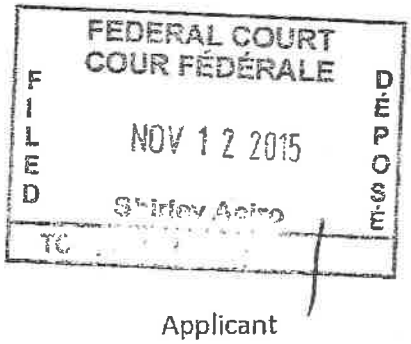
Court File No. T-1915-15

FEDERAL COURT



BETWEEN:

APOTEX INC.

Applicant

- and -

MINISTER OF HEALTH and ATTORNEY GENERAL OF CANADA

Respondents

NOTICE OF APPLICATION

TO THE RESPONDENT:

A PROCEEDING HAS BEEN COMMENCED by the applicant. The relief claimed by the applicant appears on the following page.

THIS APPLICATION will be heard by the Court at a time and place to be fixed by the Judicial Administrator. Unless the Court orders otherwise, the place of hearing will be as requested by the applicant. The applicant requests that this application be heard at Toronto.

IF YOU WISH TO OPPOSE THIS APPLICATION, to receive notice of any step in the application or to be served with any documents in the application, you or a solicitor acting for you must prepare a notice of appearance in Form 305 prescribed

by the *Federal Courts Rules* and serve it on the applicant's solicitor, or where the applicant is self-represented, on the applicant, WITHIN 10 DAYS after being served with this notice of application.

Copies of the *Federal Courts Rules*, information concerning the local offices of the Court and other necessary information may be obtained on request to the Administrator of this Court at Ottawa (telephone 613-992-4238) or at any local office.

IF YOU FAIL TO OPPOSE THIS APPLICATION, JUDGMENT MAY BE GIVEN IN YOUR ABSENCE AND WITHOUT FURTHER NOTICE TO YOU.

November 12, 2015

SHIRLEY ACIRO
REGISTRY OFFICER
AGENT DU GREFFE

Issued by: _____
Registry Officer

Address of local office: 180 Queen St. West
Suite 200
Toronto, Ontario M5V 3L6

TO: THE REGISTRAR
Federal Court of Canada
Application Division
180 Queen St. West
Suite 200
Toronto, Ontario M5V 3L6

AND TO: MINISTER OF HEALTH and ATTORNEY GENERAL OF CANADA
130 King Street West
Suite 3400, Box 36
Toronto, Ontario M5X 1K6

APPLICATION

THIS IS AN APPLICATION for judicial review by Apotex Inc. ("Apotex") of the decision of the Respondent, Minister of Health ("Minister"), to refuse to end its prohibition on granting Notices of Compliance ("NOCs") and reviewing Abbreviated New Drug Submissions ("ANDSs") and Supplementary ANDS ("SANDSs") for products manufactured at Apotex Research Private Limited ("ARPL") or having active pharmaceutical ingredient ("API") sourced from Apotex Pharmachem India Private Limited ("APIPL") without conditions precedent, in the face of the Federal Court's Judgment in T-2224-14 dated October 14, 2015.

THE APPLICANT MAKES APPLICATION FOR:

1. An order quashing the decision of the Minister to refuse to end its prohibition on granting NOCs and reviewing ANDSs and SANDSs for products manufactured at ARPL or having API sourced from APIPL;

2. An Order in the nature of *mandamus* compelling the Minister to issue NOCs in respect of all ANDSs and SANDSs for submissions for products manufactured at ARPL or having API sourced from APIPL where the Minister had, sometime in the past, completed her review and found the submissions to be satisfactory and where no statutory impediments to the issuance of an NOC exist;

3. An Order in the nature of *mandamus* compelling the Minister to return to "Patent Hold" all submissions for products manufactured at ARPL or having API sourced from APIPL that have been removed from "Patent Hold" on the basis of

the same purported and unspecified data integrity concerns on which the Minister relied to ground her improper and illegal import ban against ARPL and APIPL;

4. An order in the nature of *mandamus* that all other submissions for products manufactured at ARPL or having API sourced from APIPL be reviewed in accordance with the *Food and Drug Regulations*, without regard to a condition precedent that Apotex provide further evidence to refute the same purported and unspecified data integrity concerns which the Minister relied on to ground her improper and illegal import ban against ARPL and APIPL;

5. Costs of this application on a scale and in amount determined by this Honourable Court to be appropriate in all of the circumstances; and

6. Such further and other relief as this Honourable Court may deem just.

THE GROUNDS FOR THE APPLICATION ARE:

Overview

1. Apotex is a Canadian corporation that carries on business as a manufacturer of "generic" pharmaceutical products. A generic product is a product equivalent to an original product already on the market.

