Date: 20071214

Docket: T-1693-06

Citation: 2007 FC 1323

Ottawa, Ontario, December 14, 2007

PRESENT: The Honourable Mr. Justice Kelen

BETWEEN:

PHARMASCIENCE INC.

Applicant

and

ATTORNEY GENERAL OF CANADA

Respondent

REASONS FOR ORDER AND ORDER

[1] This is an application for judicial review of a decision by the Therapeutic Products Directorate of Health Canada (the TPD) dated August 21, 2006, whereby the TPD concluded that the applicant's application for a Notice of Compliance (NOC) for a generic drug was considered withdrawn without prejudice to re-filing because the applicant did not provide the required bioequivalence data in relation to the Canadian reference product.

[2] The existence, contents, and status of the applicant's submission for a NOC is confidential. To preserve such confidentiality, the drug in question is referred to as "pms-X/Y" rather than by its proposed brand name. The components it contains are referred to as "component X" and

"component Y" rather than by their molecular names, and the condition for which approval is sought is referred to as "condition A" rather than the condition itself. The applicant's submission for a NOC was made with reference to a Canadian reference product which, for the same reasons of confidentiality, will be referred to as "REFPRO," manufactured by another company, "Pharmacompany."

FACTS

[3] On July 29, 2005, the applicant, Pharmascience Inc., filed an Abbreviated New Drug Submission (ANDS) with the Minister of Health seeking a NOC for its product pms-X/Y, which is used for treatment of condition A.

[4] The applicant's product is a delayed release tablet containing two ingredients, component X and component Y.

[5] According to the applicant, even though REFPRO is itself a generic, it has become the Canadian reference product to which any new generic version is compared. This is due to the fact that REFPRO is the only X/Y product available in Canada for the treatment of condition A. In support of the claim that REFPRO is the appropriate Canadian reference product, the applicant notes that Health Canada itself described the applicant's ANDS as the "first generic submitted for the combination" of components X and Y.

[6] On December 16, 2002, prior to filing its ANDS, the applicant met with representatives of the TPD to discuss the submission requirements of their proposed drug. At the meeting, the applicant was informed that the TPD considered that bioequivalence of both components X and Y should be demonstrated in the applicant's submission. The TPD also made clear that if the applicant decided not to test for component Y, then it would have to justify why such a measurement was not necessary. According to the respondent, such justification should include clinical data demonstrating that component Y does not have a significant therapeutic effect in the treatment of condition A. Despite this notification, the applicant nevertheless decided that it would not conduct or submit bioavailability studies for component Y. Accordingly, the applicant's ANDS only included comparative bioavailability studies with respect to component X. It did not include comparative bioavailability studies for component Y.

[7] On September 30, 2005, after "screening" the applicant's July 29, 2005 application, the TPD informed the applicant that its submission was incomplete and, in particular, that a bioavailability study must be provided measuring the formulation's Y component. The TPD's notification provided the applicant with 45 days to address each of the identified deficiencies.

[8] On November 9, 2005, the applicant provided its response to the deficiencies identified by the TPD. In its response, the applicant raised four reasons why it believed a comparative bioavailability study of component Y was not required. Those reasons included: 1) that the Minister's general approach to bioequivalence reporting was not required for components of the class of component Y; 2) that there was no scientific support suggesting that component Y, at the

dosage in the REFPRO formulation, had any therapeutic effect in the treatment of condition A; 3) that REFPRO's previously-issued Product Monograph did not reference scientific support of such therapeutic effects; and 4) that the amount of component Y in the product was known to be safe and was within the TPD's guidelines.

[9] Despite its arguments, on January 24, 2006, the applicant received a "screening rejection letter" from the TPD, indicating that its ANDS was considered "withdrawn without prejudice to refiling." The TPD determined that the applicant's ANDS did not comply with Part C, Division 8 of the *Food and Drug Regulations*, C.R.C., c. 870 (the Regulations), since the applicant had not filed comparative bioavailability studies demonstrating bioequivalence of component Y with that in the Canadian reference product, REFPRO.

[10] On February 22, 2006, in accordance with the guidance document "Reconsideration of Final Decisions Issued for Human Drug Submissions," the applicant filed a letter outlining its intent to request a reconsideration of the January 24, 2006 screening rejection letter. Subsequently, on April 18, 2006, the applicant filed its formal "Request for Reconsideration" with the TPD.

