Patented Medicine Prices Review Board Canada | Conseil d'examen du prix des médicaments brevetés Canada

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

AND IN THE MATTER OF Horizon Pharma (the "Respondent") and the medicine Cysteamine Bitartrate sold by the Respondent under the trade name Procysbi

DECISION

(Hearing on the Merits)

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A. SUMMARY OF DECISION

1. The Panel of the Patented Medicine Prices Review Board (the "**PMPRB**" or the "**Board**") seized with this proceeding has considered the evidence adduced and submissions made by Board Staff, Horizon Pharma PLC ("**Horizon**" or the "**Respondent**") and Her Majesty the Queen in right of the Province of British Columbia, as represented by the Minister of Health (the "**BC Minister**"), and finds that the price of the medicine sold by the Respondent under the trade name Procysbi was and is excessive under sections 83 and 85 of the *Patent Act*[1] (the "**Act**").

2. The Panel orders the Respondent to (i) reduce the price of Procysbi in Canada as of the date of this decision to be no higher than the Maximum Average Potential Price ("**MAPP**") prescribed by the Moderate Improvement Test under the Guidelines and (ii) pay to Her Majesty the Queen in Right of Canada the amount, to be calculated by the Parties and approved by this Panel, which equals the amount of the excess revenues derived by the Respondent from the sale of Procysbi in Canada at the excessive price as found by this Panel.

B. BACKGROUND

3. Nephropathic cystinosis is a rare and lifelong genetic disorder. Cystinosis patients do not have the gene that enables them to remove cystine from their cells. The result is that cystine accumulates within the cells and causes cellular dysfunction. Among other symptoms, cystinosis impairs the function of the kidneys. If left untreated, cystinosis leads to end stage renal disease (requiring dialysis and/or kidney transplantation) and early death. The disease is usually diagnosed early in a child's life. There are only approximately 100 patients in Canada who suffer from this ultra-rare disease.

4. The only currently available treatment for cystinosis is cysteamine. Cysteamine removes excess cystine in the cells. The result is a reduction in tissue cystine, including a reduction in white blood cell ("**WBC**") cystine levels—which serve as a biomarker for

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[1] RSC 1985, c P-4.

the disease. Cysteamine is not a cure for cystinosis. Treatment with cysteamine is focused on preventing and delaying renal failure and other complications of the disease.

5. The patented medicine relevant to this proceeding, Procysbi, is a delayed release formulation of enterically-coated, microspherized beads of cysteamine bitartrate indicated for the treatment of nephropathic cystinosis. As a delayed release formulation, Procysbi only needs to be taken every 12 hours.

6. On December 24, 2015, Health Canada granted priority review status for Procysbi. In late 2016 and early 2017, two Canadian Patents were issued for Procysbi: (i) Canadian Patent No. CA2914770, entitled "Delayed release cysteamine bead formulation, and methods of making and using same", was issued on September 27, 2016 (the "**770 Patent**"); and (ii) Canadian Patent No. CA2640531, entitled "Enterically coated cysteamine, cysteamine and derivatives thereof", was issued on January 3, 2017 (the "**531 Patent**"). Horizon obtained a Notice of Compliance ("**NOC**") from Health Canada on June 13, 2017. Horizon made its first sale of Procysbi in Canada on September 7, 2017.

7. On December 5, 2017, the Respondent filed a Form 1 for Procysbi and, at the end of January 2018, the Respondent filed price and sales information for the period between July and December 2017. Procysbi's introductory price in Canada was set at $10.35 for each 25 mg delayed release capsule and $31.05 for each 75 mg delayed release capsule. This introductory price is below the maximum price permitted under the Median International Price Comparison ("**MIPC**") Test set out in the Board's Compendium of Policies, Guidelines and Procedures (the "**Guidelines**").

8. Cystagon is another cystine depleting medicine indicated for the treatment of nephropathic cystinosis. Cystagon has the same active ingredient as Procysbi—cysteamine bitartrate. However, unlike Procysbi, Cystagon is an immediate release formulation of cysteamine which is absorbed in the stomach and must be taken every six hours. Also unlike Procysbi, Cystagon has never been commercialized in Canada. Cystagon was made available in Canada through the Special Access Program ("**SAP**")

in 1994, and continued to be available through the SAP up to the date of first sale of Procysbi in Canada (September 7, 2017). After that date, access to Cystagon through the SAP was limited to circumstances in which a medical practitioner established that the patient was medically unable to use Procysbi.

9. On January 30, 2018, Horizon submitted its new medicine submission to the PMPRB, in which it sought breakthrough status for Procysbi.

10. On February 15, 2018, Board Staff prepared a New Medicine Scientific Staff Summary that proposed a series of questions to the Human Drug Advisory Panel ("**HDAP**"), including whether Cystagon should be used as a comparator for Procysbi.

11. On February 22, 2018, Board Staff received a complaint about the price of Procysbi from the pan-Canadian Pharmaceutical Alliance ("**pCPA**"). Receipt of a complaint is an automatic investigation trigger under the Guidelines.

12. On February 26, 2018, HDAP prepared a report entitled: "HDAP New Medicine Review", in which it recommended that: (i) Cystagon be used as a comparator for Procysbi; and (ii) Procysbi be classified as a "moderate" improvement over Cystagon.

13. On March 13, 2018, Board Staff wrote to the Respondent advising it of HDAP's conclusions and indicating that Board Staff had commenced an investigation into the introductory price of Procysbi, pursuant to the investigation criteria in the Guidelines.

14. On March 28, 2018, Horizon responded to Board Staff's letter and requested that HDAP reconsider its characterization of Procysbi as a moderate improvement and its designation of Cystagon as a comparator. On April 20, 2018, Horizon provided a further Request for Consideration to Board Staff. On April 27, 2018, Board Staff authored a New Medicine Review – Issue Paper for the purpose of asking HDAP whether Horizon's submissions of March 28, 2018 and April 20, 2018 changed HDAP's recommendations.

15. On May 18, 2018, Horizon was advised that HDAP would not be changing its initial recommendations.

16. At the commencement of the investigation into the introductory price of Procysbi, Board Staff notified the Respondent that it believed that the Guidelines should not be applied in this case because of the price differential between Procysbi and Cystagon.

17. The investigation conducted by Board Staff involved a comparison between the National Average Transaction Price ("**N-ATP**") of Procysbi to the publicly available list price of Cystagon in Canada. Board Staff also reviewed *inter alia* the prices of Procysbi and Cystagon in the comparator countries (the "**PMPRB7**") listed in the Schedule of the Patented Medicines Regulations, SOR/94-688 (the "**Regulations**"), and the review of data regarding the volume of sales of Procysbi and Cystagon in the PMPRB7. Following its investigation, Board Staff informed the Respondent that the price of Procysbi appeared to be excessive.

18. On December 6, 2018, Horizon met with Board Staff to present a draft Voluntary Compliance Undertaking ("**VCU**"). Board Staff rejected Horizon's VCU and informed Horizon that it would only continue negotiations if Horizon would commit to reduce the price of Procysbi by 75%. When Horizon refused to commit to a 75% price reduction, Board Staff referred the matter to the Chairperson of the Board and recommended the issuance of a Notice of Hearing.

19. On January 14, 2019, Board Staff filed a Statement of Allegations in which it alleges that from 2017 to date, the Respondent has been selling Procysbi in Canada at an excessive price. Board Staff seeks an order from this Panel under section 83 of the Act requiring the Respondent to, *inter alia*, reduce the price of Procysbi in accordance with one of three pricing models which Board Staff describes as: (i) the same medicine comparison; (ii) the market share approach; and (iii) the premium price approach. Application of these pricing models would reduce the price of Procysbi by approximately 71% to 98% of its current price (the "**Proposed Prices**").

20. On January 16, 2019, the Board issued a Notice of Hearing with respect to Board Staff's Statement of Allegations. After the filing of an Amended Statement of Allegations and various preliminary motions, this hearing took place on November 23-26, 2020;

November 30-December 1, 2020; December 3, 2020; January 11-15, 2021; January 18-19, 2021; and March 10-12, 2021. The purpose of the hearing was to determine whether, under sections 83 and 85 of the Act, the Respondent is selling, or has sold, Procysbi in any market in Canada at a price that, in this Panel's opinion, is or was excessive, and if so, what order(s), if any, should be made.

21. On July 29, 2021, the Federal Court of Appeal rendered its decision in *Alexion Pharmaceuticals Inc v. Attorney General of Canada* ("**Alexion FCA**") [2], in which the Court overturned the decision of the Federal Court, quashed the decision of the Board in relation to the medicine "Soliris" and remitted the matter back to the Board for reconsideration. On August 11, 2021, the Panel requested that the parties file any written submissions they wished to provide on the impact of *Alexion FCA* on the issues in this proceeding. Both parties filed written submissions on September 10, 2021 and exchanged reply submissions on September 17, 2021, all of which were considered by the Panel in reaching this decision.

C. INTERLOCUTORY DECISIONS

22. Given the lengthy procedural history, the Panel will summarize the main interlocutory motions brought in this proceeding.[3]

23. On January 15, 2020, the Panel heard Board Staff's motion to (i) bifurcate this hearing between sections 85(1) and 85(2) of the Act, (ii) redact portions of the expert report of Dr. Hay (the Respondent's witness) that relate to the cost of making and marketing Procysbi, and (iii) in the alternative, order the inspection of Horizon's books and records and the production of certain documents. The Respondent opposed the motion.

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2 2021 FCA 157 [*Alexion FCA*], leave to appeal to the Supreme Court of Canada denied, 2022 CarswellNat 714 (SCC).

3 The summary below does not include the numerous requests for confidentiality filed by the parties over the course of this proceeding.

24. The Panel issued its decision (with reasons to follow) on this motion on January 17, 2020. The Panel's reasons were issued on February 28, 2020.[4] The Panel denied Board Staff's motion to bifurcate the proceeding, redact portions of Dr. Hay's expert report, and inspect the books and records of Horizon. However, the Panel granted Board Staff's motion for production of documents in part. In this regard, the Panel ordered (i) the Respondent to produce certain requested documents, and (ii) the Parties' experts to meet and confer to endeavor to come to agreement on the remaining document requests.

25. On February 21, 2020, the Parties' experts met and conferred, in the presence of counsel and representatives of the Parties. On April 3, 2020, the Parties filed a Joint Memorandum in which they advised the Panel that six categories of document requests remained in dispute following the meet and confer. On June 26, 2020, on the basis of the written record and the Parties' oral submissions at the January 15 hearing, the Panel granted Board Staff's request for production of documents in part.[5]

26. On October 8, 2020, the Panel held a Case Conference to address the format of the merits hearing in light of the health and safety concerns raised by the COVID-19 pandemic. Board Staff maintained that as much of the hearing as practically possible should be conducted in person while maintaining adherence to health and safety protocols. The Respondent and the BC Minister maintained that the entire hearing should be conducted virtually by videoconference. On October 20, 2020, the Panel released its decision, in which it concluded that the entire hearing would be conducted

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4 Board Decision - *Horizon Pharma and the Medicine "Procysbi" (Board Staff's Motion to Bifurcate, Strike Evidence and for the Production and Inspection of Documents)* (January 17, 2020), online: PMPRB <https://www.canada.ca/en/patented-medicine-prices-review/services/hearings/status-ongoing-proceedings/decision-board-horizon.html>; Board Reasons for Decision – *Horizon Pharma and the Medicine "Procysbi" (Board Staff's Motion to Bifurcate, Strike Evidence and for the Production and Inspection of Documents*) (February 28, 2020), online: PMPRB <https://www.canada.ca/en/patented-medicine-prices-review/services/hearings/status-ongoing-proceedings/reasons-decision-bifurcation-motion.html>.

5 Board Decision – *Horizon Pharma and the Medicine "Procysbi" (Board Staff's Motion for Production of Documents)* (June 26, 2020), online: PMPRB <https://www.canada.ca/en/patented-medicine-prices-review/services/hearings/status-ongoing-proceedings/reasons-decision-production-documents.html>.

virtually, and all Parties, witnesses, counsel and the Panel would appear by videoconference.[6]

27. On December 3, 2020, the Panel heard a motion brought by the Respondent, seeking, *inter alia*, an Order disqualifying Dr. Mitchell Levine as a Panel Member in this proceeding on the basis that there was a reasonable apprehension of bias arising from statements that he made to the House of Commons Standing Committee on Health on November 23 and 27, 2020. Board Staff opposed the motion. On December 24, 2020, the Panel issued its decision denying the Respondent's motion.[7]

28. Finally, on December 22, 2020, Board Staff brought a motion to define the parameters of the testimony of Dr. Ranjan Dohil (a lay witness called by the Respondent). Board Staff sought to limit Dr. Dohil's testimony to telling the "patent story" of Procysbi, and not opining on the benefits of Procysbi over Cystagon, or any other matters that require expert opinion evidence. The Respondent opposed the motion. On January 11, 2021, the Panel advised the parties that it would take Board Staff's motion under reserve and consider Board Staff's position in light of the testimony that Dr. Dohil actually provided at the hearing. However, the Panel did provide its views about the appropriate scope of Dr. Dohil's testimony, including that Dr. Dohil's evidence should be limited to outlining the factual story of the invention of Procysbi, and should not include opinions about the superiority of one medicine over the other. To the extent that Dr. Dohil's testimony ventured into the world of opinion rather than the facts surrounding the invention of the patent, this Panel indicated it would not give any weight to those opinions.

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6 Board Decision – *Horizon Pharma and the Medicine "Procysbi" (Case Conference Regarding Hearing Format)* (October 20, 2020), online: PMPRB <https://www.canada.ca/en/patented-medicine-prices-review/services/hearings/status-ongoing-proceedings/reasons-decision-case-conference-hearing-format.html>.

7 Board Decision – *Horizon Pharma and the Medicine "Procysbi" (Respondent's Motion for Recusal)* (December 24, 2020), online: PMPRB <https://www.canada.ca/content/dam/pmprb-cepmb/documents/hearings/status-ongoing-proceedings/PMPRB%20Decision%20-%20Motion%20for%20Recusal.pdf>.

D. POSITIONS OF THE PARTIES

29. The positions of Board Staff and the Respondent are briefly summarized in this section of the decision, to assist in placing the subsequent discussion of the evidence and the Panel's analysis into context.

30. Board Staff submits that Procysbi was and is excessively priced, and seeks an order that its maximum price be reduced. Board Staff's position on the key issues in dispute is provided below.

(a) ***Board's Mandate*.** The Board's mandate is to protect consumers from excessive pricing, and the Act must be interpreted within that context.

(b) ***The Medicine***. The medicine over which the Panel has jurisdiction is cysteamine bitartrate, not Procysbi. Cystagon and Procysbi are the same medicine because the only active pharmaceutical ingredient in both is cysteamine, and both medicines treat the same condition.

(c) ***The Comparator*.** Whether or not the Panel finds that Procysbi and Cystagon are the same medicine, they are at least therapeutic comparators because: (i) they are the only two treatments for cystinosis currently available for sale; (ii) HDAP recommended that Procysbi and Cystagon be compared; and (iii) a medicine sold through the SAP is "sold" in Canada within the meaning of section 85(1)(b) of the Act, and therefore can be used as a comparator.

(d) ***Level of Therapeutic Improvement*.** This Panel should depart from the Guidelines and create a new category of therapeutic improvement. Procysbi should fall within a new "modest improvement" category, that is between the existing "slight or no improvement" and "moderate improvement" categories set out in the Guidelines.

(e) ***Applicable Price Test*.** The Panel should depart from the Guidelines and adopt one of the following pricing models: (i) the same medicine

comparison; (ii) the market share approach; and (iii) the premium price approach. It is appropriate to depart from the price tests provided for in the Guidelines because Procysbi falls within a novel category of “modest improvement”. Alternatively, if the Panel finds that Procysbi is a moderate improvement over Cystagon, the application of the test in the Guidelines for a medicine that provides a moderate improvement is not appropriate in this case because it would lead to a MAPP of Procysbi that is over 2600% greater than the price of Cystagon.

(f) ***Interaction Between Sections 85(1), 85(2) and 85(3) of the Act*.** Sections 85(1) and 85(2) are watertight compartments. The Act requires the Board to first determine whether the matter of excessive pricing can be determined pursuant to section 85(1), and it is only if the Board cannot make a determination based on the section 85(1) factors that it may have regard to section 85(2).