2. The Minister is responsible, through her delegates at Health Canada, for administering the *Food and Drugs Act* and the *Food and Drug Regulations* made thereunder. Health Canada is the federal government department that oversees the

regulation of drug products in Canada. It consists of various branches, bureaus and offices, including the Health Products and Food Branch ("HPFB"), which includes the HPFB Inspectorate, which is responsible for compliance and enforcement activities and oversight of establishment licensing for health products, and the Therapeutic Products Directorate ("TPD"), which is responsible for the regulation and market authorization for pharmaceutical drugs for human use.

Regulatory Regime

3. The Minister controls the approval of new drugs in Canada through exercise of statutory powers under the *Food and Drugs Act* and the *Food and Drug Regulations*. No person may advertise or sell a new drug in Canada unless and until the Minister grants that person an NOC in respect of that drug.

4. Section C.08.004 of the *Food and Drug Regulations* directs that a drug manufacturer may obtain an NOC in respect of a new drug only after filing a submission. A submission must contain sufficient information to enable TPD to assess the safety and effectiveness of the new drug in question. The submission may be either a New Drug Submission ("NDS") which is a submission including the results of clinical trials, or it may be an ANDS, which is a submission demonstrating equivalence to a reference product already approved and sold in Canada. Submissions from Apotex to TPD are typically in the form of ANDS.

5. Typically, an ANDS will include one or more "comparative bioavailability studies" or "bioequivalence studies" to establish equivalence to a reference product already marketed and sold in Canada. These are studies in which the product is compared to the reference product by administering the drugs to human subjects, and measuring blood levels over a period after ingestion. A statistical analysis is then performed on the results to demonstrate that both products are absorbed to a comparable extent and at a comparable rate.

6. A SANDS is a submission that a manufacturer must file for review and processing by the TPD detailing changes to be made to a drug product for which an ANDS has already been reviewed and processed and for which an NOC has already been issued. Examples of changes that require the filing of an SANDS include changes to the method of manufacture, labelling, or the recommended route of administration.

7. The Minister has the statutory duty to receive and process submissions in accordance with the *Food and Drug Regulations*. If a submission is compliant with the *Food and Drug Regulations*, the *Food and Drug Regulations* direct that the Minister shall issue an NOC. The decision as to acceptability of submissions is delegated by the Minister to Barbara Sabourin, the Director General of TPD.

8. On some occasions, the Minister completes her review and determines that a submission is approvable. However, there are statutory impediments to the issuance of an NOC, for example pursuant to the *Patented*

Medicines (Notice of Compliance) Regulations ("*PMNOC Regulations*"). In such situations, the otherwise approvable product is placed on "Patent Hold" and the Minister only issues the NOC in accordance with the *Food and Drug Regulations* once the statutory impediments have been cleared.

The Import Ban

9. In late January 2014, the United States Food and Drug Administration ("FDA") conducted an inspection of APIPL's manufacturing plant and advised APIPL of alleged observations with respect to "data reliability" and laboratory procedures. This was done via the issuance of a "Form 483" notice to APIPL under U.S. law.

10. The alleged observations did not suggest any problem with actual product quality. The issuance of a Form 483 with observations requiring improvements is very common and occurs with most inspections. Moreover, unlike what happens in the U.S., Apotex fully retests all dosage forms and ingredients imported into Canada before release for use or sale, regardless of testing done at the manufacturing plants. Hence, even if there were deficiencies in testing at the plants, same would have no relevance to quality of goods for sale in Canada.

11. The FDA has different operating guidelines for its inspection when auditing foreign facilities. Those guidelines are such that non-U.S. plants are subject to more frequent and more stringent inspections by the FDA than U.S. plants. As a result, FDA often issues Form 483s, and then warning letters and/or import alerts, on

the basis of observations that would not result in equivalent actions against plants in the United States.

12. The differential nature of the FDA's foreign plant inspection procedure is such that many of the Form 483s, warning letters and import alerts that are issued by the FDA generally result in no action by agencies of other countries, who rely on their own inspections of such facilities or on the inspections of other countries' regulatory bodies.