Decision under review

[11] On August 21, 2006, the TPD advised that, on the basis of a recommendation from the TPD's Office of Science, the original decision was being upheld. In his decision, the Director General of the TPD stated that:

> The Directorate is maintaining the initial decision since, on re-consideration, it is clear that [component Y has a condition A-related

> effect]. Evidence of bioequivalence to the Canadian reference product will be required for both [component Y and component X] of the above-named product.

ISSUE

[12] The sole issue in this application is whether the TPD erred in rejecting the applicant's submission on the ground that the applicant failed to provide a comparative bioavailability study for component Y.

RELEVANT LEGISLATION

[13] The legislation relevant to this application is the *Food and Drug Regulations*, C.R.C., c. 870. The relevant provisions are contained within Part C, Division 8, and have been attached to this judgment as Appendix "A."

STANDARD OF REVIEW

[14] In *Dr. Q v. The College of Physicians and Surgeons of British Columbia*, 2003 SCC 19, [2003] 1 S.C.R. 226, the Supreme Court of Canada reaffirmed the primacy of the pragmatic and functional approach in relation to the review of administrative decisions. Chief Justice McLachlin, writing for a unanimous Court, stated at paragraph 25:

> ¶ 25 … it is no longer sufficient to slot a particular issue into a pigeon hole of judicial review and, on this basis, demand correctness from the decision-maker. Nor is a reviewing court's interpretation of a privative clause or mechanism of review solely dispositive of a particular standard of review. … <u>The pragmatic and functional approach demands a more nuanced analysis based on consideration</u>

> of a number of factors. This approach applies whenever a court reviews the decision of an administrative body. …
>
> [Emphasis added.]

[15] In *Reddy-Cheminor Inc. v. Canada (Attorney General)*, 2003 FCT 542, 233 F.T.R. 271, aff'd 2004 FCA 102, 319 N.R. 185, Madam Justice Layden-Stevenson considered the standard of review to be applied by a reviewing court to the decisions of the Minister of Health relating to drug approval. After applying the pragmatic and functional approach, Madam Justice Layden-Stevenson found at paragraph 57:

> ¶ 57 The balancing of these four factors suggests considerable deference and thus a standard of review of patent unreasonableness. I refer to the comments of MacKay J. in [*Apotex Inc. v. Canada (Attorney General)* (1993), 59 F.T.R. 85] at p. 111-112:
>
> > "In this case the discretion granted to the executive involves more than the determination of facts and the application of the law in determining the rights of a party that do not directly affect the welfare of others. More is here involved than is often the case where courts are called upon in an application for judicial review to review the process followed by an administrator or tribunal. Discretion here vested by the Act and Regulations requires judgment in light of special expertise, in this case in related fields of applied and basic sciences, which judgment affects not merely the rights of an applicant party but is directed ultimately to the interests of, or prevention of injury to, the health of others, purchasers and consumers. In my view, discretion of this sort warrants judicial deference that recognizes the special expertise and responsibilities of the Minister and his advisers within HPH (Health Protection Branch) who must deal with numerous applications for approval of new drugs … it is now accepted that a court will intervene only where the decision

> maker has interpreted governing legislation in a manner that is so patently unreasonable that it demands intervention by the court . . .”

[16] This finding was affirmed on appeal, with Mr. Justice Evans stating at paragraph 8 of the appellate decision:

> ¶ 8 Second, I agree with Layden-Stevenson, J., that the pragmatic and functional analysis indicates that the decision under review is entitled to a high degree of deference. The drug approval process is a complex and technical area of public administration with a direct impact on the health of Canadians. Determining whether two products contain “identical medicinal ingredients” requires scientific understanding and regulatory experience, rather than knowledge of the law or legal principles.

[17] In the case at bar, the decision of whether a comparative bioavailability study is required in an ANDS falls directly within the expertise of the scientists at the TPD. Accordingly, the decision of the TPD will only be set aside if it is found to be patently unreasonable.

[18] In *Law Society of New Brunswick v. Ryan*, 2003 SCC 20, [2003] 1 S.C.R. 247, the Supreme Court of Canada stated at paragraph 52 that a patently unreasonable defect is one that can be explained “simply and easily, leaving no real possibility of doubting that the decision is defective.” This is a very high standard. Accordingly, a decision will only be set aside as being patently unreasonable if it is “clearly irrational” or “evidently not in accordance with reason.”

