PATENTED MEDICINE PRICES REVIEW BOARD

IN THE MATTER OF the *Patent Act* R.S.C. 1985, c. P-4 as amended

IN THE MATTER OF the Medicines
DIFFERIN® (adapalene)
DIFFERIN XP® (adapalene)
TACTUPUMP® (adapalene/benzoyl peroxide)
TACTUPUMP FORTE® (adapalene/benzoyl peroxide)
Sold in Canada by GALDERMA CANADA Inc.

WRITTEN REPRESENTATIONS OF GALDERMA CANADA INC.

PART 1- OVERVIEW

1. The Board seeks an order under section 81 of the *Patent Act* (the "*Act*") requiring Galderma Canada Inc. ("Galderma") to provide information referred to in section 80 of the *Act* and in sections 3 and 4 of the *Patented Medicine Regulations* (the "Regulations') for the medicines Differin, Differin XP, TactuPump, and TactuPump Forte.

2. This Application represents an attempt by the Board to extend its jurisdiction over a medicine that is not patented.

3. The medicine in issue, Differin, which is used to treat acne, has been off-patent for almost 7 years. Differin contains only one medicinal ingredient—adapalene. Galderma's only active patents for adapalene pertain to different medicines: Differin XP, TactuPump, and TactuPump Forte. Differin XP is a distinct medicine with a different concentration of adapalene. TactuPump, and TactuPump Forte are combination medicines that contain adapalene as one ingredient. The patents pertaining to Differin XP, TactuPump, and TactuPump Forte cannot be used to make Differin.

4. The pharmacological evidence demonstrates that the four medicines—Differin, Differin XP, TactuPump, and TactuPump Forte—are fundamentally different. The medicines have different uses, are regulated as different medicines by Health Canada under different Drug Identification Numbers ("DINs"), are treated as different medicines for purposes of provincial public reimbursement programs, and the Board represented to Galderma that Differin XP, TactuPump, and TactuPump Forte were "new medicines" for the purposes of price regulation.

5. The patents do not "pertain" to Differin for the purposes of the *Act* merely because the patents mention adapalene. The patents are not intended to, or capable of, being used to make Differin but rather use, or potentially use, adapalene as an ingredient in other medicines covered by the patents. The legal test for jurisdiction requires a "rational connection" or "nexus" between the patent and the medicine. In this case, it is obvious on the face of the patents that no such connection or nexus exists between the patents and Differin. While the connection need only be a "slender thread", it must exist for the Board to have jurisdiction, and it must connect the patent to "the medicine". In this case, the patents are clearly not "intended or capable of being used" for Differin, "or production of" Differin. The patents in issue pertain to wholly different medicines.

6. The patents that "pertain" to Differin expired many years ago. The Board cannot re-assert jurisdiction over a medicine by referring to new patents that pertain to other medicines, and that merely cite a common active ingredient or molecule. The plain meaning of both the *Act* and patent descriptions on their face is that the new patents "pertain" to the invention of new medicines, and not a long-unpatented ingredient.

7. In addition to falling outside the plain meaning of the *Act* and the new patents, it is procedurally unfair, and contrary to Galderma's legitimate expectations, for the Board to attempt to retroactively extend jurisdiction over off-patent medicines without informing the industry in advance and engaging in the consultation process envisaged in the *Act*.

8. The Board has no jurisdiction to impose the Order. The relief sought, which could have far-reaching implications, can only be obtained after the public consultation process required by the *Act*.

PART 2 – STATEMENT OF FACTS

9. As the caption to the Allegation states, this proceeding concerns the *"Medicines"*: Differin; Differin XP; TACTUPUMP; and TACTUPUMP FORTE.

The Medicines

10. Differin and Differin XP are both topical monotherapy prescription acne medicines manufactured and marketed by Galderma.[1]

11. TactuPump and TactuPump Forte are both topical combination therapy prescription acne medicines manufactured and marketed by Galderma.[2]

12. Each of the Medicines has been assigned a separate DIN by Health Canada. The date each medicine received a Notice of Compliance ("NOC") from Health Canada and the first sale of the product in Canada are as follows:

    (a) Differin (gel) – received an NOC on 24 January 1995 and was first sold in about May 1996;

    (b) Differin (cream) – received an NOC on 24 June 1997 and was first sold on 8 January 1998;

    (c) Differin XP – received an NOC on 29 December 2005 and was first sold in Canada on 19 July 2007;

    (d) TactuPump – received an NOC on March 21, 2011 and was first sold on 3 May 2011; and

---

[1] Affidavit of Trent Mayers sworn 12 August, 2015 ("Mayers Affidavit"), at paragraph 4.
[2] Mayers Affidavit, at paragraph 4.