Section 85(3) of the Act can only be considered if the Panel exercises its discretion to consider the costs of making and marketing Procysbi under section 85(2), which in turn is only open to the Panel if it cannot make a determination under section 85(1). Research and development costs referenced in section 85(3) cannot be considered by the Panel in its section 85(1) analysis.

Board Staff submits that the Panel can make a determination under section 85(1), and therefore does not need to consider sections 85(2) and 85(3). Consequently, Board Staff submits that the evidence of Dr. Hay and the evidence of Mr. Rosen (Board Staff’s expert witness, as further described below) is not relevant. However, if the Panel chooses to proceed with an analysis under section 85(2), the Panel should accept the evidence of Mr. Rosen that Horizon would not suffer losses if the MAPP of Procysbi was determined based on two of the three pricing models proposed by Board Staff.

31. Horizon submits that the Panel should dismiss this application, as the price of Procysbi in Canada is in accordance with the Guidelines and is not excessive. Horizon's position on the key issues in dispute is provided below.

(a) ***Board Mandate*****.** The Panel must determine excessiveness under section 85 of the Act in accordance with the Board's statutory mandate, which is to prevent the abuse of a patentee's patent monopoly. There must be a nexus between an excessive price and the abuse of a patent monopoly, and that a determination of whether there is an abuse of patent requires a consideration of the relevant context, including the economic and clinical considerations which inform the development and pricing of ultra-rare disease drugs, like Procysbi.

(b) ***The Medicine*****.** The medicine over which the Board has jurisdiction is the patented medicine: enterically-coated microspherized beads of cysteamine bitartrate, known as Procysbi. In other words, the "medicine" is the commercial formulation, not the active ingredient.

(c) ***The Comparator*****.** Cystagon is not a comparator to Procysbi. Cystagon cannot form part of the "therapeutic class" because as a SAP medicine, it was not "sold" in the "relevant market" within the meaning of section 85(1)(b) of the Act.

(d) ***Level of Therapeutic Improvement*****.** Procysbi is a breakthrough drug, or at least a substantial improvement over Cystagon.

(e) ***Applicable Price Test*****.** The appropriate test under the Guidelines is the MIPC Test because (i) Procysbi is a breakthrough, or at least a substantial improvement over Cystagon, and (ii) Cystagon is not a domestic comparator. Board Staff's three alternative pricing models should be rejected for several reasons, including because at the Proposed Prices, the Respondent will not only fail to recover its costs and earn a return, but will suffer millions of dollars in losses.

(f) **Interaction Between Sections 85(1), 85(2) and 85(3).** Sections 85(1) and 85(2) are not watertight compartments. The Board must consider all of the evidence before it, including the costs of making and marketing Procysbi, in order to determine whether it has a sufficient basis to determine whether the price of Procysbi is excessive using the section 85(1) factors alone. The evidence of Dr. Hay is relevant to the Panel's analysis under section 85(1) because it was tendered in response to Board Staff's allegations and the Proposed Prices, which Board Staff put forth under section 85(1). The exceptional circumstances of this case and the lack of reasonable comparators under section 85(1) require this Panel to consider the costs of making and marketing Procysbi under both sections 85(1) and 85(2).

Section 85(3) of the Act is not simply a provision that modifies section 85(2). Rather, is a standalone provision, pursuant to which the Panel can consider the Canadian portion of the world costs related to research in its excessiveness inquiry.

E. FACT EVIDENCE

32. Board Staff called two fact witnesses: Mr. Matthew Kellison and Dr. Muhammad Mamdani. Horizon called two fact witnesses: Mr. Vikram Karnani and Dr. Ranjan Dohil. Their evidence is briefly summarized in this section of the decision.

(i) Mr. Matthew Kellison

33. Mr. Kellison was the Director of the Regulatory Affairs & Outreach Branch of the Board from January 2017 until November 2019. As Director, Mr. Kellison was responsible for the overall management of the Branch, which included overseeing the price reviews of patented medicines and the investigation process.

34. Mr. Kellison's testimony focused on the Board's investigation of the price of Procysbi and the development and application of Board Staff's three proposed pricing models.

(ii) Dr. Muhammad Mamdani

35. Dr. Muhammad Mamdani served as one of six members of HDAP. Dr. Mamdani was the primary reviewer assigned to bring recommendations on the level of therapeutic improvement of Procysbi to the broader HDAP committee.

36. Dr. Mamdani's testimony focused on explaining the role of HDAP, the evidence-based review process that HDAP undertook with respect to Procysbi, and HDAP's recommendations to Board Staff regarding the level of therapeutic improvement of Procysbi.

(iii) Mr. Vikram Karnani

37. Mr. Karnani is the Executive Vice President and President, International of Horizon. Mr. Karnani has worked at Horizon since July 2014. Prior to assuming his current role in 2018, Mr. Karnani led a product team within Horizon's rheumatology segment.

38. Mr. Karnani's testimony focused on (i) explaining the evolution of Horizon as a leading biopharmaceutical company focused on rare diseases, and (ii) describing the major tenants of Horizon's business strategy. In particular, Mr. Karnani described Horizon's corporate mission to help those impacted by rare and rheumatic diseases by providing innovative medicines to address unmet treatment needs of these small patient populations. Mr. Karnani described the major tenants of Horizon's strategy as including: (i) filling unmet needs by listening to, learning from and engaging with the rare disease patient communities; (ii) prioritizing patient care; and (iii) utilizing a differentiated commercial model.

39. Mr. Karnani also described the challenges and costs of developing and commercializing rare disease drugs like Procysbi, including: (i) the high development costs; (ii) an extremely small patient population over which to amortize those costs; and (iii) an extremely small patient population to participate in clinical trials, which leads to difficulties with generating literature and data.

40. Mr. Karnani also provided evidence regarding Horizon's acquisition of Raptor Pharmaceuticals Inc. ("**Raptor**"), the cost to commercialize Procysbi, and Horizon's process for setting the price of Procysbi. Mr. Karnani explained that in October 2016, Horizon acquired Raptor and, as part of the transaction, Horizon acquired rights to both Procysbi and another product known as Quinsair. At the time when Horizon acquired Raptor, Procysbi had already been developed and had received marketing approval in the U.S. and Europe, but had not yet received approval in Canada. Horizon was not involved in the research, clinical studies or steps leading up to the commercialization of Procysbi.

41. Mr. Karnani testified that Horizon lowered the price of Procysbi that had been set by Raptor, so that it fell below the MIPC. He explained that Horizon's approach to pricing in Canada relied on the guidance provided by the Guidelines.

(iv) Dr. Ranjan Dohil

42. Dr. Dohil is a pediatric gastroenterologist at Rady Children's Hospital-San Diego and a professor of pediatrics at UC San Diego School of Medicine. Dr. Dohil is the named inventor of the 531 Patent, and an inventor of the 770 Patent (though not yet named in Canada).

43. Dr. Dohil explained Procysbi's "patent story". Dr. Dohil testified that in 1999, he began researching cystinosis and trying to understand the cause of the negative gastrointestinal symptoms experienced by patients. Dr. Dohil then spent over a decade seeking to solve that problem through long-term, multi-study research that ultimately led to the development of the invention of a delayed release formulation of enterically-coated microspherized beads of cysteamine bitartrate, now known as Procysbi.

44. Dr. Dohil's testimony largely focused on outlining the factual story of the invention of Procysbi, and to the extent his evidence wandered into opinions regarding the superiority of Procysbi, the Panel did not give any weight to those opinions.

F. EXPERT EVIDENCE

45. Expert evidence consumed a large portion of this proceeding. The Panel has considered the evidence thoroughly and will not reproduce it in detail in this decision, but will only refer to it where salient to the Panel's determination of the issues before it.

46. Board Staff called three expert witnesses: Dr. Julian Midgley, Professor Richard Schwindt and Mr. Howard Rosen. Horizon called two expert witness: Dr. Craig Langman and Dr. Joel Hay. The expert evidence can generally be divided into two categories: (i) medical expert evidence; and (ii) economic/accounting expert evidence. In addition to briefly summarizing the expert evidence, this section of the decision will address certain of the evidentiary issues raised by the Parties in respect of this evidence.

(i) Medical Expert Evidence

(a) Dr. Julian Midgley

47. Dr. Midgley was qualified as an expert in pediatric nephrology with experience in the treatment of cystinosis.

48. Dr. Midgley is a pediatric nephrologist who has been involved in the treatment of patients with cystinosis for over 26 years. He is on the advisory board of the Cystinosis Research Foundation, and was the president of both the Kidney Foundation and the Canadian Association of Pediatric Nephrologists.

49. Dr. Midgley's clinic has seen twenty-three cystinosis patients. He has primary responsibility for twenty patients. Dr. Midgley's clinic is unique in Canada as he sees patients from the time of diagnosis (often in the first year of life) and then follows them into adulthood.

50. Dr. Midgley prescribes Procysbi as well as Cystagon to his patients. As of November 30, 2020, nine of Dr. Midgley's patients receive Cystagon and 10 receive

Procysbi.[8] The longest period of time that any of Dr. Midgley's patients have been on Procysbi is 10 years – that is because those patients participated in the original RP-103-03 trial (further described below).

51. Dr. Midgley's opinion is that Procysbi and Cystagon are the same medicine, their clinical outcomes are not different, there is no evidence of better adherence with Procysbi versus Cystagon, it is too soon to know if Procysbi's theoretical improvement in adherence will lead to better clinical outcomes, and there does not appear to be a substantial difference in adverse effects between them.

52. Dr. Midgley's responding expert report attaches a literature review prepared by Denis Belanger and Terri O'Grady, which became the subject of a dispute between the Parties. The Respondent submits that neither the literature review nor any of its references have been properly introduced as evidence because Dr. Midgley admitted on cross-examination that he did not read the literature referenced in the literature review, and those who drafted the literature review did not swear an expert witness declaration confirming their duty to provide opinion evidence that is impartial and related only to matters within their area of expertise. Board Staff submits that the literature review is properly admitted into evidence because Dr. Midgley confirmed that he reviewed and is in agreement with the literature review, and the Respondent had the opportunity to cross-examine Dr. Midgley on the literature review.

53. This Panel has broad discretion to admit "any evidence that it considers appropriate" in this proceeding.[9] The Panel finds that it is appropriate to admit the literature review into evidence as it is relevant and material to a matter in dispute between the Parties (being the therapeutic benefit offered by Procysbi). Further, the probative value outweighs any prejudicial effect as the Respondent had the opportunity to cross-examine Dr. Midgley on the contents of the literature review and his involvement or lack thereof in its preparation. However, the Panel ascribes little weight

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8 The remaining patient is a patent who had received a stem cell transplant and was not receiving cysteamine treatment.

9 *Patented Medicine Prices Review Board Rules of Practice and Procedure*, SOR/2012-247, s 6(1).

to the literature review itself in light of Dr. Midgley's admission that he did not review the underlying literature summarized in it, and no witness was called to specifically address that literature.

(b) Dr. Craig Langman

54. Dr. Langman was qualified as an expert in pediatric nephrology, with specific expertise in the treatment of cystinosis.

55. Dr. Langman has been practicing as a board-certified pediatric nephrologist for almost 40 years. He is Division Head, Kidney Diseases at the Northwestern University Medical School and the Northwestern Memorial Hospital. He also maintains privileges as a Senior Attending Physician in the Division of Nephrology at the Ann and Robert H. Lurie Children's Hospital of Chicago and as an Associate Physician in the Department of Pediatrics at Northwestern Memorial Hospital.

56. Dr. Langman has treated or consulted on dozens of patients with nephropathic cystinosis since the early 1980s. He was also the lead investigator on the first clinical trial involving Procysbi (RP-103-03), as well as the extension study (RP-103-04).

57. Dr. Langman has treated approximately three-dozen patients with cystinosis with both Procysbi and Cystagon. However, Dr. Langman no longer prescribes Cystagon to his patients, because in his view, Procysbi is superior.

58. Dr. Langman's opinion is that Procysbi and Cystagon are not equivalent. In his view, Procysbi offers superior clinical outcomes including better control of WBC cystine levels, the potential for substantially delaying or even avoiding a cystinosis patient's need for dialysis or kidney transplant, improved therapeutic efficacy, improved quality of life, and reduced adverse events and side effects.

59. Board Staff submits that the Panel should exercise caution in reviewing Dr. Langman's evidence because he frequently assumed the role of an advocate on behalf of Horizon rather than an impartial expert. The Panel disagrees. Dr. Langman demonstrated that he understood that it was his duty to provide impartial opinion

evidence on matters within his area of expertise. As a qualified expert in pediatric nephrology, he is entitled to give opinion evidence based on his real world observations and experiences, and the fact that Dr. Langman was a lead investigator in the RP-103-03 and RP-103-04 studies does not preclude him from appearing as an expert before this Panel.

60. The Panel pauses at this point to note that while Drs. Midgley and Langman disagree on the equivalency (or not) of Cystagon and Procysbi, it was clear to the Panel that they are both respected and experienced practitioners who are dedicated to the well being of their patients and who endeavoured to provide candid, helpful and impartial evidence to this Panel.

(ii) Economic and Accounting Expert Evidence

(a) Professor Richard Schwindt

61. Professor Schwindt was qualified as an expert in microeconomics and economics of industrial organization.

62. Professor Schwindt is an emeritus professor in the Department of Economics and the Faculty of Business Administration at Simon Fraser University. His area of expertise is microeconomics and economics of industrial organization.

63. Professor Schwindt testified that from an economics standpoint, prices are excessive when they are above the competitive level (i.e., the price that would exist in a competitive market), and the difference between the two prices (i.e., the competitive price and the non-competitive price) is a measure of the degree of excessiveness. Professor Schwindt provided an opinion, from an economic perspective, on the methodologies that could be used to determine whether the price of Procysbi is excessive.

64. In Professor Schwindt’s opinion, if the Panel determines that Procysbi is a moderate improvement over Cystagon, a departure from the Guidelines is warranted for several reasons, including because the application of the Moderate Improvement Test

prescribed by the Guidelines would result in a price that is over 2600% greater than Cystagon (based on the publicly available price for Cystagon in Newfoundland and Labrador, as discussed below). In Professor Schwindt's view, applying the Moderate Improvement Test would result in a MAPP that is so much higher than the comparator that it would be difficult to defend on economic grounds.

65. Professor Schwindt also reviewed and explained the three alternative pricing models offered by Board Staff and the Proposed Prices that resulted from them:

(a) ***The Same Medicine Test***. This price of Procysbi is set at the price of Cystagon on a per-milligram basis.

(b) ***The Market Share Comparison Test***. Procysbi's price is based on the weighted average price of each of Procysbi and Cystagon, with weights based on their market shares in the PMPRB7, to the extent such data was available.

(c) ***The Premium Comparison (or "Modest Improvement") Test***. The price of Procysbi is set at the price of Cystagon, plus a twenty-five percent premium.

66. While Professor Schwindt reviewed and explained these three alternative pricing models, he expressly denied supporting or justifying any of the tests as being the one to choose.

(b) Mr. Howard Rosen

67. Mr. Howard Rosen was qualified as an expert in accounting, valuation and corporate finance related matters, with specific expertise in the pharmaceutical industry.

68. Mr. Rosen is a Chartered Professional Accountant (CPA), Chartered Business Valuator (CBV), and Accredited Senior Appraiser (ASA). He is the Managing Director of Secretariat International, an expert services firm, and has been involved in business valuation, damages quantification, and corporate finance related matters since 1981.

69. Mr. Rosen provided an opinion on the financial impact of Board Staff's Proposed Prices for Procysbi on Horizon's profits. Mr. Rosen also responded to the analysis put forward by the Respondent's expert, Dr. Joel Hay who concluded that applying any of the three pricing models meant that Horizon would fail to recover its costs and would suffer losses.

70. Mr. Rosen disagreed with Dr. Hay's analysis, followed a different approach and concluded that not only could Horizon cover all allocated costs, it would be profitable under 2 of the 3 pricing models advocated by Board Staff. As described below, the key area of disagreement between Mr. Rosen and Dr. Hay concerned how to allocate the costs of research and development and commercialization of Procysbi in the period prior to 2016.