ANALYSIS

Issue: **Did the TPD err in rejecting the applicant's submission on the ground that the applicant failed to provide a comparative bioavailability study for component Y?**

Drug approval regulatory framework

[19] Drug manufacturers wishing to sell a new drug in Canada must first obtain a NOC pursuant to Part C, Division 8 of the Regulations. Manufacturers become eligible to receive a NOC by filing a drug submission with the Minister of Health. There are several types of drug submissions that may be filed pursuant to the Regulations.

[20] Subsection C.08.002(2) establishes the content requirements for a New Drug Submission (NDS). In order to receive a NOC for a NDS, a manufacturer must establish the safety and clinical effectiveness of the drug through the submission of detailed reports and clinical testing results. Establishing the drug's safety means establishing that it is safe to use for the treatment of a specified disease. Establishing the clinical effectiveness of the drug involves establishing that the drug is effective in treating that disease or condition. Such submissions are generally very extensive and are typically filed by brand name or "innovative" drug manufacturers.

[21] Where a generic drug company seeks to copy a drug that has already been marketed in Canada, it need not file a NDS in order to establish that its product is both safe and clinically effective. Rather, the generic company can file an ANDS, which simply requires the manufacturer to establish that its product is the same as a previously-approved Canadian reference product. The

content requirements for an ANDS submission are contained within section C.08.002.1 of the Regulations.

[22] Finally, where a manufacturer has already received a NOC for a drug, any significant change made to that drug requires a Supplemental New Drug Submission (SNDS), the content requirements for which are set out in section C.08.003 of the Regulations.

Applicant filed an ANDS

[23] In the case at bar, the applicant filed an ANDS with the Minister of Health, seeking a NOC for its drug, pms-X/Y. Accordingly, while the applicant was not required to carry out clinical studies directly addressing the drug's safety and clinical effectiveness, it did need to include in its submission "sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug," including a number of factors listed in subsection C.08.002.1(2) of the Regulations.

[24] The respondent maintains that when reviewing an ANDS such as the one filed by the applicant, the TPD will conclude that the proposed generic drug is safe and clinically effective only where the evidence shows that the proposed generic drug is essentially identical to a drug that has already been shown to be safe and effective. Under subsection C.08.002.1(2) of the Regulations, this comparison is accomplished through two principal components:

a. by the applicant showing that its product is the "pharmaceutical equivalent" of the Canadian reference product, REFPRO (C.08.002.1(2)(c)(i)); and

b. by the applicant showing, where the Minister considers it necessary, that its product is "bioequivalent" with the Canadian reference product (C.08.002.1(2)(c)(ii)).

[25] The respondent further maintains that since the applicant is seeking approval for a generic version of a drug that was initially approved and sold as a "combination drug" – meaning that it contains more than one medicinal ingredient – then comparative bioavailability studies must be conducted measuring *each* active ingredient in the drug. In essence, the respondent maintains that where a drug has been sold as a "combination drug," "the minister considers it necessary" that each active ingredient of the drug be subject to a bioavailability study.

The parties' submissions regarding the TPD decision

[26] The applicant raises a number of arguments why the TPD erred in its decision, all of which relate to its position that a bioavailability study measuring component Y is not necessary to support its ANDS. First, the applicant argues that bioavailability data need not be proven for component Y since the TPD has already confirmed that the drug is both safe and clinically effective. In support of this position, the applicant points to the cross-examination of Leslie Cockell, Manager of the Division of Biopharmaceutics Evaluation 2, in the Bureau of Pharmaceutical Sciences, TPD, Health Canada, who stated in relation to the safety of component Y in REFPRO:

> Q. Is it just a safety issue or just an efficacy issue, or both? Does the safety change depending on whether you claim [component Y] as having [a condition A-related] effect?
>
> A. I understand that levels of [component Y] as far as safety has been established for a single dose, for a daily dose, so in that respect I would say the safety may not change.

and in relation to the component's clinical effectiveness:

> Q. So the Minister was satisfied as to the safety and efficacy of the new product without the need for bioequivalence data vis-à-vis the original product.
>
> A. Correct.
>
> […]
>
> Q. … We have established that the minister does not always need that bioequivalence data in the case of this product – in the case of [X/Y], the Minister does not require bioequivalence data to be satisfied as to the safety and efficacy. Is that fair to say?
>
> A. That's fair to say.