(e) TactuPump Forte – received an NOC on 16 September 2015 and was first sold on 4 January 2016.[3]

13. The active ingredients of the Medicines are as follows:

(a) Differin contains only one active ingredient—adapalene, a retinoid developed by Galderma—in a concentration of 0.1%;

(b) Differin XP contains adapalene as its sole active ingredient but at a concentration of 0.3%;

(c) TactuPump contains two active ingredients—adapalene (0.1%) and the anti-microbial agent, benzoyl peroxide ("BPO") (2.5%)—which are suspended in a gelling agent called Simulgel 600 PHA; and

(d) TactuPump Forte contains the same ingredients as TactuPump except it contains a higher concentration of adapalene (0.3%).[4]

14. In developing a combination product containing adapalene and BPO (i.e., TactuPump and TactuPump Forte), Galderma had to show that, among other things, the medicine:

(a) demonstrates therapeutic effectiveness against acne;

(b) is physically and chemically stable over time;

(c) provides a good cosmetic result;

(d) enables a single application per day rather than two applications (one of each of separate medicines), which improves patient compliance; and

(e) combines BPO and a retinoid, adapalene, for the treatment of acne.[5]

---

[3] Mayers Affidavit, at paragraph 4.
[4] Affidavit of Sandrine Segura sworn 12 August, 2016 ("Segura Affidavit"), at paragraph 6.
[5] Segura Affidavit, at paragraph 15.

15. The global development of TactuPump took more than 13 years, 2 years of which Galderma spent researching and developing a vehicle for the combination therapy. After over 300 attempts, Galderma finally selected and modified Simulgel 600 PHA so that it was suitable for this purpose. Simulgel 600 PHA was able to effectively keep both the adapalene and BPO molecules in stable suspension and chemically distinct without appreciable chemical interaction, physical separation, or chemical deterioration during the shelf-life of the medicines.[6]

16. Differin and Differin XP and TactuPump and TactuPump Forte are distinct based on:

    (a) the drug substance(s): adapalene alone for Differin and Differin XP versus adapalene in combination with BPO for Tactupump and Tactupump Forte; and

    (b) the formulation composition: comprising a conventional gelling agent for Differin versus Simulgel 600 PHA as the sole gelling agent compatible with the chemical and physical stability, and the efficacy, necessary for the TactuPump medicines.[7]

17. Differin and Differin XP are also distinct medicines. In addition to the differences between them outlined in sub-paragraphs 4 (a), (b), and (c) above and the medicines having separate DINs and NOCs, the Board itself treated Differin XP as a "new medicine" when it was introduced on the Canadian market in 2007.[8]

Expert Dermatology Evidence

18. Galderma's dermatology experts, Doctors Jerry Tan and Charles Lynde, are each well-respected and experienced dermatologists who practice in Ontario. Acne patients constitute a large component of their respective practices.

---

[6] Segura Affidavit, at paragraph 27.
[7] Segura Affidavit, at paragraph 30.
[8] Report of Dr. Jerry Tan dated 6 August, 2016 ("Tan Report"), pages 2 and 22; Affidavit of Charles Lynde sworn 10 August, 2016 ("Lynde Affidavit"), paragraphs 3 and 11.

19. Both Doctors Tan and Lynde are of the opinion that:

    (a) the Medicines are distinct from each other[9]; and

    (b) the combination medicines (i.e., TactuPump and TactuPump Forte) result in a synergistic effect in relation to absorption and penetration of the skin by the medicines and has synergistic efficacy. In other words, the efficacy of TactuPump and TactuPump Forte is greater than the sum of their individual constituents (that is, the active pharmaceutical ingredients of each of these two medicines).[10]

20. Adapalene is a retinoid, a class of medicines that exert their effects by modifying the way in which, and/or the extent to which, specific genes are expressed. These genetic traits cause hyperproliferation of skin cells which line the hair follicles of the skin. The increase in the number and keratin content of these cells leads to formation of a 'plug' that blocks the follicular tubes from which hairs protrude and form what is referred to as a comedone. Comedone formation is the first stage in the development of acne.[11]

21. Adapalene and other retinoids tend to modulate or 'down-regulate' the tendency of the cells to hyperproliferation and reduce keratin content resulting in fewer cells containing less keratin thereby 'normalizing' the cells that line the pores of the skin. These effects of adapalene prevent or mitigate comedone formation.[12]

22. BPO, when applied to the skin, has two main effects that ameliorate acne—bactericidal and keratolytic. BPO's mechanisms of action differ from adapalene. BPO kills the opportunistic bacterium (*P. acnes*) involved in the development of acne when the hair follicles become colonized with *P. acnes*. BPO oxidizes proteins in the cell walls of the bacteria leading to their rupture (lysis) and

---

[9] Tan Report, pages 2 and 22; Lynde Affidavit, paragraph 35.
[10] Tan Report, pages 2, 12-14 and 15-18; Lynde Affidavit, paragraphs 19, 22, 24 and 31.
[11] Tan Report, pages 6-7 and 8-9; Lynde Affidavit, paragraphs 3 and 11.
[12] Tan Report, pages 6-7; Lynde Affidavit, paragraphs 18-20.

destruction. One of the particularly valuable properties of BPO is that its antibacterial effects do not appear to induce the development of bacterial resistance, a phenomenon frequently observed with conventional antibiotics.[13]

23. BPO is also a keratolytic (i.e., it breaks down keratin); therefore, keratin, which forms part of the 'plug' that causes comedones, is dissolved. This effect of BPO can prevent formation of an acne lesion.[14]

24. The mechanisms of action, therefore, of the two active pharmaceutical ingredients in the combination medicines, TactuPump and TactuPump Forte, are quite different, although their clinical effect is the same. Each of the two components simply have different ways of arriving at the same result (that is, prevention of acne lesions).