(c) Dr. Joel Hay

71. Dr. Hay was qualified as an expert in health economics and pharmacoeconomics.

72. Dr. Hay is a tenured Full Professor and Founding Chair of Pharmaceutical Economics and Policy in the School of Pharmacy, with joint appointments in the Department of Economics and at the Schaeffer Center for Health Policy and Economics at the University of Southern California.

73. Dr. Hay was asked whether Horizon would recover the costs associated with commercializing Procysbi in Canada under any of Board Staff's pricing models. To answer this question, he developed an economic model of cost and revenue streams through to 2034 and conducted an analysis of Horizon's anticipated return on investment from Procysbi in Canada at the Proposed Prices under each pricing model. For the period prior to 2016, Dr. Hay used the cost of acquiring Raptor (referred to in the evidence as the Raptor Acquisition Cost), being $860.8 million (the "**RAC**"). For the period 2016 to 2034, he used Horizon's financial statements and projections.

74. Dr. Hay concluded that at the Proposed Prices, Horizon would not only fail to generate revenue sufficient to recover its costs of commercializing Procysbi in Canada but would incur tens of millions of dollars in losses through to patent expiry in 2034.

(d) Dispute Between Dr. Hay and Mr. Rosen

75. While there were other areas of disagreement between Mr. Rosen and Dr. Hay, the key and determinative dispute between them concerned how to allocate the costs of research and development and commercialization of Procysbi pre-2016. This dispute played out in the evidence in two ways.

76. First, there was a debate between Dr. Hay and Mr. Rosen about the appropriate method for allocating the RAC to Canada.

(a) Dr. Hay's initial report allocated the appropriate portion of the RAC to Canada based on number of patients. In his subsequent report, after receiving additional information, he allocated the RAC based on number of units sold, which he felt was a more accurate analysis. In Dr. Hay's view, the RAC represented the actual costs of developing Procysbi after accounting for costs of capital, which reflects the risk of investment and time value of money. He testified that whether one used the RAC or capitalized out of pocket costs the result would be the same – Horizon would not cover its costs and would suffer losses at the Proposed Prices.

(b) Mr. Rosen disagreed with this approach. He opined that the allocation of the RAC should be on the basis of revenue, not units sold. He testified that the RAC represents what Horizon was willing to pay to acquire Raptor on the basis of expected future cash flows, not on the basis of what it cost to develop and commercialize Procysbi. The RAC is therefore not a proxy for commercialization costs nor a reasonable measure of Raptor's costs to commercialize Procysbi. Mr. Rosen's view was that the allocation of the RAC should be based on where the sales and profits will be generated

because one is allocating a purchase price that was based on projected profits, not research and development costs.

(c) Dr. Hay testified that Mr. Rosen's approach was flawed in a number of respects. Dr. Hay criticized Mr. Rosen's internal rate of return (or "**IRR**") analysis because Mr. Rosen did not compare the IRR to Horizon's weighted average cost of capital ("**WACC**") rate to see whether the IRR met or exceeded Horizon's cost of capital. Dr. Hay explained that if Mr. Rosen had done so he would have seen that the IRR was less than the WACC rate in all three scenarios. Dr. Hay testified that to be profitable, the expected IRR of an investment must meet or exceed the WACC rate.

(d) Dr. Hay also testified that Mr. Rosen's approach of allocating based on revenue is inappropriate for a number of reasons, including because it results in Canada taking a "free ride" on the costs borne by US patients which is inconsistent with Canada bearing its fair share of costs, penalizes Horizon for bringing Procysbi to Canada, and is inconsistent with both section 85(3) of the Act and PMPRB guidance, which refer to units and not revenue.

(e) Finally, Dr. Hay testified that even if allocating based on revenue was the correct approach, Mr. Rosen's analysis was still flawed because (i) the denominator he used was based on Horizon's revenues from its entire drug portfolio (and not just Procysbi) over many years where there were no stable sales of Procysbi and (ii) it was limited to comparing US revenues to global revenues, as opposed to comparing Canadian revenues to global revenues.

(f) Mr. Rosen provided a number of responses to some of Dr. Hay's criticisms. He testified that Dr. Hay's reliance on Horizon's WACC rate is misguided. Research and development costs, being historical costs already spent, do not include a cost of capital. Dr. Hay also advocates

capitalizing the RAC, which is the discounted value of future cash flows, not historical research and development costs. Further, even if the IRR is less than the WACC rate, this does not mean that Horizon is suffering losses. It simply means that the company is not making as much money as it anticipated or desired on its investment.

(g) Mr. Rosen agreed that his preferred approach would have been to allocate the RAC based on the ratio of revenue reported from the sale of Procysbi in Canada to Horizon's total revenue from Procysbi worldwide, but maintained that he did not have the data necessary to do this analysis. The Respondent disputes this and insists that Mr. Rosen did in fact have the data to do this analysis and, if he had done it, the result would have been losses under all of Board Staff's proposed pricing models even before accounting for the cost of capital. Board Staff disputes this analysis, arguing that it relies on a calculation by Dr. Hay that was fundamentally wrong because it was based on projected sales in Canada which turned out to be much higher than the actual sales and also omitted the impact of the provision for PMPRB liability.

77. The second way this dispute played out in the evidence related to whether the RAC was even the right figure to allocate, as opposed to the $175 million of actual out of pocket expenses incurred by Raptor to develop and commercialize Procysbi (the "**R&D Cost**"). Until this issue arose in the course of the expert's testimony and the subsequent closing argument, neither Party questioned that the RAC was the appropriate figure to allocate. In fact, both experts allocated the RAC in their respective expert reports, joining issue not on <u>whether</u> the RAC should be allocated, but rather on <u>how</u> it should be allocated.

78. The Respondent's submission is that until Mr. Rosen testified in reply at the hearing, he accepted the RAC as the starting point for the analysis of the allocation of the cost to develop and commercialize Procysbi. The Respondent alleges that, while on the stand, Mr. Rosen shifted gears to advocate that the R&D Cost was the right starting

point, not the RAC. The Respondent objects to this evidence, noting that it is not contained in an expert report and Mr. Rosen did not actually perform any analysis to allocate any of the R&D Cost to Canada.

79. The Respondent argued that the issue was compounded by the fact that Board Staff submitted new evidence in its written closing submission, including new tables which purport to redo Dr. Hay's analysis based on Mr. Rosen's new theory to purportedly show that, had the R&D Cost been allocated, as opposed to the RAC, Horizon would be profitable under two of the three pricing models. The Respondent urged the Panel to give no weight to this evidence as it is not properly before the Panel and is grossly unfair since Horizon did not have the opportunity to respond to what is a different analysis involving different considerations. The Respondent argued that an allocation analysis based on the R&D Cost, as opposed to the RAC, required a consideration of a number of different factors, including increased risks, a greater WACC rate and the impact of financing, all of which it was not given the opportunity to address.

80. Board Staff's response is that Mr. Rosen was not inappropriately asserting a new theory during his testimony. Rather, Board Staff submits that Mr. Rosen was responding to two issues raised for the first time by Dr. Hay in his oral testimony, being: (i) that the RAC was a good measure of commercialization costs and (ii) that the R&D Cost plus the WACC rate equals the RAC.

81. The Respondent disputes that these were new matters raised by Dr. Hay for the first time in in his oral testimony. Dr. Hay noted in his first report that the RAC represented the cost of developing Procysbi. Further, Dr. Hay's discussion of WACC was simply a part of his criticism of Mr. Rosen's IRR analysis, which was reflected in his reply report.

82. While both Dr. Hay and Mr. Rosen were guilty to some extent of wandering beyond the four corners of the analysis set out in their respective reports, the Panel agrees with the Respondent that Mr. Rosen's reply evidence concerning the allocation

of the R&D Cost and Board Staff's new calculations in its written closing submissions are not justified on the basis that Dr. Hay advanced a new theory on the stand. In the Panel's view, he did not advance a new theory. Additionally and more importantly, the Panel agrees with the Respondent that the new analysis provided by way of Mr. Rosen's reply evidence and Board Staff's closing submissions should be given no weight because of the unfairness caused to the Respondent. It is not appropriate to provide new opinion evidence by way of reply evidence or by introducing new calculations in closing argument, because it deprives the Respondent of the ability to fairly respond, particularly where, as in this case, the Respondent argues that the new evidence fundamentally alters the allocation analysis and requires the consideration of additional factors and analysis.

83. The Panel will comment on the relevance of the economic and accounting evidence later in this decision when addressing the analysis under section 85 of the Act.

G. EVIDENCE OF THE BC MINISTER

84. Section 86(2) of the Act entitles a provincial minister of health to appear and make representations to the Board in respect of a proceeding.

85. On February 16, 2019, the BC Minister filed a Notice of Appearance with the Board. The provinces of Ontario, Saskatchewan and Newfoundland and Labrador have consented to the BC Minister representing them in this matter, and support the remedy sought by the BC Minister.

86. The BC Minister submits that the price at which Procysbi has been, and is being, sold in Canada is excessive, and that the Panel should order a reduction in the price of Procysbi in an amount to be determined by the Panel. The BC Minister does not endorse any of the three pricing models put forward by Board Staff.

87. The BC Minister submits that the evidence provided by Ms. Shirin Rizzardo on behalf of the BC Minister is relevant to the factors set out in sections 85(1)(a), 85(1)(b) and 85(2) of the Act.

88. With respect to section 85(1)(a), Ms. Rizzardo testified that when the BC Minister began funding the purchases of Procysbi for British Columbia patients in November 2018, the price per unit of Procysbi was $10.35 per 25 mg capsule and $31.05 per 75 mg capsule.

89. The BC Minister further submits that, since Cystagon and Procysbi share the same active ingredient (cysteamine), and are used to treat the same condition (nephropathic cystinosis), Cystagon should be considered to be in the same therapeutic class as Procysbi for the purposes of section 85(1)(b). Ms. Rizzardo provided the following evidence regarding the prices of Cystagon in British Columbia:

(a) The per unit cost of Cystagon 50 mg capsules was $0.79 in 2017 when Procysbi received marketing authorization in Canada;

(b) The per unit cost of Cystagon 150 mg capsules was $1.83 in 2017 when Procysbi received marketing authorization in Canada;

(c) The per unit cost of Cystagon 50 mg capsules was $1.93 in July 2018; and

(d) The per unit cost of Cystagon 150 mg capsules was $5.79 in July 2018.

90. Ms. Rizzardo testified that in 2018, the Province of British Columbia spent a total of $28,423.40 on Cystagon for four patients. In 2020/21, the Province of British Columbia was projected to spend $816,000 on Procysbi for three patients (based on Procysbi’s list price).

91. The BC Minister submits that if the Board is unable to make a determination under section 85(1) of the Act, the Board should consider the following evidence under section 85(2)(b) of the Act: (i) the BC Minister was not successful in its attempts to have Health Canada agree to provide continued, broader availability of Cystagon through the SAP after Procysbi entered the market in Canada; (ii) if Cystagon had remained available through the SAP, Procysbi would not have been publicly funded because the

BC Minister does not fund medications on the basis that they offer more convenience than other medications, unless either there are cost-savings to the government, or it is cost-neutral; and (iii) the pCPA had very little negotiating power with Horizon because their were no treatment options other than Procysbi after the availability of Cystagon through the SAP was reduced.

92. As explained later in this decision, this Panel is able to make a determination under section 85(1). Therefore, it is not necessary to decide whether the evidence summarized in the paragraph immediately above is appropriately considered under section 85(2)(b) as the BC Minister submits.

93. The BC Minister's concern regarding a lack of negotiating power was also raised in the pCPA's complaint to the Board. The pCPA alleged that it was being forced to negotiate with Horizon under duress. However, the pCPA complaint letter was submitted to the Board on February 22, 2018, which was less than two weeks after the pCPA sent Horizon a standard template engagement letter, and the product coverage agreement between Horizon and the BC Minister was signed on November 15, 2018, over nine months after the engagement letter had been transmitted. Moreover, throughout the negotiations, Horizon promised that no patient who wanted Procysbi would go uncovered.

94. As the Panel noted in its decision on the Respondent's motion for recusal dated December 24, 2020, the BC Minister's submission that the pCPA's negotiated agreement with the Respondent was made under duress is not relevant to any of the factors under section 85 of the Act.[10] Nonetheless, for the sake of clarity, in light of the timing and length of the negotiation process, and the Respondent's promise that no cystinosis patient would go uncovered, the Panel concludes that the evidence does not

[10] Board Decision – *Horizon Pharma and the Medicine "Procysbi" (Respondent's Motion for Recusal)* (December 24, 2020) at para 39, online: PMPRB <https://www.canada.ca/content/dam/pmprb-cepmb/documents/hearings/status-ongoing-proceedings/PMPRB%20Decision%20-%20Motion%20for%20Recusal.pdf>.

establish that the pCPA was forced to negotiate the product coverage agreements with Horizon under duress.

H. ISSUES IN THIS PROCEEDING

95. There are two issues for the Panel to determine:

(a) Is or was the price of Procysbi excessive within the meaning of sections 83 and 85 of the Act?

(b) If the answer to issue (a) is yes, what order(s), if any, should this Panel make?

I. ANALYSIS

(i) The Board's Jurisdiction

96. The Parties agree that the Board has jurisdiction in this case. Horizon is a patentee, as defined in section 79(1) of the Act, because Horizon is entitled to the benefit of the 770 Patent and 531 Patent. Moreover, pursuant to section 3(1)(h) of the Regulations, Horizon filed a Form 1 with the Board in which it admitted that the inventions in the 770 Patent and 531 Patent pertain to Procysbi, and that it is entitled to the benefits of a patent or to exercise any rights in relation to a patent.

(ii) The Board's Mandate under Sections 83 and 85 of the Act

97. Section 85 of the Act reads as follows:

> "**Factors to be considered**
>
> **85 (1)** In determining under section 83 whether a medicine is being or has been sold at an excessive price in any market in Canada, the Board shall take into consideration the following factors, to the extent that information on the factors is available to the Board:
>
> (a) the prices at which the medicine has been sold in the relevant market;
>
> (b) the prices at which other medicines in the same therapeutic class have been sold in the relevant market;

> (c) the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada;
>
> (d) changes in the Consumer Price Index; and
>
> (e) such other factors as may be specified in any regulations made for the purposes of this subsection.
>
> **Additional factors**
>
> (2) Where, after taking into consideration the factors referred to in subsection (1), the Board is unable to determine whether the medicine is being or has been sold in any market in Canada at an excessive price, the Board may take into consideration the following factors:
>
> (a) the costs of making and marketing the medicine; and
>
> (b) such other factors as may be specified in any regulations made for the purposes of this subsection or as are, in the opinion of the Board, relevant in the circumstances." [emphasis added]

98. Section 85 sets out the factors for the Board to consider when determining whether the price of a patented medicine is excessive in any market in Canada under section 83 of the Act. Section 85(1) sets out the mandatory factors that the Board must consider, and section 85(2) sets out other factors that the Board may consider if it is unable to determine whether the price of the patented medicine is excessive based on the mandatory section 85(1) factors.[11]

99. While section 85 gives the Board wide discretion, this Panel must exercise that discretion in a manner that is consistent with the text, context and purpose of that section, as well as the Board's mandate.[12]

100. In its recent decision in *Merck Canada Inc.,* the Quebec Court of Appeal recognized that, while the Act does not define "excessive", what constitutes an excessive price can be gleaned from section 85(1). The Court concluded that the

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11 *Alexion FCA*, *supra* note 14 at para 35; *Innovative Medicines Canada et al v Canada (Attorney General)*, 2020 FC 725 at paras 19-21 [*Innovative Medicines*].

12 *Alexion FCA*, *supra* note 14 at para 40.

purpose of the section 85(1) factors is to ensure an objective comparison of the price at which a patented medicine is sold in Canada (a) with the price at which medicines in the same therapeutic class are sold in Canada and (b) the prices at which the patented medicine and patented medicines in the same therapeutic class are sold in other countries. The Court further explained that the purpose is to ensure that the price charged in Canada for the patented medicine can be compared favourably in Canada and abroad for the same patented medicine and other patented medicines in the same therapeutic class. The non-excessive price so determined may then move in line with the Consumer Price Index, which is the other objective factor considered under section 85(1).