[27] Further, in relation to the safety of component Y, the applicant submits that Ms. Cockell's testimony is consistent with:

a. statements in REFPRO's previously-issued Product Monograph that "[component Y] is generally recognized as having no adverse effects";
b. the Minister's approach to not require bioavailability studies for components in the class of component Y in Drug Identification Number (DIN) submissions; and
c. the fact that the daily amount of component Y in the applicant's drug is well within the maximum daily limit in the Minister's guidelines.

[28] Accordingly, the applicant argues that the TPD's decision to reject its ANDS on the basis that it did not contain comparative bioavailability data relating to component Y was arbitrary, contrary to the Regulations, and unreasonable on its face.

[29] The respondent, however, argues that the TPD's decision in this regard was not arbitrary or inconsistent with the Regulations or the TPD's internal policy. First, the respondent submits that the applicant's reliance on the Minister's guideline document, *Preparation of Drug Identification Number Submissions*, is inappropriate since that document has no application to a product such as pms-X/Y. According to the respondent, this guideline applies solely to the class of low-risk products regulated under the less stringent drug review framework set out in Part C, Division 1 of the Regulations. New drugs, with complex risk/benefit profiles such as pms-X/Y, are not "DIN submissions," and are completely outside the scope of the guideline document.

[30] The difference, in the respondent's submission, is that use of component Y is "so well-understood" and of "sufficiently low risk" that it does not require bioavailability data in order to provide the necessary level of confidence in the safety and clinical effectiveness of the product. However, where a compound such as component Y is used in combination with another compound to treat a serious condition – such as the treatment of condition A – then the compound must be assessed in the same way as any other active ingredient pursuant to the framework contained in Part C, Division 8 of the Regulations.

[31] As well, the respondent disagrees with the applicant that the safety of component Y need not be established since REFPRO's previously-issued Product Monograph does not contain any clinical references conclusively demonstrating any therapeutic role for component Y alone in the treatment of condition A. The respondent submits that such an argument must fail since it does not recognize that REFPRO was approved as a combination product, thereby meaning that the drug's safety and

clinical effectiveness was determined based on studies using the active ingredients in combination, rather than in isolation.

[32] Further, in recognizing that the Regulations only require evidence of bioequivalence where the Minister "considers it necessary," the respondent points to the fact that the applicant was notified of the TPD's position regarding the need for bioavailability data well before the applicant filed its ANDS in July 2005.

[33] The applicant notes that Ms. Cockell's testimony concerning the safety and clinical effectiveness of component Y was made in reference to Pharmacompany's SNDS for a new formulation of REFPRO, and not in reference to the applicant's ANDS. However, the applicant maintains that there is no relevant substantive or regulatory distinction between the two submissions. Regarding the regulatory frameworks, both the requirements applicable to a SNDS – found in subsection C.08.003(3) of the Regulations – and those applicable to an ANDS – found in subsection C.08.002.1(2) – state that the submission must contain "sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug."

[34] However, the two frameworks differ in that the requirements for an ANDS go on to explicitly list a number of factors that must be included to aid the Minister's assessment. These factors include paragraph (c), which refers to:

(*c*) evidence from the comparative studies conducted in connection with the submission that the new drug is	*c*) les éléments de preuve, provenant des études comparatives menées dans le cadre de la présentation, établissant que la drogue

(i) the pharmaceutical equivalent of the Canadian reference product, and	(i) d'une part, est un équivalent pharmaceutique du produit de référence canadien,
(ii) where the Minister considers it necessary on the basis of the pharmaceutical and, where applicable, bioavailability characteristics of the new drug, bioequivalent with the Canadian reference product as demonstrated using bioavailability studies, pharmacodynamic studies or clinical studies;	(ii) d'autre part, si le ministre l'estime nécessaire d'après les caractéristiques pharmaceutiques et, le cas échéant, d'après les caractéristiques en matière de biodisponibilité de celle-ci, est bioéquivalente au produit de référence canadien selon les résultats des études en matière de biodisponibilité, des études pharmacodynamiques ou des études cliniques;

[35] No such express requirements exist in regards to a SNDS, thereby suggesting that the Minister may be satisfied of a drug's safety and effectiveness without requiring comparative bioavailability data measuring the components of a new drug's formulation. While the applicant recognizes that the framework governing a SNDS does not contain a list of particular factors that must be included in the submission, it nevertheless maintains that there is no material difference since both sections expressly require "sufficient information" to be included, and the ANDS framework only requires proof of bioequivalence where the Minister considers it necessary.