25. Doctors Tan and Lynde use adapalene-only (Differin, Differin XP or other retinoid-only) topical medicines in cases of mild acne (comedones only). In more severe cases they select from the available combination medicines and in the most severe cases they prescribe systemic (oral) medicines.[15]

26. Both Doctors Tan and Lynde reserve the higher concentration Differin XP for patients who require the higher concentration and can tolerate its more irritating properties.[16]

27. TactuPump and TactuPump Forte are indicated for a wider range of acne (that is, beyond merely comedonal acne), which also includes inflammatory acne whether classified as mild, moderate, or severe.[17]

28. As Dr. Tan observed in one of the papers he co-authored and which was published in a peer-reviewed journal, clinical studies in acne patients demonstrate that TactuPump is significantly more efficacious than its

---

[13] Tan Report, pages 7-8; Lynde Affidavit, paragraph 30.
[14] Tan Report, pages 7-8.
[15] Tan Report, pages 9-12 and 21-22; Lynde Affidavit, paragraphs 25-33.
[16] Tan Report, page 21; Lynde Affidavit, paragraph 28.
[17] Tan Report, pages 10 and 22.

'component' monotherapies in decreasing acne lesion counts and in the achievement of overall success (which he characterizes as 'clearance' or almost complete clearance of acne). In his paper, he analyzed three randomized, controlled studies comprising 3855 acne patients evenly divided into those receiving combination therapy (i.e., adapalene with BPO), adapalene alone, BPO alone or Simulgel 600 PHA alone. He found that there was a synergistic effect with the combination as characterized by lesion count reduction and overall success noted as early as week No. 1 into the study and then throughout the study's duration.[18]

29. While the precise mechanism(s) of the synergistic efficacy demonstrated in the clinical studies of TactuPump and TactuPump Forte have not been elucidated, both Dr. Tan's and Dr. Lynde's evidence is that they are thought to include adapalene's ability to reduce follicular blockage by reducing keratin production, thus enhancing the delivery of both adapalene and BPO into the follicle itself.[19] Adapalene on its own may be inadequate to reduce the populations of *P. acnes* while BPO on its own may be inadequate to penetrate into the follicle when a follicle is blocked by hyperkeratinized skin cells. As Dr. Tan also states, other fixed-dose combination acne agents do not demonstrate synergistic efficacy when lesion count and overall success are calculated.

30. In selecting between TactuPump and TactuPump Forte, Dr. Tan prescribes TactuPump in cases with mild and moderate acne and TactuPump Forte in moderate to serve acne.[20]

31. As previously stated, both Doctors Tan and Lynde conclude that each of the four Medicines are separate and distinct and are used under difference clinical conditions.[21]

---

[18] Tan Report, page 13; Tan et al "Synergystic Efficacy of Adapalene 0.1% - Benzoyl Peroxide 2.5% in the Treatment of 2855 Acne Vulgaris Patients" (2011) 22 *Journal of Dermatological Treatment* 197.
[19] Tan Report, page 14; Lynde Affidavit, paragraph 19.
[20] Tan Report, page 22.
[21] Tan Report, page 2 and 22; Lynde Affidavit, paragraphs 3 and 34-35.

Chemical Engineering Evidence

32. Sandrine Segura, a chemical engineer who specializes in the formulation of medicines and is employed by Galderma's Research and Development division, provided evidence regarding the novelty of the invention that constitutes TactuPump and TactuPump Forte (besides the obvious combination of two separate and distinct active pharmaceutical ingredients into one medicine). She advised that the true novelty of the invention was the development of a carrier molecule (or 'vehicle') in which the two distinct active pharmaceutical ingredients—adapalene and BPO—may be combined.[22]

33. Segura's evidence is that because of the physical properties of each of the active pharmaceutical ingredients, the lighter component migrates to the top of any tube or dispensing container and the heavier substance would settle at the bottom. This would prevent the uniform application of each ingredient to the skin.[23]

34. The gelling agent (Simulgel 600 PHA) enables Galderma to preserve the therapeutic effectiveness of each of the two active pharmaceutical ingredients; ensures maintenance of uniform dispersion of the ingredients throughout the suspension; ensures physical and chemical stability of the combination medicine; and retards the degradation of the combination medicine over its stated shelf-life.[24]

Pharmacist Evidence

35. Leithe Holowaty is an Alberta pharmacist who has broad prescribing authority. Her evidence is that neither of the two provinces (British Columbia and Nova Scotia) which currently permit substitution of medicines within specified

---

[22] Segura Affidavit, paragraphs 16-25, 27-29 and 31.
[23] Segura Affidavit, paragraphs 16(b) and 21; Cross-examination of S. Segura, Question 59.
[24] Segura Affidavit, paragraphs 16-29.

therapeutic classes have designated any retinoid-containing medicine as substitutable.[25]

Summary of Galderma Evidence

36. In summary, on clinical grounds each of the four Medicines is regarded as separate and distinct and prescribed in different clinical circumstance. From a chemical and formulation perspective, each medicine is unique. No government of any province of Canada has designated any other medicine as being "substitutable" for any of the four Medicines.