> [144] Ces facteurs énoncés au par. 85(1) de la Loi sur les brevets visent à assurer une comparaison objective entre le prix de vente au Canada du médicament breveté; et (a) le prix de vente au Canada des médicaments de la même catégorie thérapeutique; et (b) les prix de vente à l'étranger du même médicament et des médicaments de la même catégorie thérapeutique. Le but visé est de s'assurer que le prix exigé au Canada pour le médicament breveté puisse se comparer favorablement au Canada et à l'étranger pour le même médicament et les médicaments de la même catégorie thérapeutique. Le prix non excessif ainsi déterminé peut ensuite évoluer selon l'indice des prix à la consommation (« IPC »), lequel constitue l'autre facteur objectif à considérer.[13]

101. The Board's mandate was most recently addressed by the Federal Court of Appeal in *Alexion FCA*. In quashing the Board's decision, the Federal Court of Appeal concluded that the Board's role is not to ensure reasonable pricing, price regulation or consumer protection at large. Rather, the Board's role is strictly to prevent excessive pricing made possible by the abuse of the monopoly power given by a patent.[14]

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13 *Merck Canada Inc. c Procureur général du Canada,* 2022 QCCA at paras 143-144 [Merck]

14 *Alexion FCA*, *supra* note 14 at paras 11, 49, 51.

102. As noted above, the *Alexion FCA* decision was released after the Parties had completed closing submissions. Accordingly, the Panel invited submissions from the Parties regarding the impact of the *Alexion FCA* decision on the present case.

103. The Respondent submits that in *Alexion FCA*, the Court clarified that there must be a nexus between an excessive price and the abuse of a patent monopoly, and that a determination of whether there is an abuse of patent requires a consideration of the relevant context, including the economic and clinical considerations which inform the pricing of ultra-rare disease drugs, like Procysbi.

104. Board Staff disagrees. Board Staff submits that this Panel must follow the guidance of the Supreme Court of Canada and the Federal Court of Appeal, which have recognized that the Board has a consumer protection mandate. Moreover, Board Staff submits that the Court in *Alexion FCA* confirmed the sequential and hierarchical relationship between sections 85(1) and 85(2) of the Act, meaning that the Panel can reach a determination as to whether a medicine has been sold at an excessive price based solely on the factors contained in section 85(1), which factors do not include the economic and clinical context that the Respondent urges the Panel to consider.

105. The Panel recognizes that it must address the issue of excessiveness under sections 83 and 85 of the Act in accordance with the Board's statutory mandate as recently confirmed by the Federal Court of Appeal in *Alexion FCA*, which is to prevent excessive pricing arising from patent abuse, not consumer protection at large or general price regulation.[15]

106. That raises the question of what is meant by "patent abuse" in the context of the Board's mandate. In other words, in what circumstances does pricing become

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[15] *Alexion FCA*, *supra* note 14 at paras 49, 51. This is consistent with guidance from the Federal Court of Appeal in *Celgene Corp v Canada (Attorney General)*, 2009 FCA 378 [*Celgene FCA*], aff'd 2011 SCC 1 [*Celgene SCC*]. See also *Canada (Attorney General) v Galderma Canada Inc*, 2019 FCA 196 [*Galderma*], which was subsequently redetermined by the Board: Board Decision – *Galderma Canada Inc. and the medicines containing "adapalene" (Reasons for Decision on Redetermination Ordered by the Federal Court of Appeal on June 28, 2019)* (May 7, 2020), online: PMPRB <https://www.canada.ca/en/patented-medicine-prices-review/services/hearings/decisions-and-orders/reasons-decision-federal-court-june282019.html>, the redetermination decision currently under appeal.

excessive because it arises from patent abuse, and how, if at all, does consumer protection fit into the Board's mandate?

107. Decisions of the Supreme Court of Canada, Quebec Court of Appeal and the Federal Court provide helpful guidance. In summary, based on the key decisions discussed below, the Panel concludes that the Board's mandate is to ensure that patentees do not abuse their statutory monopoly rights by charging excessive prices and, in this respect, the Board does have a consumer protection mandate. Further, it is clear that the patent abuse relevant to the Board's mandate is the act of charging a price that is excessive within the meaning of section 85, not patent abuse under other sections of the Act (such as section 65) or some alleged general abuse of monopoly power.[16]

108. In *Celgene SCC*, the Supreme Court of Canada relied on the Board's "consumer protection goals" in upholding the Board's decision that it had jurisdiction to investigate and review the price of Thalomid.[17] The Court noted with approval that the Board's interpretation of its mandate "took into paramount account its responsibility for ensuring that the monopoly that accompanies the granting of a patent is not abused to the financial detriment of Canadian patients and their insurers."[18] The Court also relied on passages from the House of Commons debates, and cited the Federal Court's description of the Board's mandate in *ICN Pharmaceuticals FC* (which was subsequently affirmed by the Federal Court of Appeal):

> "Sections 79 to 103 of the Patent Act, creating the Patented Medicine Prices Review Board, were enacted in response to the abolition of the compulsory licensing regime. Parliament's intent was certainly to address the "mischief" that the patentee's monopoly over pharmaceuticals during the exclusivity period might cause prices to rise to unacceptable levels. Accordingly, the

16 *Innovative Medicines*, *supra* note 94 at paras 77-81.

17 *Celgene SCC*, *supra* note 102 at para 25.

18 *Celgene SCC*, *supra* note 102 at para 29.

> words of these sections of the Patent Act should be read purposively…"[19] [emphasis in original]

109. In *Celgene FCA*, the Federal Court of Appeal described the patented medicines provisions of the Act (i.e., sections 79-103) as "consumer protection provisions", and explained that the Board's mandate stems from the legislative context at the time of its creation:

> "The mandate of the Board is to ensure drug patentees do not abuse their monopoly position by charging excessive prices to consumers in Canada. The regime administered by the Board replaced the system of compulsory licensing, which was abolished in 1993. Price regulation during the life of the patent, rather than the injection of competition through compulsory licensing, thus became the means of protecting consumers from excessive prices for patented medicines."[20] [emphasis added]

110. In *ICN Pharmaceuticals FCA*, the Federal Court of Appeal rejected a restrictive interpretation of the Act which "would limit the ability of the Board to protect Canadian consumers from excessive pricing."[21] The Court of Appeal also said the following about the Board's consumer protection mandate:

> "The purpose of extending patent protection to medicines is to reward innovation and provide an incentive for pharmaceutical manufacturers … At the same time, it is believed that that objective must not overtake the need to ensure that Canadians have access to patented medicines which are reasonably priced."[22]

111. Other appellate authorities have made similar findings. Dismissing a separate application brought by Alexion to challenge the constitutionality of the patented

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19 *Celgene SCC*, *supra* note 102 at para 28, citing *ICN Pharmaceuticals Inc v Canada (Patented Medicine Prices Review Board)*, [1996] FCJ No 206 (FC) at para 24 [*ICN Pharmaceuticals FC*], aff'd [1996] FCJ No 1065 (FCA) [*ICN Pharmaceuticals FCA*]

20 *Celgene FCA*, *supra* note 102 at para 16. The Quebec Court of Appeal has also recently confirmed the consumer protection role played by sections 79 to 103 of the Act. The Court described those sections as a regime to control abuse of the patent monopoly that is necessary to protect the Canadian public: *Merck*, *supra* note 96 at para 48.

21 *ICN Pharmaceuticals FCA*, *supra* note 106 at para 60.

22 *ICN Pharmaceuticals FCA*, *supra* note 106 at para 3.

medicines provisions of the Act, the Federal Court of Appeal noted that the Board was created for a consumer protection purpose. As explained by Laskin J.A.:

> "The Act as it stood in the period from 1987 until the enactment of the 1993 amendments continued to provide for compulsory licensing of patents applicable to medicines, but gave patentees a period of exclusivity … To address concerns that prices during the exclusivity period might be unacceptably high from the consumer's perspective, the legislation provided for the establishment of the Board to monitor and review patented drug prices."[23] [emphasis added]

112. In *Sandoz Canada*, the Federal Court of Appeal considered a Board determination that its enabling provisions are meant to protect consumers from excessive pricing of patented medicines.[24] The Court found this to be "a defensible interpretation of the Act as construed to date by the case law".[25] The Court also applied *Celgene SCC* as instructive on the objectives of the patented medicines provisions: namely, ensuring patentees do not abuse their monopolies to the detriment of Canadian patients and their insurers.[26]

113. The Federal Court of Appeal in *Galderma,* in the context of discussing the Board's mandate, confirmed that the abuse of patent the Board is concerned with is the abuse of excessive pricing:

> "Before examining the Board's decision, it may be useful to briefly review the legislative context in which this dispute arises. The Board is established pursuant to section 91 of the Act and its composition, powers, procedures and attributes are set out in sections 92-100 of the Act. The Board's mandate is to ensure that the statutory monopoly granted to patentees of medicines is not abused by excessive pricing of those medicines."[27] [emphasis added]

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23 *Alexion Pharmaceuticals Inc v Canada (Attorney General)*, 2017 FCA 241 at para 20.

24 *Canada (Attorney General) v Sandoz Canada Inc*, 2015 FCA 249 at para 65 [*Sandoz Canada*].

25 *Sandoz Canada*, *supra* note 111 at paras 66-67.

26 *Sandoz Canada*, *supra* note 111 at para 89.

27 *Galderma*, *supra* note 102 at para 10. This matter was subsequently redetermined by the Board: Board Decision – *Galderma Canada Inc. and the medicines containing "adapalene" (Reasons for Decision on Redetermination Ordered by the Federal Court of Appeal on June 28, 2019)* (May 7, 2020), online: PMPRB <https://www.canada.ca/en/patented-medicine-prices-review/services/hearings/decisions-and-

114. Similarly, in *Innovative Medicines*, the Federal Court explained what is meant by patent abuse in the context of the Board's mandate:

> "Created by Parliament in 1987, the Board is a quasi-judicial body that regulates the prices that patentees can charge for patented medicines during the statutory monopoly period. The Board's mandate includes a type of consumer protection: ensuring that patentees do not abuse their patent rights by charging "excessive" prices for patented medicines. The Board's mandate is not to set prices for patented medicines, but to ensure patentees do not sell patented medicines at excessive prices (*Pfizer Canada Inc v Canada (Attorney General)*, 2009 FC 719 at para 11 [*Pfizer*]; *Sanofi Pasteur Limited v Canada (Attorney General)*, 2011 FC 859 at para 17 [*Sanofi*]).
>
> […]
>
> That said, I agree with the Respondent that the jurisprudence does not suggest that Courts have equated the "abuse" of excessive pricing with "patent abuse" under section 65 of the Patent Act. Instances of "patent abuse" and the powers of the Commissioner of Patents in such cases are detailed in sections 65 and 66 of the Patent Act. The Board's mandate is limited to the specific and separate "abuse" of excessive pricing, and the powers conferred on the Board are limited to those found in sections 79 to 103 of the Patent Act." [28] [emphasis added]

115. Finally, contrary to Horizon's initial closing submissions, the Board's mandate does not involve balancing consumer protection against both the rights of patentees and the desire to increase innovation. Rather, the Act contains that balance. The patented medicines regime in sections 79 to 103 of the Act is a distinct division of the Act which was implemented to serve as the consumer protection counterbalance to the increased statutory monopoly rights given to patentees in other parts of the Act. The Act itself balances patentee rights/innovation and consumer protection, not the Board.[29]

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orders/reasons-decision-federal-court-june282019.html>, the redetermination decision currently under appeal.

28 *Innovative Medicines, supra* note 94 at paras 7, 81.

29 *Innovative Medicines*, *supra* note 94 at paras 76-89, 93.

(iii) The Guidelines

116. The Board's Compendium of Policies, Guidelines and Procedures (previously defined as the "**Guidelines**") provides non-binding guidance and methodologies for applying section 85 of the Act to determine whether the price of a patented medicine sold in Canada is excessive.

117. The Guidelines provide for a two-step process: (a) the Scientific Review Process; and (b) the Price Review Process.

(a) The Scientific Review Process

118. The "Scientific Review Process" is an evidence-based process that assesses the level of therapeutic improvement of a patented medicine. Section C.5 of the *Guidelines* provides for the following four levels of therapeutic improvement:

> **Breakthrough:** A breakthrough drug product is the first one to be sold in Canada that treats effectively a particular illness or addresses effectively a particular indication.
>
> **Substantial Improvement:** A drug product offering substantial improvement is one that, relative to other drug products sold in Canada, provides substantial improvement in therapeutic effects.
>
> **Moderate Improvement:** A drug product offering moderate improvement is one that, relative to other drug products sold in Canada, provides moderate improvement in therapeutic effects.
>
> **Slight or No Improvement:** A drug product offering slight or no improvement is one that, relative to other drug products sold in Canada, provides slight or no improvement in therapeutic effects."

119. Section C.6 of the Guidelines provides that in determining the level of therapeutic improvement, both primary factors (increased efficacy and reduction in incidence or grade of important adverse reactions) and secondary factors (including patient convenience, caregiver convenience and compliance improvements leading to improved therapeutic efficacy) are to be considered. However, the primary factors are given the greatest weight, followed by an assessment of any additional improvement as

a result of secondary factors.[30] Moreover, additional factors including “a different pharmacokinetic profile”, will generally not be taken into consideration, unless the impact of these factors results in either increased efficacy and/or a reduction in the incidence or grade of important adverse reactions.[31]

120. Section C.7 of the Guidelines provides that the methodology for evaluating the level of therapeutic improvement is based on the hierarchy of evidence from the Oxford Centre for Evidence-Based Medicine, with the greatest weight given to “Level 1” evidence.[32] The Guidelines do provide that other levels of evidence may be considered, as required, on a case by case basis in order to assess the secondary factors”,[33] however, the secondary factors are limited to being assessed “up to the level of moderate therapeutic improvement”.[34]

121. As discussed above, on February 26, 2018, HDAP prepared a report entitled, “HDAP New Medicine Review”, in which it recommended that (i) Cystagon be used as a comparator for Procysbi; (ii) Procysbi be classified on the primary factors as providing “slight or no therapeutic improvement” over Cystagon in the treatment of cystinosis; and (iii) Procysbi be classified on the secondary factors as providing “moderate” improvement over Cystagon (the highest level of improvement for secondary factors permitted under the Guidelines).

122. As previously noted, after being advised of HDAP’s conclusions, Horizon requested that HDAP reconsider its characterization of Procysbi as a “moderate improvement” and designation of Cystagon as a comparator. HDAP reconsidered these matters and concluded that there would be no changes to its initial recommendations.

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30 Canada, Patented Medicine Prices Review Board, "Compendium of Policies, Guidelines and Procedures", (February 2017) at C.8 [*Guidelines*].

31 *Guidelines*, *supra* note 117 at C.6.3.

32 *Guidelines*, *supra* note 117 at C.7.2.

33 *Guidelines*, *supra* note 117 at C.7.4.

34 *Guidelines*, *supra* note 117 at C.6.5.

123. Dr. Mamdani testified that although other literature had been reviewed, HDAP's recommendation was based, primarily, on conclusions reached in the RP-103-03 study because it was the only randomized, cross-over study directly comparing Cystagon and Procysbi that achieved the status of Level 1 evidence. In cross-examination, Dr. Mamdani admitted that Board Staff's instructions to HDAP did not include section C.7.4 of the Guidelines, which provides that HDAP may consider evidence, other than Level 1 evidence, as required on a case by case basis. Dr. Mamdani was of the view that while the Guidelines provide that Level 1 evidence is preferred (not required), he considered this to mean that Level 1 evidence is "highly, highly, highly" preferred.

124. RP-103-03 was designed as a non-inferiority trial to demonstrate that Procysbi is not inferior to or worse than Cystagon. It was not designed to demonstrate a benefit of Procysbi over Cystagon. By primarily basing its conclusions on RP-103-03, HDAP's assessment of Procysbi's level of therapeutic improvement was effectively limited to evidence of non-inferiority.

125. The Respondent submits that HDAP's "blinkered approach" is not appropriate given the paucity of literature relating to orphan drugs, especially in the case of an ultra-rare orphan drug like Procysbi.