13. On April 2, 2014, the FDA issued an import alert in respect of APIPL products (i.e., APIs) entering the United States (the "APIPL Import Alert"). This was done solely on the basis of the Form 483 issued in January 2014, and without regard for Apotex's responses explaining that the observations were minor, partially erroneous, and already addressed, such that there was no reasonable basis of concern. The effect of the import alert was to refuse entry into the United States of all drug products originating from material made at APIPL except for riluzole which was deemed to be medically necessary.

14. From April to August 2014, Apotex regularly communicated with Health Canada in respect of APIPL (and ARPL), including providing copies of materials submitted to the FDA as part of the FDA's ongoing investigations.

15. Between August 7, 2014 and August 14, 2014, Health Canada, supported by the Australian Therapeutic Goods Administration ("TGA"), Health

Canada's counterpart regulatory agency in Australia, inspected APIPL. Neither Apotex nor APIPL was advised of any significant concerns by Health Canada or the TGA inspectors regarding compliance with Good Manufacturing Practices ("GMP") at that time, this despite Health Canada being cognizant of the FDA's alleged data reliability and laboratory procedure concerns.

16. On September 25, 2014, Health Canada provided Apotex with confirmation that APIPL would be assigned a Compliant (C) rating, and that no observations had been made of issues related to data integrity (which had purportedly been found by the FDA).

17. A similar inspection had been carried out in February, 2014 by the United Kingdom Medicines and Healthcare Products Regulatory Agency ("MHRA"), Health Canada's counterpart regulatory agency in the U.K., supported by Health Canada, at the ARPL facility. Following the February 2014 inspection, on May 6, 2014, the MHRA issued a GMP Certificate of Compliance for ARPL. The GMP Certificate of Compliance is valid for 3 years.

18. On or about May 6, 2014, Health Canada similarly recognized that ARPL was GMP compliant pursuant to the above joint MHRA/Health Canada inspection.

19. During the month of September, 2014 the Toronto Star published several articles impugning Indian pharmaceutical manufacturing facilities generally

and Apotex's Indian facilities specifically. In the days which followed these publications, the Minister was compelled to respond to vigorous questioning in Parliament in respect of the content of the articles.

20. Then, on September 30, 2014, Apotex was advised by Health Canada that the Minister had decided to restrict the importation into Canada and sale in Canada of products from APIPL and ARPL (the "Import Ban").

21. The Minister implemented the Import Ban in two ways. First, the Minister instructed the Canadian Border Services Agency ("CBSA") to restrict importation of APIs from APIPL and finished product from ARPL. Second, she advised that she would be imposing terms and conditions on Apotex's establishment licences with respect to the importation or sale of products from ARPL or APIPL.

22. At the same time, a similar decision was taken with respect to only one other plant, an API facility operated by IPCA Laboratories ("IPCA"). IPCA was the only other Indian facility named in the Toronto Star articles.

23. The Minister's action came as a complete surprise to Apotex because, at all times up to September 29, 2014, there had been no indication from Health Canada of any significant concern about GMP compliance at either APIPL or ARPL. To the contrary, as result of inspections carried out jointly with other regulatory agencies, Health Canada had explicitly confirmed that both plants were and are compliant.

24. Even when the Import Ban was issued, Health Canada issued a statement advising consumers that "no specific safety issues have been identified with products...". There was no recall of product already on the market made by APIPL or ARPL. It was clear that there was no safety issue.

25. In the two years prior to September 30, 2014, approximately 40 foreign plants, including plants in Canada, had been subject to similar Warning Letters and/or Import Alerts by the FDA. Yet, Health Canada had never previously announced an import ban with respect to any, apparently in recognition that the US actions are often unreasonable and discriminatory, instead relying on Health Canada's own inspections, in accordance with Canadian regulations and policies. The only apparent basis of distinguishing the plants of APIPL, ARPL and IPCA from all others was that only these plants were cited in the Toronto Star articles, which asserted that the Minister was negligent to not also ban these three plants.

26. On October 29, 2014, Apotex commenced a judicial review bearing the Court File No. T-2223-14 asserting, *inter alia*, that the Import Ban was, among other things, unlawful and was implemented for an ulterior purpose.

27. On October 14, 2015, the Federal Court released its decision in Court File No. T-2223-14 quashing the import ban on the basis that "the Minister acted for an improper purpose and did not act in accordance with the duty of procedural fairness when she implemented the Import Ban". The Federal Court further found that "the Import Ban was motivated by the Minister's desire to ease pressure

triggered from the media and in the House of Commons – a purpose falling outside her delegated authority from the enabling legislation, which must be exercised in accordance with the rule of law".