[36] Further, the applicant argues that even though section C.08.003 may "theoretically" allow a manufacturer to establish the effectiveness of its SNDS through a means other than including information addressing bioequivalence, there is no evidence of what such other methods might be, nor is there any evidence that Pharmacompany adopted such other methods in order to independently establish the safety and effectiveness of component Y in REFPRO.

[37] The applicant goes on to compare the requirements placed on it by the TPD with Pharmacompany's SNDS for a new delayed-release formulation of REFPRO, stating that that submission did not contain a comparative bioavailability study in the "fasted and fed" states demonstrating the bioequivalence of component Y in the new formulation with reference to the old formulation. Accordingly, the applicant submits that this fact is clear evidence that a comparative bioavailability study for component Y is not actually considered necessary by the TPD in order to assess the safety and clinical effectiveness of an X/Y product. In relying on this argument, the applicant submits that the TPD's decision to reject the applicant's ANDS directly contradicts the evidence and was, therefore, unreasonable.

[38] The respondent notes the differences between the two regulatory frameworks and the fact that the requirements for a SNDS are silent with respect to the type information needed to "enable the Minister to assess the safety and effectiveness of the new drug." Accordingly, the respondent argues that the TPD has "broad discretion" as to what information and material will be sufficient to support the proposed change under a SNDS, and that this framework is completely different from that required with respect to an ANDS.

[39] The respondent does, however, take note of the unique circumstances surrounding Pharmacompany's SNDS. The respondent submits that while bioavailability studies are commonly part of a SNDS concerning a change in formulation, such a study was not possible in the circumstances surrounding Pharmacompany's submission. Accordingly, the TPD was required to find an alternate means of assessing the new formulation's safety and clinical effectiveness. The

respondent maintains, however, that despite these unique circumstances, the alternate means taken by the TPD were justified by the SNDS requirements, which are substantially different from the content requirements for an ANDS.

Court's analysis

[40] In the case at bar, the TPD considered it necessary for the applicant to file bioavailability studies for both component X and component Y of its proposed new drug in order to show that the drug was bioequivalent with the Canadian reference product, REFPRO.

[41] Understanding this consideration, the question then becomes whether the TPD's outright rejection of the applicant's ANDS was inconsistent with the requirements provided for in the Regulations in a way that was patently unreasonable. In my view, the TPD's requirement that the applicant file bioavailability studies for both component X and component Y was not patently unreasonable. Such a decision was entirely within the purview of the TPD. The decision stated that "it is clear that [component Y has a condition A-related effect]." The applicant has not provided any scientific evidence that this component does not work to offset the effects of condition A in this product.

[42] The respondent directed the Court to the evidence that component Y has a condition A-related effect. The evidence was:

1. the NOC for REFPRO that the medicinal ingredients are component X and component Y and that their therapeutic classification is as a treatment for condition A. This means that both ingredients have this therapeutic effect;
2. the new REFPRO Product Monograph states at page 9 that the drug provides the action of two unrelated compounds which provide treatment for condition A. This shows that both ingredients have a role to play, and the drug would not be approved in combination if component Y did not have any therapeutic role; and
3. two scientific studies were before the TPD. The titles of these studies show that component Y is used for the treatment of condition A. Therefore, when used in combination with component X, it acts as much more than in its usual role.

The Court is satisfied that the decision, based on this evidence, was reasonably open to the decision-maker, and was not "patently unreasonable," *i.e.*, clearly irrational.

[43] The applicant filed its ANDS in reference to REFPRO. This drug contains identical amounts of the two active ingredients as the applicant's product. The applicant submitted that since the Minister of Health recently approved a SNDS for the new REFPRO without requiring the manufacturer to file a study comparing the bioavailability of component Y in the new formulation to that in the old formulation, or any other evidence of the effectiveness of component Y in the new formulation, then the applicant should not have had to do so either.