126. The Panel agrees that blinded, long-term head-to-head comparative studies between Cystagon and Procysbi related to therapeutic efficacy would be virtually impossible to complete given the dosing regimen of each medicine. It is important for the Board to consider and give weight, as appropriate, to all credible sources and levels of evidence proffered, in addition (and not limited) to Level 1 evidence, when considering the level of therapeutic improvement for ultra-rare orphan drugs, like Procysbi. Accordingly, the Panel has not limited its review of this issue to Level 1 evidence but rather has considered all sources and levels of evidence proffered by the Parties. However, as discussed in greater detail below, at the end of the day, the Panel agrees with HDAP's ultimate conclusion that Procysbi offers a moderate improvement over Cystagon.

(b) The Price Review Process

127. The second step of the review process under the Guidelines is the "Price Review Process", in which the level of therapeutic improvement of the patented medicine is used to determine the highest possible price of the drug, known as the Maximum Average Potential Price or "MAPP".

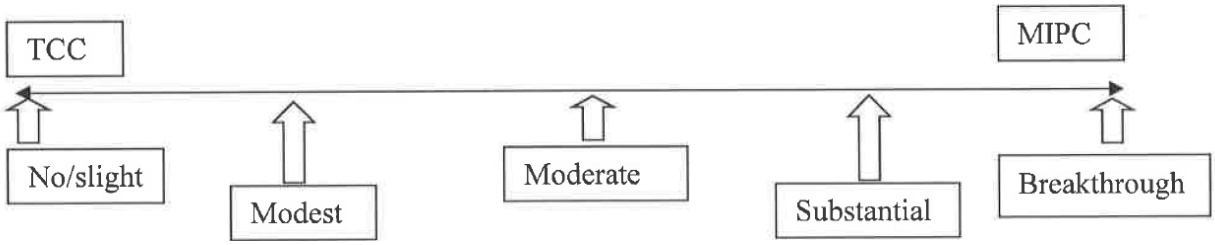
128. The Guidelines provide that the test applicable to the introductory price of a new patented medicine is dependent on the level of therapeutic improvement recommended for that medicine during the Scientific Review Process. Professor Schwindt summarized the price tests in his report as follows:

Level of Therapeutic Improvement	**New Medicine Price Test**
Slight or No Improvement	Price is constrained by the price(s) of medicines in the same therapeutic class, i.e., the Therapeutic Class Comparison ("**TCC**") Test.
Moderate Improvement	Price is constrained by the higher of: a. The highest non-excessive price determined by the TCC Test; b. The midpoint between (a.) and the median international price, i.e., the Median International Price Comparison ("**MIPC**") Test.
Substantial Improvement	Price is constrained by the higher of: a. The highest non-excessive price determined by the TCC Test; b. The median international price as determined by the MIPC Test.
Breakthrough	Price is constrained by the median international price as determined by the MIPC Test.

(c) Applicability of the Guidelines

129. Board Staff asks this Panel to deviate from the categories of therapeutic improvement and associated pricing tests set out in the Guidelines. Board Staff

advocates for a new category of therapeutic improvement, a “modest improvement” category, that is between the “slight or no improvement” and “moderate improvement” categories, as represented in the chart below:



Source: Expert Report of Professor Richard Schwindt dated September 6, 2019, Figure 1.

130. In Board Staff’s submission, the creation of this new category is necessary because the evidence only establishes that Procysbi may provide some therapeutic improvement over Cystagon, but its proven benefit does not rise to the level of being a moderate improvement. Board Staff submits that this new “modest improvement” category is necessary to recognize new products that are not that much better than existing treatment options.

131. Moreover, Board Staff submits that even if the Panel concludes that Procysbi is a “moderate improvement” over Cystagon, the Board should still depart from the Guidelines. In Board Staff’s submission, the Moderate Improvement Test set out in the Guidelines would not be an appropriate implementation of the factors in section 85(1) of the Act in the unique circumstances of this case because the starting prices of the two products (Cystagon and Procysbi) are so far apart that the test generates a grossly disproportionate result, being a MAPP that is over 2600% greater than the price of Cystagon.

132. Accordingly, Board Staff submits that the Panel should not follow the Guidelines in this instance, and should instead adopt one of its three pricing models, none of which appear in the Guidelines (although one is similar to the TCC test), or have ever been applied by the Board.

133. There is no doubt that the Guidelines are not binding on this Panel, and that it is open to this Panel to depart from the Guidelines by recognizing a new category of therapeutic improvement or pricing methodology if necessary to ensure an appropriate implementation of the factors in section 85 of the Act and to fulfill its mandate under the Act. As recently explained by the Federal Court of Appeal in *Alexion FCA*: "As non-binding guidance, the Guidelines can be departed from. But any departures from the Guidelines must be reasonable, at least in the sense that they are not inconsistent with a reasonable interpretation of section 85. And there must be a reasoned explanation for any departures from the Guidelines".[35]

134. The Panel finds that a departure from the Guidelines is not reasonable or necessary to appropriately implement section 85 of the Act in this case. For the reasons set out below, the Panel is of the view that (i) Procysbi is a moderate improvement over Cystagon and, therefore, there is no need or justification for creating a new "modest" category of therapeutic improvement in the circumstances of this case; and (ii) the application of the Moderate Improvement Test prescribed by the Guidelines (subject to using the international as opposed to the Canadian prices of Cystagon) appropriately operationalizes the section 85(1) factors and fulfils the Board's mandate.

(iv) The Benchmark for Determining Whether the Price of Procysbi is Excessive

(a) Cystagon and Procysbi Are Not the Same Medicine

135. Board Staff submits that Cystagon and Procysbi are the same medicine because the only active ingredient in both is cysteamine bitartrate, and both are indicated for the treatment of nephropathic cystinosis. Board Staff argues that the fact that the medicine is available in two different formulations (namely, immediate release and delayed release) does not change the fact that it is a single medicine.

136. The Respondent disagrees. The Respondent submits that the medicine at issue is not cysteamine bitartrate. Rather, it is the patented medicine, Procysbi. To look only

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[35] *Alexion FCA*, *supra* note 14 at para 39.

at the active pharmaceutical ingredient would, the Respondent argues, ignore Dr. Dohil's evidence regarding Procysbi's patent story, and important evidence regarding the improvements offered by Procysbi's enterically coated, microspherized beads.

137. The Panel agrees with the Respondent. The term "medicine" refers to the commercial formulation (Procysbi), and not simply the active ingredient (cysteamine bitartrate).[36] Dr. Dohil spent over a decade seeking to improve the treatment of cystinosis through long-term, multi-study research that ultimately lead to the development of the invention of a delayed release formulation of enterically-coated microspherized beads of cysteamine bitartrate now known as Procysbi. It is this invention (not the active ingredient, cysteamine bitartrate) that is the subject of two Canadian patents, which gives rise to the Board's jurisdiction in this case and is the medicine for purposes of the section 85 analysis.

(b) Cystagon is a Therapeutic Comparator for Procysbi

138. Previous panels of this Board have consistently defined therapeutic class to mean clinical equivalence, and this Panel agrees with that interpretation.

139. For example, the panel in *Dovobet* noted that "the therapeutic class of a medicine includes those medicines that are similar to the medicine under review in ways that are relevant to the pricing of the medicine, such as the condition the medicines treat, the way the medicines are delivered to the body, their chemical compositions, and the way they work in the body."[37]

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36 See *Galderma*, *supra* note 102 at para 61. This matter was subsequently redetermined by the Board: Board Decision – *Galderma Canada Inc. and the medicines containing "adapalene" (Reasons for Decision on Redetermination Ordered by the Federal Court of Appeal on June 28, 2019)* (May 7, 2020), online: PMPRB <https://www.canada.ca/en/patented-medicine-prices-review/services/hearings/decisions-and-orders/reasons-decision-federal-court-june282019.html>, the redetermination decision currently under appeal. See also *Hoechst Marion Roussel Canada Inc v Canada (Attorney General)*, 2005 FC 1552 at paras 119-121.

37 Board Decision – *Leo Pharma Inc. and the Medicine "Dovobet"* (19 April 2006), online: PMPRB <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=827&lang=en>, rev'd in part *Leo Pharma Inc v Canada (Attorney General)*, 2007 FC 306.

140. Further, in *Penlac*, the panel noted that "therapeutic class" should be defined as "clinical equivalence" and "[i]f the new medicine is not demonstrated to be comparable in efficacy and safety to existing medicines in Canada, it will not be considered to be clinically equivalent and thus there will be no therapeutic class for price comparison purposes."[38] This approach was also adopted by the panel in the *Quadracel* and *Pentacel* proceeding.[39]

141. Board Staff and the BC Minister submit that Cystagon should be considered to be in the same therapeutic class as Procysbi. The Panel agrees. While Cystagon and Procysbi are not the same medicine, Cystagon is a therapeutic comparator for Procysbi because they are clinically equivalent. As described above: (i) Cystagon and Procysbi are both cystine depleting therapies indicated for the treatment of nephropathic cystinosis; (ii) the therapeutic effect of both Cystagon and Procysbi is primarily assessed by WBC cystine levels; and (iii) the only active medicinal ingredient in both medicines is cysteamine bitartrate. When Procysbi was not available in Canada, nephropathic cystinosis was treated with Cystagon, and Cystagon is still available for those patients who cannot tolerate Procysbi.

142. The Respondent submits that Cystagon cannot form part of Procysbi's "therapeutic class" for the purposes of section 85(1)(b) of the Act because it is only available in Canada through the SAP, and therefore is not sold within a functioning, competitive market within the meaning of section 85(1)(b). The Respondent argues that the Board must compare market prices in a properly functioning competitive market. The Respondent also submits that access to Cystagon through the SAP is considerably different from access to Procysbi through a NOC for several reasons, including:

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38 Board Decision – *sanofi-aventis Canada Inc. and the Medicine "Penlac Nail Lacquer"* (31 January 2011) at paras 18, 20, online: PMPRB <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=848&lang=en> [*Penlac*].

39 Board Decision – *sanofi pasteur Limited and the Medicines "Quadracel and Pentacel"* (21 December 2009) at para 68, online: PMPRB <http://www.pmprb-cepmb.gc.ca/CMFiles/Hearings%20and%20Decisions/Decisions%20and%20Orders/Quadracel-Pentacel-Merits-Reasons-D5-Amended-March-1-2010.pdf>, amended 1 March 2010, implemented by order issued March 16, 2010, rev'd on other grounds *Sanofi Pasteur Ltd v Canada (Attorney General)*, 2011 FC 859.

(a) Health Canada does not receive studies on efficacy or safety for medicines accessed through the SAP, as it does for medicines applying for a NOC. Given the lack of data, Health Canada does not provide patients with an opinion on the efficacy or safety of medicines accessed through the SAP;

(b) Prices of drugs accessed through the SAP are unreliable because they are at the sole discretion of the manufacturer, who may provide the medicine at deep discounts or no cost; and

(c) There is no access to the medicine through normal distribution channels because access through the SAP requires a physician to file a separate application to Health Canada under the SAP guidelines.

143. The Panel disagrees with the Respondent and finds that Cystagon, despite only being available through the SAP, has been "sold" in the "relevant market" for the purposes of section 85(1)(b) of the Act.

144. Following the decision in *Celgene SCC*,[40] there is no doubt that medicines accessible through the SAP can properly be considered to be medicines that are "sold" under the Act. The Respondent attempts to distinguish *Celgene SCC* from the present case on the basis that *Celgene SCC* considered the phrase "sold in *any* market", whereas the current phrase before the Panel is "sold in the *relevant* market". The Respondent argues that the scope of a "relevant" market is narrower than the scope of "any" market, and does not include sales through the SAP.

145. The Panel disagrees. While the scope of a "relevant" market is narrower than the scope of "any" market, there is nothing in the wording or context of section 85(1)(b) of the Act to suggest that this provision necessarily excludes sales through the SAP, or requires that the medicine be sold in a "functioning", "competitive market", as the Respondent argues. Rather, a plain reading of the words "relevant market" within their

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[40] *Celgene SCC*, *supra* note 102.

context supports Board Staff's position that this phrase is simply referring to the particular market that the Board has decided to examine. In determining whether a medicine is being or has been sold at an excessive price "in any market in Canada" in accordance with section 85(1) of the Act, the Board can decide to examine the price of a medicine in a particular market. Once the Board makes a determination under section 85(1) as to the market in which it is examining the price, then that becomes "the relevant market" under section 85(1)(a) and (b). In this case, the Board has decided to examine the price of Procysbi in the national market and that is therefore the relevant market for the purposes of section 85(1)(b) of the Act. Cystagon is sold in that relevant market, albeit through the SAP.

(c) Procysbi is a Moderate Improvement Over Cystagon

146. As described above, HDAP concluded, on the primary factors, that Procysbi offered no/slight improvement over Cystagon and, on the secondary factors, that Procysbi offered a moderate improvement over Cystagon. This Panel is not bound by the findings and conclusions of HDAP. Rather, this Panel has considered the evidence adduced by the Parties and has come to its own determination of the level of therapeutic improvement of Procysbi.[41]

147. The Respondent's position, in brief, is that the pharmacokinetics of Procysbi results in reduced dosing which leads to improved adherence which leads to improved kidney function. The Respondent submits that Procysbi is a breakthrough drug, or at least a substantial improvement over Cystagon.

148. The Panel disagrees with the Respondent's categorization of Procysbi. Procysbi cannot be a "breakthrough drug" because it is not the first drug to be sold in Canada that effectively treats nephropathic cystinosis. As explained above, the Panel considers Cystagon to have been "sold" in Canada, despite the fact that it is only available through

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41 Board Decision - *Hoechst Maron Roussel Canada Inc. and the medicine "Nicoderm" (PMPRB-99-D9-Nicoderm - Motion for Particulars and Production)* (16 December 2008), online: PMPRB <http://www.pmprb-cepmb.gc.ca/CMFiles/Hearings%20and%20Decisions/Decisions%20and%20Orders/MotionforParticulars_and_Production-Dec16_0841LEV-12192008-4824.pdf> at para 10.

the SAP. In addition, as explained further below, the evidence does not establish that Procysbi offers a substantial improvement over Cystagon.

149. Board Staff submits that Procysbi and Cystagon are the same medicine, or in the alternative, that Procysbi only offers a modest improvement over Cystagon (*i.e.*, less than a moderate improvement, but more than slight/no improvement). The Panel disagrees. For the reasons already set out above, Procysbi and Cystagon are not the same medicine. Further, it is not necessary to deviate from the Guidelines and establish a whole new therapeutic category because, as explained further below, the Panel is satisfied that Procysbi offers a moderate improvement over Cystagon.

150. The Panel was provided with a significant volume of evidence regarding the level of therapeutic improvement offered by Procysbi. The Panel has considered the expert evidence, literature and studies thoroughly. While the Panel will not reproduce this evidence in detail in this decision, the following paragraphs summarize the key evidence and findings that are salient to the Panel's determination of the level of therapeutic improvement of Procysbi.

(A) Therapeutic Effect

151. The therapeutic effect of cysteamine is primarily assessed by WBC cystine levels. It is likely that lower WBC cystine levels are better for long term outcomes in cystinosis, including preventing renal functional decline and kidney failure.

152. Dr. Midgley testified that Procysbi and Cystagon are both very effective at depleting WBC cystine, generally on a milligram-to-milligram basis and that he has observed that WBC cystine levels in patients have been similar before and after a change from Cystagon to Procysbi.

153. Dr. Langman testified that he has been better able to control WBC cystine levels with Procysbi as compared to Cystagon. Dr. Langman directed the Panel to the study of the clinical effects of Procysbi on 41 patients in RP-103-03, and 40 patients in RP-103-

04, which demonstrated, over two years, that Procysbi was able to maintain the WBC cystine biomarker in an ideal range.

154. The Panel accepts that RP-103-03 and RP-103-04 demonstrated that Procysbi was able to maintain the WBC cystine biomarker in an ideal range. However, given that RP-103-03 was designed as a non-inferiority study, it does not establish that Procysbi is better able to deplete WBC cystine, or control WBC cystine levels, than Cystagon.

155. The literature predicts that Procysbi's delayed release formulation may encourage better adherence, and therefore enable Procysbi patients to better control their WBC cystine levels than Cystagon patients. For example, a review paper by Cassiman et al. (2016), concluded that it is highly likely that Procysbi's 12-hour dosing schedule promotes better compliance than Cystagon, and therefore could result in more sustained low WBC cystine levels. Similarly, an article by Levtchenko (2006) concluded that departing from a strict dosing regimen can lead to ineffectiveness of treatment because of the accumulation of WBC cystine in the cells. However, as Dr. Midgley explained, this paper concluded that although Cystagon patients who skipped their nighttime dose had higher WBC cystine levels, their WBC cystine levels remained, on average, around 0.73 nmol cystine/mg protein—well below the recommended threshold of 1 nmol cystine/mg protein (which is often cited as the target level for effective treatment).