Board Staff's Expert Evidence

37. Dr. Vincent Ho, the dermatologist retained by the Board Staff to provide his expert opinion, has only one material dispute with Doctors Tan and Lynde. He disagrees with their conclusion that a synergistic effect has been demonstrated with respect to the combination medicines, TactuPump and TactuPump Forte. Dr. Ho believes that nothing short of a randomized, double blind, controlled trial will suffice and criticizes the meta-analyses and pooled analyses that have been conducted upon which (among other things) Doctors Tan and Lynde conclude that a synergistic effect has been demonstrated for the adapalene and BPO combinations.[26]

38. Dr. Ho denies there is any advantage to the medicines other than the convenience of applying a product once a day instead of two products at different times on the same day. Indeed, in his cross-examination Dr. Ho rejected the self-evident proposition that patient adherence is improved by using a once-daily medicine.[27] His evidence is that "a lot" of his patients do not find it inconvenient to use a product in the morning and a second product at night. However, even Dr. Ho states that it is unclear if the effects of the two medicines are additive or

---

[25] Report of L. Holowaty dated 12 August, 2016, pages 2-3.
[26] Affidavit of V. Ho dated 22 August, 2016, at pages 8-9.
[27] Ho Cross-Examination, Question 178.

synergistic.[28] If one accepts that a synergistic effect has not been proven, it stands to reason that a single, once-daily application of the medicine is likely to elicit greater adherence over the separate applications of two different medicines at different times on the same day.

The Patents

39. During the period Galderma Canada has been selling the Medicines in Canada, the company has obtained the following patents:

(a) Canadian Patent No. 1266646 entitled "Benzonaphtalenic Derivatives, Process for their preparation and uses as Pharmaceutic and Cosmetic Agents", which was issued on March 13, 1990 and expired on March 13, 2007;[29]

(b) Canadian Patent No. 1312075 entitled "Process for the Preparation of Adamant-1 Derivatives", which was issued on December 29, 1992 and expired on December 29, 2009 (the "'075 patent");[30]

(c) Canadian Patent No. 2,656,451 entitled "Composition Comprising a Retinoid and Benzoyl Peroxide", issued on January 27, 2015 and expiring on July 11, 2027 (the "451 patent");[31]

(d) Canadian Patent No. 2,478,237 entitled "Use of Adapalene for the Treatment of Dermatological Disorders", issued on May 12, 2009 and lapsed on March 14, 2016 (the "'237 patent");[32] and

(e) Canadian Patent 2,466,321 entitled "Gel Comprising at Least a Retinoid and Benzoyl Peroxide", issued on November 8, 2011 and expiring on December 9, 2022 (the "'321 patent").[33]

---

[28] Affidavit of V. Ho dated 13 June, 2016, at paragraph 22.
[29] Mayers Affidavit, paragraph 6(i) and Exhibit "A".
[30] Mayers Affidavit, paragraph 6(ii) and Exhibit "B".
[31] Mayers Affidavit, paragraph 6(iii) and Exhibit "C".
[32] Mayers Affidavit, paragraph 6(iv) and Exhibit "D".

40. The abstract of the '451 patent states:

> The invention relates to a composition comprising, in a physiologically acceptable medium, at least one retinoid, dispersed benzoyl peroxide and a gelling system comprising at least two categories of compounds.[34]

41. The abstract for the '237 patent states:

> The present invention relates to the use of 6-[3-(1-adamantyl)-4-methoxypheny]-2-naphthanoic acid (adapalene), or its salts, for producing a pharmaceutical product composition intended for the treatment of dermatological elements with an inflammatory or proliferative component, comprising 0.3% by weight of adapalene relative to the total weight of the composition.[35]

42. John Cook is the only "Senior Regulatory Officer" assigned to the "enforcement team" for this proceeding. Before joining the Board in 2009, Mr. Cook worked for 20 years in the pharmaceutical industry. In the *Curriculum Vitae* appended to his affidavit, Mr. Cook indicates "in-depth knowledge" of "patent law and patent instruments."[36]

43. Mr. Cook, and other regulatory officers, are responsible for examining patentee's submissions "to ensure accuracy, completeness, and conformance to form and content as prescribed in the legislation." In his affidavit, Mr. Cook addressed Form 1 and Form 2 documents filed by patentees and described the requirements of the *Patent Act* ("*Act*") and *Patented Medicines Regulations* (the "*Regulations*").[37] Mr. Cook stated that "patentees are required to provide Board Staff with information *identifying the medicine (Form 1)*" which "need only be

---

[33] Mayers Affidavit, paragraph 6(v) and Exhibit "E".
[34] Mayers Affidavit, Exhibit "C".
[35] Mayers Affidavit, Exhibit "D".
[36] Cross Examination of John Cook ("Cook Cross-Examination"), at page 8; Affidavit of John Cook sworn on 13 June, 2016 ("Cook Affidavit"), Exhibit "A".
[37] Cook Cross-Examination, at pp. 10-11.

filed once *the medicine* has received a Notice of Compliance from Health Canada." [Italics added.][38]

44. Mr. Cook acknowledged in his affidavit that Galderma received a NOC for Differin, in gel and cream format, in January 1995 and June 1997 respectively.[39] He also acknowledged that Galderma had complied with reporting requirements under the *Regulations* from the date of first sale of the gel (in the second half of 1996) and the cream (in the first half of 1998).[40]

45. Galderma stopped reporting for the Differin medicines at the end of December 2009 because the patent pertaining to Differin, the '075 patent , expired on 29 December 2009.[41]