[44] First, the requirements for a SNDS are substantially different from the requirements for an ANDS, as the lack of express requirements in relation to a SNDS gives the TPD more discretion in

determining what is necessary to enable the Minister to assess a drug's safety and clinical effectiveness. This significant difference was addressed by the Federal Court of Appeal in *Reddy-Cheminor*, above, where Mr. Justice Evans stated at paragraph 11:

> ¶ 11 In my opinion, this argument is misconceived because the statutory criteria for obtaining a NOC on the basis of a SNDS are materially different from those governing the issue of a NOC on the basis of an ANDS. A SNDS may be filed by a person when a NOC has been issued in respect of a drug and some change has been made to the product, its manufacture or marketing.

[45] Second, the jurisprudence establishes that while consistency in drug regulation is an admirable objective, it cannot overrule the objective consideration of individual submissions on a case-by-case basis. Moreover, the existence of a conflict in administrative decisions, if a conflict does in fact exist, does not constitute a basis for the Court setting aside a decision for drug approval: see *Reddy-Cheminor*, above, per Layden-Stevenson J. at paragraphs 35-36 (affirmed on appeal).

[46] Instead of requiring Pharmacompany to conduct and file a bioavailability study on component Y, Health Canada accepted the two years of post-market data, which showed how the new product performed in the market. As the applicant submitted, this post-market data does not show that the new product is as effective, only that it is safe. However, Health Canada was prepared to grant the concession since Pharmacompany was introducing an extended release of its product, which had actually been sold in Canada for quite some time.

[47] With respect to the differences between the TPD's consideration of Pharmacompany's SNDS and the applicant's ANDS in the case at bar, such different treatment is reflective of the

significant differences in the regulatory framework governing the different types of submissions. Further, the issue of the TPD's treatment of the Pharmacompany SNDS is not before the Court in this matter. All the Court is concerned with here is whether the TPD was patently unreasonable in requiring the applicant to file bioavailability studies supporting its ANDS for pms-X/Y. As outlined above, such a requirement was within the expertise of the TPD, and will not be set aside by this Court as being patently unreasonable.

CONCLUSION

[48] The Court concludes that:

1. the decision under review was reasonably open to the decision-maker on the basis of the evidence;
2. the applicant's reliance upon the regulatory approval for the Canadian reference product is misguided. The Canadian reference product was approved under the regulations for a SNDS, which are different than the regulations applicable to the applicant's product;
3. even if Health Canada made a mistake in approving the Canadian reference product, that mistake does not affect the obligation of Health Canada to undertake an objective consideration of the applicant's submission on a stand alone basis. Otherwise, Health Canada would be repeating its previous mistake. Moreover, the existence of a conflict in administrative decisions with respect to drug approvals does not constitute a basis for the Court to intervene; and

4. the fact that component Y, when used alone, is well known to be safe and effective, does not mean that it is safe and effective when used in combination with another medicinal ingredient. In such cases, Health Canada requires a bioavailability study for all the ingredients, including component Y.

ORDER

THIS COURT ORDERS that:

This application for judicial review is dismissed with costs.

"Michael A. Kelen"
Judge

APPENDIX "A"

Food and Drug Regulations, C.R.C., c. 870

C.08.002.1 (1) A manufacturer of a new drug may file an abbreviated new drug submission for the new drug where, in comparison with a Canadian reference product,

(*a*) the new drug is the pharmaceutical equivalent of the Canadian reference product;

(*b*) the new drug is bioequivalent with the Canadian reference product, based on the pharmaceutical and, where the Minister considers it necessary, bioavailability characteristics;

(*c*) the route of administration of the new drug is the same as that of the Canadian reference product; and

(*d*) the conditions of use for the new drug fall within the conditions of use for the Canadian reference product.

(2) An abbreviated new drug submission shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug, including the following:

(*a*) the information and material described in paragraphs C.08.002(2)(*a*) to (*f*) and (*j*) to (*l*);

(*b*) information identifying the Canadian reference product used in any comparative studies conducted in connection with the submission;

(*c*) evidence from the comparative studies conducted in connection with the submission that the new drug is

(i) the pharmaceutical equivalent of the Canadian reference product, and

C.08.002.1 (1) Le fabricant d'une drogue nouvelle peut déposer à l'égard de celle-ci une présentation abrégée de drogue nouvelle si, par comparaison à un produit de référence canadien :

a) la drogue nouvelle est un équivalent pharmaceutique du produit de référence canadien;

b) elle est bioéquivalente au produit de référence canadien d'après les caractéristiques pharmaceutiques et, si le ministre l'estime nécessaire, d'après les caractéristiques en matière de biodisponibilité;

c) la voie d'administration de la drogue nouvelle est identique à celle du produit de référence canadien;

d) les conditions thérapeutiques relatives à la drogue nouvelle figurent parmi celles qui s'appliquent au produit de référence canadien.