(B) Clinical Outcomes

156. Clinical outcomes of cystinosis include the onset of end stage kidney disease requiring dialysis or a kidney transplant, and the onset of other significant organ dysfunction such as pancreatic insufficiency, hypothyroidism, muscle weakness or hypogonadism (in males).

157. In Dr. Midgley's opinion, the clinical outcomes for Cystagon and Procysbi patients are not different. He also testified that there is no data to suggest that patients on Procysbi will never need a kidney transplant. Dr. Midgley explained that we don't have data yet regarding the important outcomes, such as end-stage renal disease, the

development of hypothyroidism, diabetes, and myopathy, because these are very long-term outcomes, and Procysbi has not been in use long enough to assess those long-term outcomes. While Dr. Midgley recognized that increased adherence from an every 12-hour dosing regimen theoretically may result in a meaningful difference in clinical outcomes, he maintained that this would only become apparent in the next 10 to 15 (or more) years. Therefore, Dr. Midgley testified that he would not advise cystinosis patients or their families that Procysbi offered a definite advantage over Cystagon in terms of clinical outcomes.

158. In Dr. Langman's opinion, Procysbi is the first drug that shows potential for substantially delaying or avoiding a cystinosis patient's need for dialysis or kidney transplant. In his practice, Dr. Langman has seen clinical success with Procysbi in an overwhelming majority of his patients whereas, with Cystagon, his patients devolved to end stage renal failure and transplantation. Since Dr. Langman started treating patients with Procysbi in 2013, none have required a kidney transplant.

159. Moreover, Dr. Langman suggests that while we do not yet have long term data on clinical outcomes, recent data shows that Procysbi was able to maintain kidney function over at least 18 months. The Vaisbich poster (which was accepted for presentation at the 2018 American Society of Nephrology Annual Meeting) reported on the results of RP-103-08, and presented initial data for patients with nephropathic cystinosis who were treatment-naïve and started on Procysbi. Unlike all other data, which shows a general trend of decline in kidney function, this data showed normal kidney maturation and maintenance of physical growth in 80% of patients taking Procysbi over the first 18 months of the study. The poster reported that it cannot conclude that Procysbi was solely responsible for the improvements in health, however, it provides optimism for maintenance of good kidney function over the long term.

160. In Dr. Langman's opinion, simply because we do not have a crystal ball which allows us to quantitatively assess the full impact of Procysbi over a patient's lifespan does not mean that we should dismiss the benefits that have already been demonstrated, or the scientific rationale that suggests that Procysbi will, in time,

demonstrate significant clinical benefits for patients over their lives (including by increasing longevity and quality of life).

(C) Adherence

161. Dr. Langman testified that Procysbi is a significant improvement over Cystagon in terms of patient adherence. He explained that the twice-daily dosing improves patient adherence because it limits the negative side-effects associated with cysteamine (such as halitosis) and allows patients and their caregivers to sleep through the night. This improved patient adherence likely leads to improved therapeutic efficacy because strict adherence to the dosing schedule is required in order to prevent nocturnal cystine accumulation and thereby prevent the inevitable consequences of the disease.

162. Dr. Midgley accepts that it is generally recognized that adherence to long-term medication is difficult and that medications that require less frequent dosing during a day to achieve a desired effect are preferred because of improved adherence to the regimen. However, he notes that there are no direct, comparative studies on adherence differences between Cystagon and Procysbi and he believes that it is too soon to know if Procysbi's theoretical improvement in adherence will lead to better clinical outcomes.

(D) Administration

163. Dr. Midgley recognizes that a benefit reported by patients is that Procysbi is only taken twice per day. However, Dr. Midgley cites several disadvantages associated with the administration of Procysbi, including: (i) the pill burden; and (ii) the requirement to take Procysbi on an empty stomach and space it in time from food and bicarbonate or carbonate containing medications.

164. Dr. Langman submits that Procysbi's twice-daily dosing offers a significant improvement over Cystagon in terms of administration. Dr. Langman notes that Dr. Midgley's concerns regarding the pill burden and administration requirements do not accord with his understanding of his patients' experience. Moreover, Dr. Langman notes that there is no suggestion in the literature or the clinical studies that the pill burden or process of administration associated with Procysbi causes adherence, efficacy, or

quality of life issues for patients. Indeed, at the end of RP-103-03, all but one patient opted to remain on Procysbi, which suggests that the pill burden is not a significant hurdle to treatment.

165. In addition to the 12-hour dosing regimen, Dr. Langman notes that RP-103-03 found that Procysbi is also effective at doses that are generally 20-30% lower than Cystagon. Dr. Midgley disagrees with this assertion, noting that it is inconsistent with the product monograph and his own experience in that, of the four patients at Alberta Children's Hospital that have switched from Cystagon to Procysbi, the dose in mg/day has not been decreased (except in one patient after a recent kidney transplant).

(E) Quality of Life

166. Dr. Langman submits that Procysbi offers significant improvements in patients' quality of life. In support of this conclusion, Dr. Langman notes that: (i) 40 of the 41 patients (97.6%) in the crossover study (RP-103-03) elected to participate in the extension study (RP-103-04) and remain on Procysbi when given the choice; (ii) the PedsQL model itself demonstrated statistically significant improvements in quality of life when patients switched from Cystagon to Procysbi; (iii) in the RP-103-04 extension study, investigators were able to take even the most-controlled Cystagon patients and generate a statistically significant increase in quality of life (school function, social function, total function) and maintain those levels for the two-year duration of the study; and (iv) Procysbi's 12-hour dosing schedule allows patients and caregivers to sleep through the night, and there is evidence to support a relationship between sleep quality and cognitive performance, behavior, and quality of life.

167. Although Dr. Midgley testified that he was not satisfied that Dr. Langman had, in fact, established an improvement in the quality of life of Procysbi patients over a two-year period, he did agree that the paper by Langman et al (2014) reported that the increased quality of life noted in the initial RP-103-03 trial was maintained in patients treated for two-years with Procysbi.

(F) Adverse Events

168. Halitosis (bad breath), body odour and gastrointestinal ("**GI**") symptoms (including vomiting, anorexia, diarrhea, nausea and abdominal pain/discomfort) are among the most common adverse events associated with treatment using cysteamine. Dr. Midgley's view is that there does not appear to be a substantial difference in adverse events between Procysbi and Cystagon. Dr. Langman, by contrast, believes that Procysbi is associated with a reduction in adverse events.

169. ***Halitosis and Body Odour.*** Dr. Midgley testified that while some patients believe that there has been an improvement, there is very little evidence overall on the incidence of halitosis and body odour with Procysbi and insufficient evidence to conclude that halitosis and body odour are reduced for Procysbi patients compared to Cystagon patients.

170. Dr. Langman's view is that Procysbi eliminates or significantly diminishes halitosis and the "rotten egg" gas associated with the elevated peak serum concentration ("**Cmax**") of Cystagon. Dr. Langman testified that the halitosis and body odour experienced by cystinosis patients appears to be related to the fact that cysteamine eventually metabolizes into a volatile sulphur compound called dimethyl sulphide ("**DMS**"). The highest concentrations of this compound (and therefore, the worst halitosis and body odour side effects) occur at the drug's Cmax. With 6-hour dosing (as required by Cystagon), patients have four separate peak serum concentrations within the day at which these side effects will be more pronounced. Procysbi's slower rate of absorption, delayed Cmax, and overall fewer Cmax peaks are in his view the likely cause of the reduced body odour and halitosis experienced with Procysbi.

171. Dr. Langman referred to literature that supports his view that halitosis and body odour are improved for Procysbi patients. For example: (i) Greenbaum et al. (2017) showed that patients taking Procysbi had a 26% reduction in exhaled DMS as compared to patients taking Cystagon; and (ii) a 2012 poster presentation prepared by

Dr. Langman, reported a statistically significant ($p<0.05$) reduction in DMS in patients taking Procysbi compared to Cystagon.

172. Board Staff takes issue with Dr. Langman's reliance on the 2012 poster as it is not peer-reviewed, and because on cross-examination, Dr. Langman conceded: (i) Besouw (2012) dealt with the exact same subset of four patients from the RP-103-03 trial who were the subject of Dr. Langman's 2012 poster, and concluded that the difference in DMS area under the curve did not reach statistical significance in this small cohort; (ii) the same subset of four patients was also the subject of Veys (2016), who observed that the measured DMS values remained above the threshold levels that cause halitosis; and (iii) in 2020, Dr. Langman co-authored an article with Kasimer (which he did not cite in any of his expert reports), that references the same subset of four patients and notes that while the breath of patients on Procysbi had less DMS, the difference was not statistically significant.

173. ***GI Symptoms.*** Dr. Midgley testified that patients generally seem to tolerate either preparation of cysteamine similarly. By contrast, Dr. Langman testified that Procysbi is associated with a reduction in GI adverse events. Dr. Langman explained that immediate absorption of large concentrations of Cystagon in the stomach is associated with increased nausea and other GI adverse events. He suggests that because Procysbi is a delayed release formulation that bypasses the stomach and is absorbed over a longer time period, it is associated with a lower incidence of GI-related adverse events.

174. Some Procysbi patients in the RP-103-03 clinical trial experienced GI side-effects, however, the investigators posited that this may have resulted from the reduction in PPI use during this study. Further, Dr. Langman testified that these GI side-effects could have been caused by a carry-over effect of prior Cystagon treatment. However, in cross-examination, Dr. Langman admitted that the results from the RP-103-08 clinical trial also established that the same GI disorders were experienced by children who were previously naïve to treatment and were then placed on Procysbi.

175. Finally, during the cross-examination of Dr. Langman, Board Staff attempted to introduce into evidence certain findings related to GI adverse effects from RP-103-07. The Respondent objected to questions about RP-103-07 being put to Dr. Langman because Dr. Langman testified that he had never seen the RP-103-07 report, and therefore the rule in *R v Marquard*[42] precluded Board Staff from questioning Dr. Langman on the study.

176. Board Staff submits that the Panel is entitled to consider the results from RP-103-07 because it was referenced in the literature review appended to Dr. Midgley's responding expert report, and referenced at paragraph 73 of Dr. Langman's reply expert report where he states: "There is no need to do a further cross-over or parallel trial in view of RP-103-03, RP-103-04 and the further extension studies RP-103-07 and 08".

177. In light of Dr. Langman's express reliance on RP-103-07 in his expert report, the Panel permitted Board Staff to question Dr. Langman on the study and held that it would consider the weight of the evidence after hearing Dr. Langman's testimony on the issue. Ultimately, the Panel ascribes little weight to RP-103-07 because it was clear from Dr. Langman's examination that he had not reviewed the report (which was thousands of pages in length) and therefore could not credibly comment on it, and no other witness was called to speak to the substance or import of the report.

(G) Proton Pump Inhibitor ("**PPI**") Use

178. Dr. Langman testified that treatment with PPIs has been shown to control the GI side effects arising from Cystagon. However, because PPI use is associated with increased bone fractures and kidney issues in adults, it is generally recommended that PPI use and duration be minimized as much as possible.

179. Dr. Langman testified that in his experience, PPI usage for Procysbi patients is not required to the same extent that it is required for Cystagon patients. Accordingly,

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[42] *R v Marquard*, [1993] 4 SCR 223.

Procysbi allows patients with already compromised kidney function to avoid PPIs, and therefore the undesirable side effects associated with PPI use.

180. Dr. Midgley testified that available evidence does not support that PPI use can be reduced with Procysbi compared to Cystagon without a consequent increase in GI adverse events. Contrary to Dr. Langman's assertion that patients taking Procysbi generally do not take a PPI, Dr. Midgley notes that of the 12 patients taking Procysbi that are seen in the Calgary Cystinosis Clinic, 50% of them are taking a PPI, whereas of the nine patients taking Cystagon, only 22% are taking a PPI.

181. Moreover, the experts disagree over the conclusions that can be drawn from the RP-103 studies with respect to PPI use. Dr. Langman testified that the investigators saw an 87% reduction in PPI use in the Procysbi arm of the RP-103-03 study. Dr. Langman also noted that only five out of eighteen patients in the initial Cystagon arm resumed use of PPIs. Dr. Langman thought that the fact that some patients went back on PPIs suggested that some of the GI effects from the Cystagon arm continued even after the drug had been switched. In cross-examination, Dr. Langman admitted that the results from the RP-103-08 clinical trial established that the same GI disorders were experienced by children who were previously naïve to treatment and were then placed on Procysbi, which calls into question Dr. Langman's theory that the GI upsets were a runoff effect from treatment with Cystagon.

182. Dr. Midgley testified that the rate of PPI use during RP-103-03 does not support Dr. Langman's conclusion that Procysbi patients generally do not take a PPI. The trial protocol specifically indicated that patients on the Procysbi arm could only use PPIs in cases of intolerable gastric upset at the discretion of the investigator. Also, although PPI use during the Procysbi arm of the cross-over trial decreased, the incidence of adverse GI effects significantly increased. Dr. Midgley concluded that, while it is true that patients on Procysbi can reduce PPI use, this may result in increased adverse effects (which PPI use is intended to control). Dr. Midgley also noted that during the RP-103-08 trial, 89% of the Procysbi patients had GI issues, and 80% experienced vomiting.

(H) Conclusion on Level of Therapeutic Improvement

183. The Panel recognizes that in the case of an ultra-rare orphan drug like Procysbi, there is a small patient population to participate in clinical trials, which results in a paucity of Level 1 evidence. This problem is exacerbated in this case by the fact that (i) clinical outcomes such as end-stage renal disease are very long-term outcomes, and Procysbi has not been in use long enough to definitively confirm whether these long-term clinical outcomes are improved for Procysbi patients, and (ii) blinded, long-term, head-to-head comparative studies between Cystagon and Procysbi related to therapeutic efficacy would be very difficult to complete given the dosing regimen of each medicine. Accordingly, this Panel has not limited itself to considering only Level 1 evidence. This Panel has considered all sources and levels of evidence presented by the Parties, and has made its decision on the level of therapeutic improvement of Procysbi based on the inferences it can fairly draw from the evidence as a whole.

184. Viewing the evidence as a whole, and in the context of Procysbi being a recently available ultra-orphan drug, the Panel has concluded that Procysbi offers a moderate improvement over Cystagon, and that improvement for the most part stems from its dosing regimen. The ability to sleep through the night for both the patient and caregiver is a considerable benefit offered by Procysbi that should not be underemphasized. In particular the Panel was persuaded by the evidence of (i) increased quality of life, (ii) that medications that require less dosing during a day are preferred because of improved adherence coupled with evidence of a high likelihood that Procysbi's dosing schedule promotes better compliance than Cystagon and (iii) the positive data from RP-103-08 showing that Procysbi was able to maintain kidney function, not seen in studies of Cystagon. While the therapeutic improvement offered by Procysbi appears to be promising, there is insufficient evidence at this stage to satisfy the Panel that Procysbi is more than a moderate improvement over Cystagon.

(d) Applicable Pricing Test for Procysbi

185. The Respondent submits that the applicable test is the MIPC test under the Guidelines and that Procysbi is in compliance with that test. The accuracy of this

submission depends on the Panel accepting the Respondent's position that (i) Procysbi's level of therapeutic improvement was "breakthrough", or at least a "substantial improvement" over Cystagon, and (ii) there is no domestic comparator sold in a relevant market. The Panel has rejected both submissions. The MIPC Test is not applicable to Procysbi because Cystagon is a therapeutic comparator sold in the relevant market within the meaning of section 85(1)(b) of the Act, and Procysbi's level of therapeutic improvement over Cystagon is only moderate.

186. For the reasons already discussed, Board Staff submits that the Panel should deviate from the Guidelines and use one of its three pricing models, even if Procysbi is found to provide a moderate improvement over Cystagon. The Respondent objects to all three of Board Staff's pricing models. The Respondent submits that they are not economically rational and would curtail development, they are inconsistent with the Board's mandate to encourage innovation because each of the Proposed Prices would not allow Horizon to recover its costs or earn a return, and they are novel, arbitrary and not justified, adopted or endorsed by any of Board Staff's experts.