46. In his affidavit, Mr. Cook confirmed that: Galderma obtained a NOC for Differin XP in 2005; the first sales of Differin XP took place in 2007; Galderma has reported information required under the *Regulations* to the Board for Differin XP; and that a separate patent, the '237 patent , pertains to Differin XP.[42]

47. In the cross-examination, Mr. Cook identified a letter sent by the Board to Galderma in July 2008 relating to Differin XP. The letter, and an attached compliance report prepared by the Board, characterized Differin XP "as a category 1 new medicine."[43] The letter and attachment also show that "Reasonable Relationship" and "International Price Comparison" tests were conducted for Differin XP and that the introductory price of Differin XP was "within the Guidelines". The Compliance Report appended to the letter described Differin XP as a "New Medicine" and the gel and cream forms of Differin as "Comparable Medicines."[44]

---

[38] Cook Affidavit, at paragraph 4.
[39] Cook Affidavit, at paragraphs 6-10.
[40] Cook Affidavit, at paragraph 7.
[41] Cook Affidavit, at paragraphs 9-10; Cook Cross-Examination at pp 30-32.
[42] Cook Affidavit, at paragraphs 14-15.
[43] Letter dated 23 July 2008, Exhibit "A" to Cook Cross-Examination.
[44] Letter dated 23 July 2008, Exhibit "A" to Cook Cross-Examination; Cook Cross – Examination, at pp. 37-38.

48. Mr. Cook acknowledged that: TactuPump was a combination medicine that combined, in gel format, 0.1% adapalene and BPO; there was a separate DIN for TactuPump; the NOC for TactuPump was granted in March 2011; and the year of first sale of TactuPump was 2011.[45] He further acknowledged that TactuPump Forte also has a separate DIN, NOC, and year of first sale (2016).[46] The combination medicines were, like Differin XP, subject to separate pricing review by the Board upon introduction in Canada.

49. As part of his normal job duties, Mr. Cook "engages pharmaceutical companies' representatives and their consultants in voluntary compliance discussions and initiatives to achieve compliance with the Guidelines." He also provides "patentees with interpretation of legislation and regulations", including regulations that relate to submissions or filings."[47] He acknowledged that he has had no discussions with Galderma in relation to the filings in this case.[48] Nor has he, or anyone else at the Board, assembled any documents, prepared any analysis, or developed any position papers for this case or the issues raised against Galderma.[49]

50. The only relevant communication between the Board and Galderma that Mr. Cook was able to point to was an exchange of correspondence initiated by Beatrice Mullington, then a manager in the Board's Outreach and Investigations Unit, in February 2010[50] relating to expiry of various patents, including three patents relating to the Differin 0.1% mg medicine.[51] Galderma confirmed that no other patents pertained to Differin 0.1% gel, cream, or solution.[52] When cross-examined, Mr. Cook acknowledged that Ms. Millington's letter says "a patent

---

[45] Cook Cross-Examination, at p. 25.
[46] Cook Cross-Examination, at pp. 25-26
[47] Cook Cross-Examination, at p. 12-13.
[48] Cook Cross-examination, at p. 13.
[49] Cook Cross-examination, at p. 16.
[50] Cook Cross-Examination, at pp. 13-15; Exhibit "B" to Cook Affidavit.
[51] Cook Affidavit, Exhibit "B".
[52] Cook Affidavit, Exhibit "C".

pertains to a medicine where it is intended or capable of being used for *the medicine* or for the preparation or production of *the medicine*."[53]

51. Neither Mr. Cook, nor anyone else at the Board, has prepared any briefings, strategies, advice, or recommendations concerning the allegations against Galderma.[54] At this stage, the board is only "trying to establish" whether other patents held by Galderma may apply to the Differin 0.1% medicine.

52. Mr. Cook appended to his affidavit an apparent complaint from a consumer in relation to Differin. He did not personally investigate the complaint.[55] The complaint was received in June 2013, and then repeated in September 2015. In November 2015, Ms. Ginette Tognet wrote to Galderma expressing the view that the '451 combination patent for TactuPump "pertained to Differin."[56] In January 2016, Galderma responded to Ms. Tognet expressing the view that the '451 patent did not apply to Differin, the patent for which had expired in 2009.[57] The Board responded by issuing a Notice of Application in February 2016.[58]

53. The November 2015 letter from Ms. Tognet to Galderma does not mention the '237 patent for Differin XP.[59] The only assertion in Ms. Tognet's letter is that an amended Form 1 for Differin should make reference to the '451 patent covering the combination therapy. In his cross-examination, Mr. Cook could point to no communication from the Board to Galderma concerning the '237 patent until the Notice of Application was issued in February 2016.[60]

54. The Board was well aware in this case that a new strength adapalene medicine, Differin XP, and a new combination product using adapalene 0.1% as an ingredient, TactuPump, were being introduced. Indeed, the Board treated the two medicines as *"new medicines."* No question was raised about new reporting

---

[53] Cook Cross-Examination, at pp. 54-55.
[54] Cook Cross-Examination, at pp. 17-18.
[55] Cook Cross-Examination, at p. 42
[56] Cook Affidavit, at paragraph 21.
[57] Cook Affidavit, at paragraph 22.
[58] Cook Affidavit, at paragraph 23.
[59] Letter from Ginette Tognet dated 25 November 2015. (Provided by undertaking.)
[60] Cook Cross-Examination, at pp. 48-49

requirements for the older, off-patent, medicine Differin until the Board received a complaint about the price of a medicine that it no longer regulated. The Notice of Application, in effect asserts novel, and shifting, theories about how the Board re-acquires jurisdiction over an old, off-patent, medicine that, on the basis of the existing law and administrative practice, has not required any reporting for almost 7 years.