(2) La présentation abrégée de drogue nouvelle doit contenir suffisamment de renseignements et de matériel pour permettre au ministre d'évaluer l'innocuité et l'efficacité de la drogue nouvelle, notamment :

a) les renseignements et le matériel visés aux alinéas C.08.002(2)*a*) à *f*) et *j*) à *l*);

b) les renseignements permettant d'identifier le produit de référence canadien utilisé pour les études comparatives menées dans le cadre de la présentation;

c) les éléments de preuve, provenant des études comparatives menées dans le cadre de la présentation, établissant que la drogue

(ii) where the Minister considers it necessary on the basis of the pharmaceutical and, where applicable, bioavailability characteristics of the new drug, bioequivalent with the Canadian reference product as demonstrated using bioavailability studies, pharmacodynamic studies or clinical studies;

(*d*) evidence that all test batches of the new drug used in any studies conducted in connection with the submission were manufactured and controlled in a manner that is representative of market production; and

(*e*) for a drug intended for administration to food-producing animals, sufficient information to confirm that the withdrawal period is identical to that of the Canadian reference product.

(3) The manufacturer of a new drug shall, at the request of the Minister, provide the Minister, where for the purposes of an abbreviated new drug submission the Minister considers it necessary to assess the safety and effectiveness of the new drug, with the following information and material:

(*a*) the names and addresses of the manufacturers of each of the ingredients of the new drug and the names and addresses of the manufacturers of the new drug in the dosage form in which it is proposed that the new drug be sold;

(*b*) samples of the ingredients of the new drug;

(*c*) samples of the new drug in the dosage form in which it is proposed that the new drug be sold; and

nouvelle :

(i) d’une part, est un équivalent pharmaceutique du produit de référence canadien,

(ii) d’autre part, si le ministre l’estime nécessaire d’après les caractéristiques pharmaceutiques et, le cas échéant, d’après les caractéristiques en matière de biodisponibilité de celle-ci, est bioéquivalente au produit de référence canadien selon les résultats des études en matière de biodisponibilité, des études pharmacodynamiques ou des études cliniques;

d) les éléments de preuve établissant que les lots d’essai de la drogue nouvelle ayant servi aux études menées dans le cadre de la présentation ont été fabriqués et contrôlés d’une manière représentative de la production destinée au commerce;

e) dans le cas d’une drogue destinée à être administrée à des animaux producteurs de denrées alimentaires, les renseignements permettant de confirmer que le délai d’attente est identique à celui du produit de référence canadien.

(3) Le fabricant de la drogue nouvelle doit, à la demande du ministre, lui fournir, selon ce que celui-ci estime nécessaire pour évaluer l’innocuité et l’efficacité de la drogue dans le cadre de la présentation abrégée de drogue nouvelle, les renseignements et le matériel suivants:

a) les nom et adresse des fabricants de chaque ingrédient de la drogue nouvelle et les nom et adresse des fabricants de la drogue nouvelle sous sa forme posologique proposée pour la vente;

b) des échantillons des ingrédients de la drogue nouvelle;

(*d*) any additional information or material respecting the safety and effectiveness of the new drug.

c) des échantillons de la drogue nouvelle sous sa forme posologique proposée pour la vente;

d) tout renseignement ou matériel supplémentaire se rapportant à l'innocuité et à l’efficacité de la drogue nouvelle.