187. The Panel has concluded that it is not appropriate to implement any of Board Staff's three proposed pricing models, for the following reasons.

188. First, there is no justification to depart from the applicable test in the Guidelines, the application of which appropriately implements the section 85(1) factors in this case. The Panel has concluded that Procysbi is a moderate improvement over Cystagon and that it is appropriate to apply the Moderate Improvement Test prescribed by the Guidelines. As described further below, the Panel concludes that as long as the median international price of Cystagon (rather than the Newfoundland Formulary price) is used for the TCC test, the Panel is satisfied that the Moderate Improvement Test prescribed by the Guidelines appropriately operationalizes the section 85(1) factors and fulfils the Board's mandate.

189. Second, and in any event, the application of any of Board Staff's proposed pricing models would not appropriately implement the Act in the circumstances of this case:

(a) ***Same Medicine Test*****.** This test is not appropriate given that, for the reasons set out above, Cystagon and Procysbi are not the same medicine.

(b) ***Market Share Comparison Test***. This test is not appropriate because it requires consideration of units and market share which go beyond the factors in section 85(1) of the Act. Moreover, this test is based on incomplete IQVIA data and does not accurately reflect the fact that Procysbi offers a moderate level of therapeutic improvement over its comparator.

(c) ***Premium Comparison Test*****.** This test is not appropriate because the suggested premium is arbitrary and, in any event, is intended to address the price of a "modest" improvement drug. For the reasons set out above, this Panel finds that there is no need for the introduction of a modest improvement category in the circumstances of this case.

190. Neither of Board Staff's experts endorsed or supported any of the proposed pricing models. In particular, Professor Schwindt expressly stated he was not endorsing or proposing any of them, even though he was retained to give an opinion from an economic perspective on an appropriate method to determine whether the price of Procysbi is excessive.

191. Lastly, during the cross-examination of Mr. Kellison, it became clear that Board Staff reverse-engineered the three new pricing models to generate results that would reduce the price of Procysbi by a greater order of magnitude than the reduction prescribed by Guidelines. The Panel does not accept that this is a principled approach that properly implements the section 85(1) factors or one that is consistent with the

Board's mandate, which is to protect against excessive prices, not to engineer a lower price or engage in price regulation.[43]

(v) The Price of Procysbi is Excessive Under Section 85(1)

(a) Section 85(1)(a) – the prices at which the medicine has been sold in the relevant market

192. As described above, the medicine at issue is Procysbi. The Panel considers the relevant market to be Canada.

193. What are the relevant prices is clear from the Act and the Regulations.

194. Section 80(1)(b) of the Act provides that patentees shall, as required by and in accordance with the Regulations, provide the Board with information respecting "the price at which the medicine is being or has been sold in any market in Canada and elsewhere." The purpose of this section of the Act is to provide the Board with the information necessary for it to fulfill its mandate.[44]

195. Section 101(1) of the Act provides that the Governor-in-Council may make regulations specifying the information to be provided to the Board under section 80(1)(b).

196. The Courts have interpreted sections 80(1)(b) and 101(1) of the Act to mean that any regulations which specify the information that must be provided by a patentee to the Board under section 80(1)(b) must relate to the sale of medicines by the patentee to its customers.[45] Consistent with this interpretation, section 4(1)(f)(i) of the Regulations, specifically requires patentees to indicate the price at which the medicine was "sold by the patentee…to each class of customer in each province and territory". In other words, the Regulations only require patentees to report the price at the initial point of sale by the patentee; commonly referred to as the "ex-factory" or "factory gate" price. Unless a

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43 *Alexion FCA*, *supra* note 14 at paras 49, 51.

44 *Merck*, *supra* note 96 at para 51.

45 *Innovative Medicines*, *supra* note 94 at paras 184-187.

party chooses to introduce additional pricing information into evidence, the Board has no further information regarding the patentee's pricing of a patented medicine beyond the ex-factory prices.

197. The corollary is that the Regulations do not require a patentee to report financial transactions, such as rebates and discounts, with third parties who are strangers to the original sale transaction (such as public drug plans or other insurers that reimburse consumers for the costs of the patented medicine). Rebates and discounts provided by patentees to third party insurers are unrelated to the price at which patented medicines are sold within the meaning of section 80(1)(b) of the Act.[46] Relatedly, both the Federal Court and the Quebec Court of Appeal have recently decided, albeit on different bases, that requiring patentees to report pricing unrelated to the factory gate prices is legally invalid, and that the Act and Regulations, as well as the constitutional restraints on federal jurisdiction, limit the Board's review to only the ex-factory prices of patented medicines.[47]

198. It is the information filed by a patentee under the Act that allows the Board to determine the first factor in the section 85(1) analysis, being the price at which the medicine has been sold by the patentee in the relevant market. Accordingly, for Procysbi, the relevant price is the N-ATP, which is calculated based on the factory gate prices as disclosed in Horizon's filings with the Board. Procysbi's introductory prices in Canada are set out in the following table:

Strength	**Price / Capsule (CAD)**	**Price / MG (CAD)**	**Max Dosage Regimen Per Day**	**Cost Per Day (CAD)**	**Cost Per Year (CAD)**
25 mg/capsule	$10.3500	$0.4140	60 Capsules	$621.00	$226,665.00
75 mg/capsule	$31.0500	$0.4140	20 Capsules	$621.00	$226,665.00

46 *Innovative Medicines*, *supra* note 94 at paras 53, 205.

47 See *Pfizer Canada Inc v Canada (Attorney General)*, 2009 FC 719; *Innovative Medicines*, *supra* note 94 at paras 53, 215-217; *Merck*, *supra* note 96 at paras 197-199, 206.

(b) Section 85(1)(b) – the prices at which other medicines in the same therapeutic class have been sold in the relevant market

199. For the reasons set out above, the Panel finds that Cystagon and Procysbi are therapeutic comparators, and that Cystagon has been "sold" in the "relevant market" within the meaning of section 85(1)(b) of the Act. Accordingly, the Panel will consider the price of Cystagon in Canada under this subsection of the Act.

200. ***Newfoundland and Labrador*.** To determine the price of Cystagon, Board Staff selected a public price from the Newfoundland and Labrador provincial formulary (the "**Newfoundland Formulary**"). Board Staff submits that it is the only public price available in Canada. On the date that Procysbi was first sold in Canada (September 2017), the Newfoundland Formulary had a publicly listed price for the 150mg capsule of Cystagon, which is set out in the table below:

Strength	Price / Capsule (CAD)	Price / Mg (CAD)	Max Dosage Regimen Per Day	Cost Per Day (CAD)	Cost Per Year (CAD)
150 mg/capsule	$1.1481	$0.0077	10 Capsules	$11.4810	$4,190.565

201. Horizon submits that the Panel should not rely on the Newfoundland Formulary price because: (i) Mr. Kellison testified that, in selecting this price, Board Staff sought to find the lowest publicly available price; and (ii) when selecting a public price, Board Staff focused solely on whether a public list price existed, and was not concerned with whether there were patients for the drug, or whether the drug was sold at the publicly available list price. Dr. Hay testified that in the absence of evidence of any sales, it is inappropriate to rely on the Newfoundland Formulary price because it is not a true market price and therefore does not provide a reasonable benchmark for the price of Procysbi. In reply to this argument, Board Staff submits that the presence of Cystagon on the Newfoundland Formulary necessarily leads to the conclusion that Cystagon is available for sale in Newfoundland and Labrador.

202. The Panel agrees that the Newfoundland Formulary price represents a public price for Cystagon in Canada that the Panel may consider for the purposes of its

analysis under section 85(1)(b). However, the Panel concludes that little weight should be given to the Newfoundland Formulary price of Cystagon considering the lack of any evidence of actual sales in respect of Newfoundland patients at this price and the fact that higher prices appeared to be charged in British Columbia (as described below).

203. ***British Columbia*.** Ms. Rizzardo provided evidence regarding prices of Cystagon in British Columbia, which appear to be higher than the Newfoundland Formulary price. In particular, Ms. Rizzardo provided evidence regarding the prices of Cystagon that were pulled from "PharmaNet"—a province-wide data network administered by the BC Minister that keeps a record of every prescription dispensed in a British Columbia community pharmacy. As Ms. Rizzardo explained, the price of a drug in PharmaNet is updated each time the price is changed by the manufacturer.

204. Ms. Rizzardo testified that when Procysbi received marketing authorization in Canada (June 13, 2017), the price of Cystagon listed on PharmaNet was as follows:

Strength	**Price / Capsule (CAD)**	**Price / Mg (CAD)**	**Max Dosage Regimen Per Day**	**Cost Per Day (CAD)**	**Cost Per Year (CAD)**
50 mg/capsule	$0.79	$0.0158	-	-	-
150 mg/capsule	$1.83	$0.0122	10 Capsules	$18.30	$6,679.50

205. Ms. Rizzardo testified that, a year later, in July 2018, the price of Cystagon listed on PharmaNet was as follows:

Strength	**Price / Capsule (CAD)**	**Price / Mg (CAD)**	**Max Dosage Regimen Per Day**	**Cost Per Day (CAD)**	**Cost Per Year (CAD)**
50 mg/capsule	$1.93	$0.0386	-	-	-
150 mg/capsule	$5.79	$0.0386	10 Capsules	$57.90	$21,133.50

206. In addition to the PharmaNet prices, Ms. Rizzardo testified to a wide range of costs for Cystagon in British Columbia, which varied from $12,000 per year for an adult

patient before Procysbi entered the Canadian market, to approximately $18,259 per year for a pediatric patient and $30,714 per year for an adult patient, after Procysbi entered the Canadian market.

207. In addition, Ms. Rizzardo referred to emails sent to the British Columbia Minister of Health, reporting that the price for Cystagon ranged from $40,000 to $45,000.

208. The Panel accepts that the PharmaNet prices for Cystagon in British Columbia at the time that Procysbi entered the Canadian market are prices that the Panel may consider for the purposes of its analysis under section 85(1)(b). However, the Panel finds these prices to be of little assistance to its analysis under section 85(1) given the wide range of prices referenced by Ms. Rizzuto in her evidence, and the lack of clarity regarding the reason for the discrepancy of the per milligram price of Cystagon between the 50 mg and 150 mg capsules in 2017.

209. Finally, Horizon submits that there is evidence before the Panel that the manufacturer of Cystagon was considering applying to Health Canada for marketing approval, and that it intended to sell Cystagon at a price up to one-third that of Procysbi. However, the evidence referenced by Horizon is a letter from the Canadian Association of Paediatric Nephrologists, not the manufacturer of Cystagon. There is nothing in the record that establishes that the manufacturer of Cystagon has taken steps to apply to Health Canada for marketing approval at that price and it is not a price at which Cystagon is now being sold in Canada. Accordingly, the Panel gives this evidence no weight.

210. ***Other Provinces*****.** The Panel received evidence regarding the total costs for Procysbi and Cystagon patients in Ontario in 2019 plus the number of patients who received each medicine. However, these figures do not allow the Panel to determine the price at which Cystagon was sold, including because there is a potential overlap in patients who received Procysbi and Cystagon. The Panel also received evidence from Dr. Midgley which confirms that there are cystinosis patients in Alberta, however, neither party introduced evidence regarding the price of Cystagon in Alberta.

211. Board Staff conceded that if the Panel is questioning the Canadian prices for Cystagon, it is free to consider the international prices of Cystagon in the PMPRB7 under section 85(1)(c). The Panel agrees. Ultimately, the Panel finds the Canadian prices of Cystagon to be unreliable for the reasons expressed above and therefore has given them little weight. The Panel places greater weight on the international prices under section 85(1)(c), as described further below.

(c) Section 85(1)(c) – the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada

212. Under section 85(1)(c), the Panel must consider the price at which Cystagon and Procysbi have been sold in countries other than Canada. The relevant countries are set out in the Regulations as the PMPRB7.

213. The Panel recognizes that, in performing the comparison required under section 85(1)(c), it is limited to comparing the ex-factory price of Procysbi in Canada as filed by Horizon in accordance with the Regulations, with the publicly available ex-factory prices in the comparator countries.

214. ***Procysbi*.** The ex-factory international prices for Procysbi (25mg) are set out in the table below:

Country	**Price / Mg in Domestic Currency**	**Price / Mg (CAD$ as at Apr 2017)**	**Price / Mg (CAD$ as at Dec 2017)**	**Price / Mg (CAD$ as at Jun 2018)**
France	No price filed	-	-	-
Germany	0.2902 (EURO)	$0.4179	$0.4207	$0.4289
Italy	No price filed	-	-	-
Sweden	No price filed	-	-	-
Switzerland	No price filed	-	-	-
United Kingdom	0.2240 (GBP)	$0.4115	$0.4049	$0.4003
United States	3.3402 (USD)	$4.2136	$4.3449	$4.3687

215. The ex-factory international prices for Procysbi (75mg) are set out in the table below:

Country	Price / Mg in Domestic Currency	Price / Mg (CAD$ as at Apr 2017)	Price / Mg (CAD$ as at Dec 2017)	Price / Mg (CAD$ as at Jun 2018)
France	No price filed	-	-	
Germany	0.2902 (EURO)	$0.4179	$0.4207	$0.4289
Italy	No price filed	-	-	
Sweden	No price filed	-	-	
Switzerland	No price filed	-	-	
United Kingdom	0.2240 (GBP)	$0.4115	$0.4049	$0.4003
United States	1.1134 (USD)	$1.4045	$1.4483	$1.4562

216. Board Staff questions the appropriateness of relying on the international prices of Procysbi for several reasons, including because: (i) there is only evidence of the price of Procysbi in three countries; (ii) one of those countries – Germany – has a regime that supports high prices for rare disease drugs because they are presumed to have an additional therapeutic benefit upon receipt of market authorization so long as total annual health insurance expenditures remain below €50 million; (iii) another one of those countries – the U.S. – can set the price of a drug regardless of therapeutic benefit; and (iv) Cystagon is available in each of these markets and so buyers may be less sensitive to Procysbi's price.

217. The Respondent disagrees. Dr. Hay's evidence is that the price of Procysbi in other countries is probative evidence on the extent of differentiation between Cystagon and Procysbi because Procysbi is sold in countries where Cystagon has been sold for years, and the fact that Procysbi is priced at a substantial premium to Cystagon where both medicines are sold supports the view that Procysbi is of a higher quality than Cystagon. Moreover, the Respondent submits that the Canadian price of Procysbi is one of the lower ones and that this is deserving of weight.

218. The Panel agrees with the Respondent that it is appropriate to give weight to the international prices of Procysbi. The fact that Procybi is sold in only 3 of the PMPRB7 countries does not affect the reliability of the 3 prices that are available. Further, Board Staff's argument that because Cystagon is available where Procysbi is sold means that buyers may be less sensitive to Procysbi's price is based on a comment made by Professior Schwindt in his oral testimony, without any supporting analysis, and is speculative at best. Lastly, the Panel notes that Board Staff offered no specific criticism of the UK price.

219. ***Cystagon*.** The publicly available ex-factory international prices for Cystagon (150mg) are set out in the table below:

Country	**Price / Mg in Domestic Currency**	**Price / Mg (CAD$ as at Apr 2017)**	**Price / Mg (CAD$ as at Dec 2017)**
France	0.0129 (EURO)	$0.0186	$0.0187
Germany	0.0177 (EURO)	$0.0255	$0.0257
Italy	0.0093 (EURO)	$0.0134	$0.0135
Sweden	0.1356 (SEK)	$0.0208	$0.0207
Switzerland	-	-	-
United Kingdom	0.0127 (GBP)	$0.0233	$0.0230
United States	0.0080 (USD)	$0.0101	$0.0104

220. The publicly available ex-factory international prices for Cystagon (50mg) are set out in the table below:

Country	**Price / Mg in Domestic Currency**	**Price / Mg (CAD$ as at Apr 2017)**	**Price / Mg (CAD$ as at Dec 2017)**
France	0.0138 (EURO)	$0.0199	$0.0200
Germany	0.0225 (EURO)	$0.0324	$0.0326
Italy	0.0095 (EURO)	$0.0137	$0.0138
Sweden	0.1360 (SEK)	$0.0209	$0.0208

Switzerland	-	-	-
United Kingdom	0.0140 (GBP)	$0.0257	$0.0253
United States	0.0082 (USD)	$0.0103	$0.0107

221. Neither party took issue with the reliability of the international prices of Cystagon as represented in the above tables.