PART 3 – ISSUES

55. The issue for determination in this Application is whether the Board has jurisdiction over Galderma's sales of:

(a) Differin (gel and cream) as a result of the '237 patent and the '451 patent; and

(b) Differin XP as a result of the '451 patent.

PART 4 – STATEMENT OF LAW AND ARGUMENT

Test for Board assumption of jurisdiction

56. For the Board to assume jurisdiction over the pricing of the Medicines under s. 83(1) of the *Act*, three condition precedents must be met:

(i) the Board must determine that Galderma is a patentee of an invention;
(ii) Galderma's invention must pertain to a medicine; and
(iii) Galderma must be selling the medicine in a market in Canada.

> *ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board)*, [1996] F.C.J. No. 1065 (QL) at para. 47 (F.C.A.)

57. The second condition—an invention that pertains to a medicine—is the only issue in dispute in this application.

58. In *ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board)* ("*ICN*"), and *Sandoz Canada Inc. v. Canada (Attorney General)* ("*Sandoz*"), the Federal Court of Appeal held the following with respect to this requirement:

(a) the Board's jurisdiction to review a given set of prices requires the existence of a rational connection between a patented invention and the medicine being sold in Canada;

(b) the rational connection can be one of "the merest slender thread"; and

(c) the Board need not construe the claims of the patent, and must determine the existence of the required connection without going beyond the face of the patent.

ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board), [1996] F.C.J. No. 1065 (QL) at para. 46 (F.C.A.)

Sandoz Canada Inc. v. Canada (Attorney General), [2015] F.C.J. No. 1311 (QL) at para. 104 (F.C.A.)

The patents must be intended or capable of ultimately creating the medicines

59. The clear wording of the Act states that the patent must pertain *to the medicine* being sold in Canada:

> 79 (2) For the purposes of subsection (1) and sections 80 to 101, *an invention pertains to a medicine* if the invention is intended or capable of being used for medicine or for the preparation or production of medicine.
>
> 83 (1) Where the Board finds that a patentee of *an invention pertaining to a medicine* is selling the medicine in any market in Canada at a price that, in the Board's opinion, is excessive...
>
> *Patent Act*, R.S.C. 1985, c. P-4, s. 83(1)

60. The fundamental flaw in the Board's assertion of jurisdiction in this case is its attempt to reverse that logic—namely, the medicine pertains to the patents. The Board alleges that because retinoids and adapalene are mentioned in the '451 patent, and because adapalene is referenced in the '237 patent, the two patents pertain to adapalene in general and therefore to Differin. This assertion is made

even though neither patent is "intended or capable" of being used to prepare, produce or otherwise create Differin (0.1% adapalene gel).

61. The wording of the *Act* only permits even a "merest slender thread" to be pulled in one direction—the patent must somehow result in the medicine. Although the Court in *ICN* pointed out that the wording of s. 83(1) of the *Act* does not require a patent to "actually be used in the production of the medicine", it still *does* require that the patent "be intended or capable of being used for medicine or for the preparation or production of medicine".

> *ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board)*, [1996] F.C.J. No. 1065 (QL) at paras. 57 and 65 (F.C.A.)

62. The '451 patent is not intended to, nor is it capable of producing adapalene, in any concentration. In fact, adapalene (or any other retinoid) is a component of a combined medicine created by the '451 patent, just like BPO. As discussed below, as both of these components (0.1% adapalene and BPO) are not subject to patents, their pricing is beyond the jurisdiction of the Board.

63. Put differently, when a patent for an "ingredient" medicine expires, any thread creating the Board's jurisdiction over the ingredient itself is cut. The Board's jurisdiction only remains in relation to the medicine with the new delivery system, strength, combination, or use. An expired patent cannot be revived, *ex post facto*, when it becomes an ingredient in a new medicine.

64. In addition, the '237 patent is not intended to, nor is it capable of producing a 0.1% adapalene gel. The Board has conceded as much in considering Differin (0.1% adapalene) as a comparator drug in approving the introductory price of Differin XP (0.3% adapalene) in Canada.

65. Unlike the situation in the *Hoechst Marion Roussel Canada Inc.* decision, where the Board found it had jurisdiction over the pricing of a Nicoderm patch containing nicotine, Galderma does not in this case dispute that either of the patents ('451 and '237) pertain to medicines. Indeed, Galderma points to the

obvious proposition, supported by the separate DINs for each medicine, that the medicines produced under these patents are distinct from the older medicine produced under the now expired Differin patent. The new medicines are a higher strength version and a combination medicine that the Board itself has treated as distinct.

PMPRB-99-D6-NICODERM, Decision on Jurisdiction – Part II

The patents must pertain to the pharmaceutical end products in question

66. Section 83(1) grants the Board jurisdiction where "a patentee of an invention pertaining to *a medicine* is selling ***the*** *medicine* in any market in Canada". Section 79(2) provides that "an invention pertains to *a medicine* [the medicine referred to in s. 83(1)] if the invention is intended or capable of being used for medicine or for the preparation or production of medicine".