C.08.003 (1) Notwithstanding section C.08.002, no person shall sell a new drug in respect of which a notice of compliance has been issued to the manufacturer of that new drug and has not been suspended pursuant to section C.08.006, if any of the matters specified in subsection (2) are significantly different from the information or material contained in the new drug submission or abbreviated new drug submission, unless

(*a*) the manufacturer of the new drug has filed with the Minister

(i) a supplement to that new drug submission, or

(ii) a supplement to that abbreviated new drug submission;

(*b*) the Minister has issued a notice of compliance to the manufacturer of the new drug in respect of the supplement;

(*c*) the notice of compliance in respect of the supplement has not been suspended pursuant to section C.08.006; and

(*d*) the manufacturer of the new drug has submitted to the Minister specimens of the final version of any label, including any package insert, product brochure and file card, intended for use in connection with the new drug, where a change with respect to any of the matters specified in subsection (2) is made that would require a change to the label.

C.08.003 (1) Malgré l'article C.08.002, il est interdit de vendre une drogue nouvelle à l'égard de laquelle un avis de conformité a été délivré à son fabricant et n'a pas été suspendu aux termes de l'article C.08.006, lorsqu'un des éléments visés au paragraphe (2) diffère sensiblement des renseignements ou du matériel contenus dans la présentation de drogue nouvelle ou la présentation abrégée de drogue nouvelle, à moins que les conditions suivantes ne soient réunies :

a) le fabricant de la drogue nouvelle a déposé auprès du ministre :

(i) soit un supplément à la présentation de drogue nouvelle,

(ii) soit un supplément à la présentation abrégée de drogue nouvelle;

b) le ministre a délivré au fabricant un avis de conformité relativement au supplément;

c) l'avis de conformité relatif au supplément n'a pas été suspendu aux termes de l'article C.08.006;

d) le fabricant de la drogue nouvelle a présenté au ministre, sous leur forme définitive, des échantillons de toute étiquette—y compris une notice jointe à l'emballage, un dépliant et une fiche sur le produit—destinée à être utilisée pour la drogue nouvelle, dans le cas où la modification d'un des éléments visés au paragraphe (2) nécessite un changement dans l'étiquette.

(2) The matters specified for the purposes of subsection (1), in relation to the new drug, are the following:

(*a*) the description of the new drug;

(*b*) the brand name of the new drug or the identifying name or code proposed for the new drug;

(*c*) the specifications of the ingredients of the new drug;

(*d*) the plant and equipment used in manufacturing, preparation and packaging the new drug;

(*e*) the method of manufacture and the controls used in manufacturing, preparation and packaging the new drug;

(*f*) the tests applied to control the potency, purity, stability and safety of the new drug;

(*g*) the labels used in connection with the new drug;

(*h*) the representations made with regard to the new drug respecting

(i) the recommended route of administration of the new drug,

(ii) the dosage of the new drug,

(iii) the claims made for the new drug,

(iv) the contra-indications and side effects of the new drug, and

(v) the withdrawal period of the new drug; and

(*i*) the dosage form in which it is proposed that the new drug be sold.

(3) A supplement to a new drug submission or to an abbreviated new drug submission, with respect to the matters that are significantly different from those contained in the submission, shall contain sufficient information and material

(2) Pour l'application du paragraphe (1), les éléments ayant trait à la drogue nouvelle sont les suivants :

a) sa description;

b) sa marque nominative ou le nom ou code sous lequel il est proposé de l'identifier;

c) les spécifications de ses ingrédients;

d) les installations et l'équipement à utiliser pour sa fabrication, sa préparation et son emballage;

e) la méthode de fabrication et les mécanismes de contrôle à appliquer pour sa fabrication, sa préparation et son emballage;

f) les analyses effectuées pour contrôler son activité, sa pureté, sa stabilité et son innocuité;

g) les étiquettes à utiliser pour la drogue nouvelle;

h) les observations faites relativement :

(i) à la voie d'administration recommandée pour la drogue nouvelle,

(ii) à sa posologie,

(iii) aux propriétés qui lui sont attribuées,

(iv) à ses contre-indications et à ses effets secondaires,

(v) au délai d'attente applicable à celle-ci;

i) sa forme posologique proposée pour la vente.

(3) Le supplément à la présentation de drogue nouvelle ou à la présentation abrégée de drogue nouvelle doit contenir, à l'égard des éléments qui diffèrent sensiblement de ce qui figure dans la présentation, les renseignements et

to enable the Minister to assess the safety and effectiveness of the new drug in relation to those matters.

le matériel nécessaires pour permettre au ministre d'évaluer l'innocuité et l'efficacité de la drogue nouvelle relativement à ces éléments.

FEDERAL COURT

SOLICITORS OF RECORD

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