Refusal to Complete the Review of ANDS or SANDS

28. On or about November 17, 2014, the Minister, through her delegates at the TPD, decided that she would not complete the review of ANDSs or SANDSs for any products manufactured at ARPL and/or manufactured using API sourced from APIPL and that the Minister would not issue NOCs in respect of those products.

29. On November 17, 2014, the Director General of TPD, telephoned Apotex's President and CEO, Dr. Jeremy Desai and advised that the Minister would not complete the review of ANDSs or SANDSs for any products manufactured at ARPL and/or manufactured using API sourced from APIPL and that the Minister would not issue NOCs in respect of those products.

30. The sole basis for the Minister's decision was that ARPL and APIPL had been subject to an import ban since September 30, 2014. As set out above, on October 14, 2015, the decision to implement the import ban was quashed among other things because on the basis that the Minister acted for an improper purpose when she implemented the Import Ban.

31. Accordingly, the sole reason for the Minister's decision to refuse to review or process ANDSs or SANDSs for any products manufactured at ARPL and/or

manufactured using API sourced from APIPL had been quashed and no longer existed.

32. On that same day, in light of the Federal Court's decision quashing the 2015 Import Ban, Apotex wrote to Health Canada asking that the TPD (i) process the ANDS and/or SANDS for which NOCs had been withheld, (ii) restore the "approvable status" for products awaiting the expiry of a market exclusivity period of another manufacturer; or (iii) complete the review and processing of any ANDS and SANDS which had been delayed as a result of the Minister's decision, as the case may be.

33. On October 15, 2015, Health Canada advised Apotex that it had received the Federal Court's decision, but that it needed to "do some analysis and understand the implications before moving forward". On the same day, Apotex repeated its request that Health Canada act promptly in light of the decision, given the large harm that the delay in the review and would cause.

34. On October 20, 2015, Health Canada advised that it was still reviewing its position in light of the judgment.

35. As of the date of this Notice of Application, Health Canada has stonewalled, provided no meaningful response to Apotex's inquiries, nor altered its unlawful course of behaviour.

36. Although the unlawful and improper 2014 Import Ban has been quashed by this Court, the Minister, through the TPD, is attempting to perpetuate its

unlawful decision by maintaining decisions based solely upon the unlawful Import Ban. The Minister, through the TPD, has steadfastly ignored the findings of this Court and refused to alter its course of behaviour, notwithstanding it was found by this Court to have selected its present unlawful course of behaviour for an improper purpose.

37. Absent the Minister's intransigence in attempting to perpetuate the effects of the unlawful and improper 2014 Import Ban, each of the ANDS or SANDS for the Affected Products (defined below) would have either:

(a) been reviewed and found satisfactory, resulting in the grant of an NOC in respect of the ANDS and/or SANDS;

(b) been reviewed and found satisfactory, resulting in the TPD advising Apotex that the ANDS or SANDS was satisfactory, but that the issuance of the NOC was on hold, awaiting the expiry of a market exclusivity period of another manufacturer and determination of applications for prohibition under the *PMNOC Regulations*; or

(c) been reviewed in the ordinary course and found to contain *bone fide* deficiencies, if any, which TPD would have communicated to Apotex such that they could be addressed by Apotex.

The Affected Products

38. The submissions for the following drug products have been and continue to be adversely affected by the Minister's improper prohibition:

(a) Abacavir Tablets;

(b) Abacavir-Lamivudine Tablets;

(c) Alendronate/D3 Tablets;

(d) Cabegoline Tablets;

(e) Candesartan Tablets (SANDS);

(f) Candesartan/HCTZ Tablets (SANDS);

(g) Capecitabine Tablets;

(h) Cinacalcet Tablets;

(i) Dabigatran Tablets;

(j) Darifenacin Tablets;

(k) Deferasirox Tablets;

(l) Donepezil Tablets (SANDS);

(m) Doxylamine/D6 Tablets;

(n) Emtricitabine/Tenofovir Tablets;

(o) Felodipine ER Tablets;

(p) Gatifloxacin Oph Solution;

(q) Lamivudine Tablets (100 mg);

(r) Lamivudine-Zidovudine Tablets;

(s) Moxifloxacin Tablets;

(t) Olmesartan Tablets;

(u) Olmesartan/HCTZ Tablets;

(v) Olopatadine (SANDS);

(w) Perindopril/Indapamide Tablets;

(x) Rasagiline Tablets;

(y) Sitagliptin Tablets;

(z) Solifenacin Tablets;

(aa) Tacrolimus Capsules;

(bb) Tenofovir Tablets;

(cc) Tolterodine Tablets; and

(dd) Varenicline Tablets ((a) to (dd) together, the "Affected Products").