67. These two provisions (79(2) and 83(1)) must be "read in their entire context and in their grammatical and ordinary sense harmoniously with the scheme of the Act, the object of the Act, and the intention of Parliament."

Rizzo & Rizzo Shoes Ltd. (Re), [1998] 1 SCR 27, 1998 CanLII 837 at para. 21 (SCC)

68. In *ICN*, the Federal Court of Appeal made clear that the relationship (pertaining to) is between the patent and the "pharmaceutical end product in question":

> Under subsection 83(1) of the Act, the second condition precedent is that the invention must pertain to a medicine. In turn, this condition precedent can be broken down into two subrequirements. First, ***the*** *pharmaceutical end product* in question, whether it be described as ribavirin or Virazole, must qualify as a medicine. Second, there must be *a rational connection between* ***the*** *invention and* ***the*** *pharmaceutical end product. That is to say between the invention and the medicine being sold in Canada*. [Emphasis added.]

ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board), [1996] F.C.J. No. 1065 (QL) at para. 50 (F.C.A.)

69. The Board expressly acknowledged this interpretation in its 2006 Newsletter regarding the *ICN* decision:

> there must be a rational connection or nexus between the invention described in the patent and ***the*** *pharmaceutical end product*, that is between the invention described in the patent and the medicine.
>
> PMPRB, "The Scope of the PMPRB's Jurisdiction: When Does a Patent Pertain to a Medicine?" (2006)

70. This interpretation has never been changed by the Federal Court of the Federal Court of Appeal, including in the Federal Court of Appeal's recent decision in *Sandoz*:

> As was held by this Court in ICN, the Board's jurisdiction to review a given set of prices requires the existence of a rational connection between a patented invention and ***the medicine being sold in Canada*** ... Subsection 79(2) of the Act defines the parameters of such a connection in providing for when an invention will "pertain" to ***a given medicine*** for the purposes of applying subsection 79(1)...
>
> *Sandoz Canada Inc. v. Canada (Attorney General)*, [2015] F.C.J. No. 1311 (QL) at para. 104 (F.C.A.)

71. With these directions, the Federal Court of Appeal referred back to the Federal Court the issue of whether the patents in question pertain to medicines. On this issue, therefore, the Board's reasoning was not upheld in *Sandoz*.

> *Sandoz Canada Inc. v. Canada (Attorney General)*, [2015] F.C.J. No. 1311 (QL) at para. 55 (F.C.A.)
>
> *Sandoz Canada Inc. v. Canada (Attorney General)*, [2014] F.C.J. No. 522 (QL) at para. 5 (F.C.)
>
> PMPRB-10-D2-SANDOZ at para. 69

72. Any differing interpretations of the Board would be inconsistent with the Federal Court of Appeal's decisions in both *ICN* and *Sandoz*.

73. There is no dispute in this case that the '451 and '237 patents are "used for medicine" or for "the preparation or production of medicine". The medicines in question, however, are not Differin. The evidence is clear that the '451 and '237 Patents create different medicines from Differin *and* play no role in the preparation or production of Differin. The '237 and '451 Patents relate to a new dosage strength and a combination medicine (TactuPump and TactuPump Forte) and a stronger concentration of adapalene (Differin Forte and TactuPump Forte)—none of which are the medicine found in Differin.

Patent that pertains to Differin is expired and therefore the Board has no jurisdiction over pricing for Differin

74. The express language of s. 83(1) of the *Act* contemplates an existing patent:

> Where the Board finds that *a patentee of an invention* pertaining to a medicine is selling the medicine in any market in Canada at a price that...
>
> *Patent Act*, R.S.C. 1985, c. P-4, s. 83(1)

75. The requirement for an existing patent as a basis for Board jurisdiction (at the time the patent was in force) was reiterated several times by the Federal Court of Appeal in *ICN*:

> ... subsection 83(1) speaks of an ***existing patent***...
>
> ... the Board's statutory mandate is limited to the pricing of ***patented medicines***.
>
> *ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board)*, [1996] F.C.J. No. 1065 (QL) at paras. 48 and 61 (F.C.A.)

76. While the Board retains the jurisdiction to determine whether excessive prices were charged for a medicine *before* expiration of a patent, it does not have jurisdiction to determine excessive pricing, or to request pricing information, for the time period *after* the patent expires. Similarly, the Board does not attain jurisdiction until a patent is issued.

Hoechst Marion Roussel Canada Inc. v. Canada (Attorney General), [2005] F.C.J. No. 1928 (QL) at paras. 134-136 (F.C.)

Shire Biochem Inc. v. Canada (Attorney General), [2007] F.C.J. No. 1688 (QL) at para. 23 (F.C.)

77. This is the only reasonable interpretation given the language of s. 83(1) as a whole:

(a) First, the provision refers to "a patentee of an invention". "Patentee" is defined at s. 2 of the Act as "the person for the time being entitled to the benefit of a patent." A person is only entitled to the benefit of a patent from the time it is issued until it expires.

(b) Second, the provision refers to selling "*the* medicine in any market in Canada at [an excessive price]". Only a patented medicine could be found to be excessively priced.

