Part I. Some proponents, such as the biopharmaceutical manufacturers, requested that the new data protection regulations apply to data relating to products that have been marketed for less than eight years prior to the coming into force of the regulations for which there is no subsequent-entry manufacturers' submission filed prior to December 11, 2004, the date the generic drug industry was given notice of the proposed 8-year data protection term.

The provincial and territorial Ministers of Health recommended that the 30-day consultation period be extended an additional 60 days to allow for dialogue between the key stakeholders, so as to garner a better understanding of the impact of the proposed regulatory amendments. Specifically, the Ministers expressed concern that the proposed data protection regulations appear to impede access to non-patented medicines. Further consultations with provincial and territorial representative have since taken place.

Compliance and Enforcement

This amendment does not alter existing compliance mechanisms under the provisions of the Act and the regulations enforced by Health Canada inspectors.

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