Unlawful Decision not to Review ANDS or SANDS, nor Issue NOCs

39. There is no lawful basis upon which to refuse to complete the review of ANDSs or SANDSs for products that are manufactured at ARPL and/or are manufactured using API sourced from APIPL, nor issue NOCs in respect of them where all the legal requirements for the issuance of an NOC have been met. More particularly:

(a) the Import Ban, upon which the decision was founded, has been quashed as it was implemented for an unlawful and improper purpose;

(b) even when it was extant, the Import Ban had no bearing on the requirements for the issuance of an NOC;

(c) there is no legitimate safety concern related to any of the Affected Products, nor has one been offered by the Minister;

(d) no safety (or efficacy) concerns have been identified during the reviews, to the extent they have been conducted, of Apotex's submissions for the Affected Products;

(e) Heath Canada has acknowledged in both its words and actions that there is no health and safety concern with respect to products manufactured at ARPL or products made using API sourced from APIPL;

(f) Health Canada's inspectors have consistently found ARPL and APIPL to be GMP-compliant; and

(g) Health Canada's guidance entitled: *Post-Notice of Compliance (NOC) Changes - Quality Guidance* permits a manufacturer to change the manufacturing site of a drug substance (API) or drug product (finished dosage form) after receipt of an NOC without requiring the prior approval of Heath Canada, confirming that the site of manufacture is an irrelevant consideration for the issuance of an NOC.

40. The decision not to complete the review of ANDSs or SANDSs, nor issue NOCs where all the legal requirements have been met, was made contrary to facts known to the Director General that the Affected Products met all lawful requirements to be reviewed and processed by the TPD and, where appropriate, issued an NOC. Accordingly, the decision was made for some ulterior, improper, irrelevant or arbitrary reason. Moreover, Apotex was afforded no opportunity to be heard in advance of the decision being made.

41. For Affected Products for which Apotex has met all lawful requirements for the issuance of an NOC, the Minister is obligated to now issue an NOC. The Minister has no discretion to do otherwise as her discretionary decisions must be prescribed by law and fall within the confines of her mandate. The withholding of NOCs in the face on the Minister's statutory duty to issue same is unlawful and a denial of natural justice, and compels this Court's intervention.

42. For Affected Products for which Apotex has met all lawful and relevant health and safety requirements for the issuance of an NOC, but for which certain other statutory impediments remain (i.e. the statutory impediments pursuant to the *PMNOC Regulations*), the Minister is obligated to advise that her review in respect of all relevant safety and efficacy considerations is complete and that the granting of the NOC is subject only to a "Patent Hold" pursuant to the *PMNOC Regulations*.

43. For Affected Products which the Minister has not yet completed her review of the ANDSs or SANDSs to determine if all lawful and relevant health and safety requirements have been met, the Minister is obligated to review and process the ANDS or SANDS for those Affected Products in accordance with *Food and Drug Regulations* and without regard for irrelevant considerations.

44. The Minister and her delegates have treated Apotex unfairly, unlawfully, arbitrarily, discriminatorily and contrary to its legitimate expectations such that this Honourable Court should intervene.

THE APPLICANT REQUESTS, PURSUANT TO RULE 317, THE FOLLOWING MATERIAL IN THE POSSESSION OF THE MINISTER BE PRODUCED:

1. All documents relating to:

   (a) communication within and between the TPD and the Minister's Office in respect of the decision to not to issue NOCs for the Affected Products, or any one of them; and

(b) communication within and between the TPD and the Minister's Office in respect of the ANDSs or SANDSs, or any one of them.

THIS APPLICATION WILL BE SUPPORTED BY THE FOLLOWING MATERIAL:

1. The Affidavits to be affirmed;

2. Such further and other material as counsel may advise and this Honourable Court may permit.

November 12, 2015

GOODMANS LLP/MW.

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Barristers & Solicitors
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Solicitors for the Applicant

Court File No.

FEDERAL COURT

B E T W E E N :

APOTEX INC.

Applicant

- and –

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DUPLICATE
DUPLICATA

NOV 12 2015

TORONTO

NOTICE OF APPLICATION

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Solicitors for the Applicant

GOODMANS\6507269

I HEREBY CERTIFY that the above document is a true copy of the original issued out of / filed in the Court on the ____ day of NOV 12 2015 A.D. 20____

Dated this ____ day of NOV 12 2015 20____

SHIRLEY ACIRO
REGISTRY OFFICER
AGENT DU GREFFE