Patent Act, R.S.C. 1985, c. P-4, ss. 2 and 83(1)

78. As the court noted in *ICN*, there must be a rational connection between an existing patent and the pharmaceutical end product, or there would be no jurisdiction in the Board to control pricing:

> That there must be a rational connection or nexus between the invention outlined in a patent and ***the*** *medicine which is being sold in Canada* cannot be doubted. *Without such a statutory requirement the constitutional authority of Parliament to enact price control legislation would be in issue.*

ICN Pharmaceuticals, Inc. v. Canada (Staff of the Patented Medicine Prices Review Board), [1996] F.C.J. No. 1065 (QL) at para. 55 (F.C.A.)

79. In this case, the patent for Differin has expired. The Board therefore has no legal basis to request pricing information for that medicine. The '237 and '451 patents do not pertain to the pharmaceutical end product Differin and cannot form the basis of the Board's jurisdiction over Differin.

Procedural Fairness and Legitimate Expectations

80. Furthermore, in bringing this application, the Board has failed to follow the principles of procedural fairness and legitimate expectations.

81. The Federal Court has held that the duty of fairness applies to the Board's decisions.

> On the basis of the foregoing, I conclude that the basic requirements of procedural fairness, as described by the Supreme Court of Canada in *Lakeside Colony of Hutterian Brethren v. Hofer*, [1992] 3 S.C.R. 165, that is the right to an unbiased tribunal, the right to notice and the opportunity to make representations, apply to the Board's actions.
>
> *Hoechst Marion Roussel Canada Inc. v. Canada (Attorney General)*, [2006] 3 FCR 536, 2005 FC 1552 at para. 73
>
> See also: *Sanofi-Aventis Canada Inc. v. Canada (Attorney General)*, 2009 FC 965 at paras. 41-42

82. The Supreme Court has held that:

> Where a government official makes representations within the scope of his or her authority to an individual about an administrative process that the government will follow, and the representations said to give rise to the legitimate expectations are clear, unambiguous and unqualified, the government may be held to its word, provided the representations are procedural in nature and do not conflict with the decision maker's statutory duty. Proof of reliance is not a requisite. It will be a breach of the duty of fairness for the decision maker to fail in a substantial way to live up to its undertaking.
>
> *Canada (Attorney General) v. Mavi*, 2011 SCC 30, [2011] 2 S.C.R. 504 at para. 68 (citations omitted)

83. In addition, section 96(5) of the *Act* requires the Board to consult with the industry before making any changes to the Board's Guidelines:

> Before the Board issues any guidelines, it shall consult with the Minister, the provincial ministers of the Crown responsible for health and such representatives of consumer groups and representatives of the pharmaceutical industry as the Minister may designate for the purpose.

84. The Board failed to inform the industry in any document that an off-patent medicine that became an ingredient in a new medicine would create new reporting requirements for the old medicine, or that the Form 1 filed for the new medicine would have to mention the old, off-patent medicine.

85. The Board was well aware in this case that a new strength adapalene medicine, Differin XP, and a new combination product using adapalene 0.1% as an ingredient, TactuPump, were being introduced. Indeed, the Board treated the two medicines as *"new medicines."* No question was raised about new reporting requirements for the older, off-patent, medicine Differin until the Board received a complaint about the price of a medicine that it no longer regulated. The Notice of Application, in effect asserts novel, and shifting, theories about how the Board somehow re-acquires jurisdiction over an old, off-patent, medicine that, on the basis of the existing law and administrative practice, has not required any reporting for almost 7 years.

86. The Board has not informed the industry in any document that an off-patent medicine that became an ingredient in a new medicine would create new reporting requirements for the old medicine, or that the Form 1 filed for the new medicine would have to mention the old, off-patent medicine. This requirement, if it exists, could have far-reaching implications for the industry because, for example, it would mean medicines with new delivery or extended release systems would, in effect, "revive" reporting requirements for off-patent ingredients. New patented combinations, strengths, or uses of older off-patent

medicines would similarly "revive" reporting requirements of older off-patent medicines. The Board's Guidelines fail to address this issue and no document has ever been published to notify the industry of such a significant development in reporting requirements.

PART IV – ORDER SOUGHT

87. Galderma seeks an order dismissing this Application.

Dated at Toronto this 19th day of September 2016.

ALL OF WHICH IS RESPECTFULLY SUBMITTED

Original signature redacted

Malcolm Ruby

GOWLING WLG (CANADA) LLP
1 First Canadian Place
100 King Street West, Suite 1600
Toronto ON M5X 1G5

Malcolm N. Ruby
Tel: 416-862-4314
Fax: 416-862-7661
malcolm.ruby@gowlings.com

Alan West
Tel: 416-862-4308
Fax: 416-862-7661
alan.west@gowlings.com
Lawyers for the Respondent

TO: **PATENTED MEDICINE PRICES REVIEW BOARD**
Legal Services Branch
Standard Life Centre
333 Laurier Avenue West, Suite 1400
Ottawa ON K1P 1C1
Tel: (613) 954-8299
Fax: (613) 952-7626

Guillaume Couillard *(Secretary of the Board)*
guillaume.couillard@pmprb-cepmb.gc.ca

AND TO: **CONWAY BAXTER WILSON LLP/s.r.l.**
401 - 111 Prince of Wales Drive
Ottawa, ON K2C 3T2
Tel: 613-780-2019
Fax: 613-688-0271

David Wilson
dwilson@conway.pro

Calina N. Ritchie
critchie@conway.pro

Lawyers for Board Staff