222. Considering (i) the issues noted above with the evidence of the Canadian prices for Cystagon and (ii) the evidence of the international prices of Cystagon and the lack of any objection to them, the Panel finds that the international prices are more reliable and therefore more appropriate to be used for purposes of the TCC Test.

(d) Section 85(1)(d) – changes in the Consumer Price Index

223. The Parties agree that changes in the Consumer Price Index or "**CPI**" are not applicable in this case, as the issue is solely the introductory price of Procysbi.

(e) Section 85(1)(e) – such other factors as may be specified by the Regulations

224. There are no such other factors.

(f) The Costs of Making and Marketing, Research and Development, and Commercialization Are Not Relevant to the Section 85(1) Analysis

225. The Panel does not accept the Respondent's submission that the Board's mandate requires it to consider, in the section 85(1) analysis, the overall economic and clinical context that informed the development of Procysbi, including the cost of making and marketing it. To do so would disregard the plain wording of the Act.

226. As already explained above, section 85(1) of the Act sets out the factors that the Board must consider in determining whether the price of a medicine sold in a Canadian market is excessive. They do not include consideration of the costs of research, development, making, marketing or commercialization of the medicine. Rather, these

matters are solely to be considered in a panel's discretion under an analysis conducted under section 85(2) of the Act.

227. The Respondent submits that this Panel can make a determination based on the section 85(1) factors but, at the same time, submits that in deciding this case under section 85(1), the Panel must consider costs related to making and marketing Procysbi. The Panel does not accept this submission. It is only if the Board is unable to determine whether the price of the medicine is excessive *after* having considered the section 85(1) factors that the Board *may* consider the costs of making and marketing the medicine or any other factors that the Board deems relevant.[48]

228. The Respondent further submits that section 85(3) is a standalone provision, pursuant to which the Panel can consider research and development and commercialization costs in its excessiveness inquiry under section 85(1). The Panel does not accept this submission as it is contrary to the express wording of the Act. Section 85(1) does not permit the Panel to consider any factors in addition to those listed in sections 85(1)(a) through (e) of the Act. Section 85(1)(e) of the Act contemplates that additional factors may be specified in regulations made for the purposes of this subsection, however, no such additional factors have been specified by the regulations to date. The Respondent ignores this fact, and instead asks the Panel to simply read section 85(3) as an additional factor to consider under section 85(1), despite the fact that there is no provision of the Act that permits it to do so.

229. Moreover, section 85(3) is expressed in the negative. It states: "… the Board shall <u>not</u> take into consideration research costs other than the Canadian portion of the world costs related to the research that led to the invention pertaining to that medicine or to the development and commercialization of that invention…" [emphasis added].

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[48] *Alexion FCA*, *supra* note 14 at paras 46-47; Board Decision – *ratiopharm Inc. and the medicine "ratio-Salbutamol HFA"* (May 27, 2011) at paras 56, 86, online: PMPRB <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=866>; Board Decision – *ICN Canada Ltd. and ICN Pharmaceuticals Inc.* (July 26, 1996) at pp. 8, 11, online: PMPRB <http://www.pmprb-cepmb.gc.ca/CMFiles/Hearings%20and%20Decisions/Decisions%20and%20Orders/db-95d5v-e14LGJ-492003-8710.pdf>; *ICN Pharmaceuticals Inc v Canada (Patented Medicine Prices Review Board)*, [1996] FCJ No 1112 at paras 3, 8.

The only way section 85(3) would be applicable to section 85(1) is if research and development costs were listed as a factor in section 85(1) and they are not.

230. Research costs are a component of making and marketing a medicine under section 85(2) of the Act. As such, section 85(3) modifies section 85(2), not section 85(1). It is only in the limited circumstances where the Panel cannot make a determination under section 85(1) and exercises its discretion to consider the cost of making and marketing a medicine under section 85(2) that the Panel may consider a patentee's claim for research and development costs within the constraints required by section 85(3).

231. The Respondent argues that the Canadian price for Procysbi simply cannot be excessive because it is one of the lowest prices of Procysbi in the world and it does not enable Horizon to cover its costs of capital. Even if it is true that the Canadian price is one of the lowest and even if it is true that the price does not allow Horizon to cover its costs of capital, those are not relevant factors under section 85(1). In short, section 85(1) does not permit the Panel to engage in a cost or profit-based analysis to determine "excessiveness" – such analysis is not provided for in section 85(1)(a) through (e).

232. The Respondent further suggests that the Board cannot use its mandate to impose prices that "deprive" consumers of innovative drugs, and that the Board must consider the practical consequences of any reduction in the price of a medicine. Specifically, the Respondent submits that the Board must consider whether the price reductions would impair commercialization of and access to innovative medicines for Canadians. The Panel disagrees. Whether consumers may be "deprived" of drugs is speculative and beyond the scope of the Panel's role in the section 85(1) analysis which is to determine if a medicine is being sold at an excessive price. In any event, the Panel notes that Horizon made a strategic decision to enter the Canadian market at a price that Horizon says would not enable it to recover its costs. This is inconsistent with the Respondent's submissions that patentees will not enter the Canadian market (or will

leave the Canadian market) if their costs for a particular drug are not being covered by the price of that drug in the country.

233. For all of these reasons, and the fact that the Panel is able to make a determination based on the section 85(1) factors, the Panel limits its analysis to the factors expressly listed in section 85(1) of the Act, and denies the Respondent's request to consider additional contextual factors.

(g) Analysis Under Section 85(1) of Act

234. This section of the decision contains the Panel's application of the section 85(1) factors in the context of the findings and conclusions already reached in this decision.

235. In summary, the Panel finds that the price of Procysbi is and was excessive for the purposes of sections 83 and 85(1) of the Act.

236. The Panel finds that the Moderate Improvement Test set out in the Guidelines appropriately operationalizes the section 85(1) factors consistent with the Board's mandate and there is no need to create a new test in the circumstances of this case. The Moderate Improvement Test involves an analysis of the TCC Test, the MIPC Test, and the midpoint between those two tests. The price of a moderate improvement drug is then constrained by the higher of the TCC Test and the midpoint between the TCC Test and the MIPC Test.

237. ***TCC Test.*** As already noted, the Panel finds that it is appropriate to rely on the international prices of Cystagon for the TCC Test. The median international price of Cystagon based on the ex-factory international prices for Cystagon (150 mg), using rolling exchange rates as of December 2017, is C$0.0197 / mg.[49]

238. ***MIPC Test.*** For the reasons set out above, the Panel finds that it is appropriate to have regard to the international prices of Procysbi. The median international price of

[49] Given that there is an even number of countries, the Guidelines prescribe that the median be calculated by taking the simple average of the two middle prices (being France and Sweden).

Procysbi based on the ex-factory prices of Procysbi (75mg), using month rolling exchange rates as of December 2017, is C$0.4207 / mg.

239. ***The Midpoint.*** The midpoint between the TCC Test and the MIPC Test is C$0.2202 / mg.

240. ***Conclusion.*** The Moderate Improvement Test provides that the price of Procysbi is constrained by the higher of the TCC Test (C$0.0197 / mg) and the midpoint (C$0.2202 / mg). Accordingly, the MAPP of Procysbi in Canada under the Moderate Improvement Test is **C$0.2202 / mg**.

241. Given that the introductory price of Procysbi in Canada is C$0.4140, Procysbi was and is being sold at a price that is excessive under the Act.

242. Given that the Panel has made a decision under section 85(1) of the Act, sections 85(2) and 85(3) of the Act are not relevant and no analysis will be conducted under these subsections.

(vi) The Economic and Accounting Evidence

243. As noted above, Board Staff submits that the evidence of Dr. Hay, and the responding evidence of Mr. Rosen, are relevant only to an analysis under section 85(2) of the Act. By contrast, the Respondent submits that Dr. Hay's evidence was tendered in response to Board Staff's Proposed Prices, which Board Staff put forward under section 85(1). Moreover, the Respondent submits that in light of the exceptional circumstances of this case, the Panel must consider this evidence under both sections 85(1) and 85(2) of the Act.

244. The evidence of Dr. Hay and Mr. Rosen focused on what costs associated with the research and development and making, marketing, and commercializing of Procysbi should be allocated to Canada and, as such, is not relevant to the section 85(1) analysis. This evidence may only be relevant to an analysis under section 85(2), which will not be undertaken in this case as the Panel has been able to make a determination

under section 85(1). It follows that it is not necessary for the Panel to resolve the many conflicts and issues raised by Dr Hay and Mr. Rosen's evidence.

245. The Parties spent considerable time and expense on the expert economic evidence provided by Dr. Hay and Mr. Rosen and a considerable part of the hearing was taken up by this evidence. Although, because of its decision, the Panel does not have to determine which expert's analysis was accepted or preferred, it will make a few comments about this evidence.

246. Even if this was one of the exceptional cases where the Panel could not make a determination under section 85(1) and found there were compelling reasons to exercise its discretion to determine the issue under section 85(2), the Panel's view is that there was no clear and reliable evidence in the record that would have allowed it to make a determination under section 85(2).[50]

247. The summary of the evidence of Dr. Hay and Mr. Rosen earlier in this decision refers to the numerous issues and disputes raised by their evidence. Considering this evidence as a whole, the Panel would have concluded that it did not have the clear and reliable evidence necessary to make a decision under section 85(2).

248. By way of example, after considering all of the evidence, the Panel concluded that it did not have clear and reliable evidence that the RAC was the correct starting point for allocating the costs to develop Procysbi to Canada. This is because, while both expert's analysis started from the RAC, there was no consensus as to what the RAC represents.

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[50] Board Decision – *ICN Canada Ltd. and ICN Pharmaceuticals Inc.* (26 July 1996) at pp. 11, 12, online: PMPRB <http://pmprb-cepmb.gc.ca/CMFiles/Hearings%20and%20Decisions/Decisions%20and%20Orders/db-95d5v-e14LGJ-492003-8710.pdf> application for stay of board decision dismissed *ICN Pharmaceuticals Inc v Canada (Patented Medicine Prices Review Board)*, [1996] FCJ No 1112 (FC); Board Decision –*Teva Neuroscience and the Medicine "Copaxone"* (25 February 2008) at para 48, online: PMPRB <http://www.pmprb-cepmb.gc.ca/CMFiles/Hearings%20and%20Decisions/Decisions%20and%20Orders/COPAXONE_Merits-Reasons_-_D2-_Feb_25_0838KCU-3102008-2953.pdf > set aside on other grounds in *Teva Neuroscience G.P.-S.E.N.C. v Canada (Attorney General)*, 2009 FC 1155.

(a) Mr. Rosen's evidence was that the RAC represented what Horizon was willing to pay based on expected future cash flows and not on the basis of costs already incurred, which appeared to be consistent with the evidence surrounding the acquisition of Raptor, including that of KPMG.

(b) Dr. Hay, on the other hand, indicated that the RAC actually represented the costs of developing Procysbi after accounting for the cost of capital. He also testified that whether one started with the RAC or the R&D Cost, the result would be the same, but did not provide a clear analysis to support this conclusion.

249. Another example arises from Dr. Hay's analysis relying on the appropriateness of applying a WACC rate. The evidence was not clear as to whether WACC was a relevant consideration in the context of allocating the RAC (including because of the dispute about what the RAC actually represents), but, even if it was, the Panel was not convinced that an analysis comparing a WACC rate with the IRR is all that helpful. If the WACC rate exceeds the IRR, a company may not be achieving the return it had planned or hoped for on an investment, but this is something different from profitability and the Panel did not receive clear evidence regarding the relationship, if any, between the two.

250. A third example relates to Mr. Rosen's analysis of the RAC based on revenue (in contrast to Dr. Hay's analysis based on units). The reliability of this analysis was undermined by the fact that it was based on revenues from Horizon's entire drug portfolio (and not just Procysbi) and did not analyze Canadian revenue compared to global revenue. Whether Mr. Rosen had or did not have the information to perform the correct analysis is beside the point. The Panel was left with an analysis based on revenue that was not clear and reliable.

J. Order re Excessive Prices

251. Sections 83(1) and (2) of the Act provide:

> 83 (1) If the Board finds that a rights holder for 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, the Board may, by order, direct the rights holder to cause the maximum price at which the rights holder sells the medicine in that market to be reduced to the level that the Board considers not to be excessive and that is specified in the order.
>
> (2) Subject to subsection (4), if the Board finds that a rights holder for an invention pertaining to a medicine has, while a rights holder, sold the medicine in any market in Canada at a price that, in the Board's opinion, was excessive, the Board may, by order, direct the rights holder to do any one or more of the following things that will, in the Board's opinion, offset the amount of the excess revenues estimated by it to have been derived by the rights holder from the sale of the medicine at an excessive price:
>
> (a) reduce the price at which the rights holder sells the medicine in any market in Canada, to the extent and for the period that are specified in the order;
>
> (b) to the extent and for the period that are specified in the order, reduce the price at which the rights holder sells, in any market in Canada, any other medicine to which a patented invention, or invention protected by a certificate of supplementary protection, of the rights holder pertains;
>
> (c) pay to Her Majesty in right of Canada an amount that is specified in the order."

252. The Panel has found that Horizon is selling Procysbi in Canada at a price that is excessive (C$0.4140). Consistent with its mandate to ensure that patented medicines are not sold in Canada at an excessive price, the Panel directs Horizon to cause the maximum price at which Procysbi is sold by Horizon in Canada to be reduced to no higher than C$0.2202 / mg.

253. The Panel has also found that Horizon was selling Procysbi in Canada at a price that was excessive since September 2017 in that the ex-factory price reported by Horizon in its filings (C$0.4140) exceeded the MAPP prescribed by the Moderate Improvement Test (C$0.2202 / mg) as applied by the Panel.

254. Section 83(2) of the Act gives the Panel the discretion to direct a patentee to, amongst other things, make a payment to Her Majesty the Queen in Right of Canada that will, in the Panel's view, offset the amount of any excess revenues derived by a patentee from the sale of the patented medicine at an excessive price. In providing the Board with such a power, Parliament clearly intended it to be one of the Board's tools in fulfilling its mandate to protect against the abuse of excessive pricing.

255. Based on the discretion granted to it under section 83(2), the Panel orders Horizon to pay to Her Majesty in right of Canada the amount, to be calculated by the Parties and approved by this Panel, which equals the amount of the excess revenues derived by Horizon from the sale of Procysbi in Canada at the excessive price as found by this Panel.

256. The Panel directs the Parties to consult and submit a joint submission setting out the calculation of the excess revenue payment to the Panel by 4:00 pm EST on September 30, 2022. If the Parties cannot agree, each Party shall provide by 4:00 pm EST on September 30, 2022 the calculation that it submits is accurate along with written submissions which clearly and concisely set out the dispute between the Parties and why its calculation should be approved by the Panel as being consistent with this decision and the Act and Regulations.

257. A Case Conference will be scheduled in the event the Panel has any questions about the calculation(s).

258. The Panel will review the joint calculation or separate calculations, as applicable, and issue a decision confirming the amount of the excess payment required to be made. Horizon shall make the payment within 30 days following the Panel's decision.

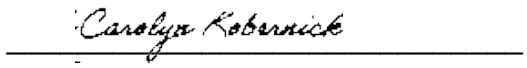
259. The Panel therefore makes the following two orders:

(a) Horizon shall reduce the price of Procysbi in Canada to no higher than the Maximum Average Potential Price prescribed by the Moderate

Improvement Test as applied by the Panel in its decision (C$0.2202 / mg); and

(b) Horizon shall pay to Her Majesty in Right of Canada the amount, to be calculated by the Parties and approved by this Panel, which equals the amount of the excess revenues derived by Horizon from the sale of Procysbi in Canada at the excessive price as found by this Panel, according to the process and timing set out in this decision.

Dated at Ottawa, this 1st day of September, 2022.



Signed on behalf of the Panel by
Carolyn Kobernick

Panel Members

Carolyn Kobernick
Mitchell Levine

Counsel for Board Staff

David Migicovsky
Christopher Morris
Courtney March

Counsel for the Respondent

Sheila Block
Andrew Shaughnessy
Stacey Reisman

Counsel for the Panel

Sandra Forbes