January 31, 2011 **Decision: PMPRB-07-D2-PENLAC - Merits**

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

AND IN THE MATTER OF sanofi-aventis Canada Inc. (the "Respondent") and the medicine "Penlac Nail Lacquer"

Introduction

1. These Reasons for Decision pertain to allegations by Board Staff that the patented medicine Penlac was sold by the Respondent sanofi-aventis Canada Inc. ("sanofi-aventis") at excessive prices, within the meaning of that term in the *Patent Act* (the "Act"). These allegations were the subject of a hearing by a panel of the Board (the "Panel"), at which some lay evidence and a substantial volume of expert evidence was received and tested in cross-examination. The Panel heard seven days of evidence and two days of oral final submissions, and received written final submissions.

Overview: Issues and Position of Parties

2. Penlac is a nail lacquer that is applied to finger and toe nails as part of a program of treatment for a fungal nail infection, onychomycosis due to the fungus Trichophyton rubrum, which is prevalent in approximately 5%-10% of the population. Onychomicosis causes disfigurations in the shape of the nail. Penlac is indicated for mild to moderate cases of onychomycosis in patients whose infection has not affected the lunula of the nail.

3. Three medicines have been approved by Health Canada for the treatment of mild to moderate onychomycosis: the topical lacquer Penlac (ciclosporox) and the oral systemic medicines Lamisil (terbinafine) and Sporanox (itraconazole).

4. Penlac was introduced to the Canadian market in July 2004 by Dermik Laboratories Canada Inc. ("Dermik"). As the result of a corporate merger in 2006, sanofi-aventis is the current corporate entity responsible for the potential excessive revenues that might have been earned between July 2004 and April 18, 2008, when the patent that pertained to Penlac expired. In these Reasons, references to sanofi-aventis should be taken to refer, where applicable, to the predecessor corporate entity, Dermik.

5. The hearing involved a considerable volume of evidence from an impressive group of expert and lay witnesses, and raised a number of complex issues involving subsection 85(1) of the Act, which sets out the factors that the Board must consider when determining whether a medicine is being or has been sold at an excessive price:

> **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:
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> (*a*) the prices at which the medicine has been sold in the relevant market;
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> (*b*) the prices at which other medicines in the same therapeutic class have been sold in the relevant market;
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> (*c*) the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada;
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> (*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.

6. Subsection 85(1) will be considered more completely later in these Reasons, but it can be seen that paragraph 85(1)(*b*) of the Act obliges the Board to consider the prices of other medicines "in the same therapeutic class" as the medicine under review. Paragraph 85(1)(*c*) requires the Board to consider the prices of the medicine in "countries other than Canada" (often referred to as the international pricing of the medicine). Both of these provisions, and the interaction between them, gave rise to debate between the parties. Paragraphs 85(1)(*a*) (establishing the price at which Penlac was sold in Canada) and 85(1)(*d*) (changes in the Consumer Price Index or "CPI") were potentially relevant but not contentious.

7. The Board has developed non-binding *Excessive Price Guidelines*[1] (the "Guidelines", about which more will be said later) to implement the provisions of the Act and more particularly, as the Guidelines pertain to this case, to implement subsection 85(1) of the Act. The Guidelines provide several tests by which Board Staff and patentees can determine the maximum price at which a given medicine will be presumed not to be excessive – the "maximum non-excessive price" (the "MNE" price).

8. As regards the prices of medicines in the same therapeutic class as the medicine under review, the Guidelines implement paragraph 85(1)(*b*) of the Act by stipulating that the MNE price of the medicine under review is equal or lesser than the price of the highest-priced medicine in the same therapeutic class. This is known as the Therapeutic Class Comparison.

9. As regards the international pricing of the medicine, the Guidelines implement paragraph 85(1)(*c*) of the Act in several ways, including (as was relevant in this case) by stipulating that the price of a medicine in Canada will be presumed not to be excessive if

[1] References in these Reasons are to the Guidelines that were in effect during the relevant time period 2004-2008. In 2009, some features of the Guidelines were revised and implemented in January 2010.

its price in Canada is no higher than the median of the prices of the medicine in countries specified by the *Patented Medicines Regulations* (the "Regulations"). This is known as the Median International Price Comparison (MIPC).

10. If there are no medicines in the same therapeutic class as the medicine under review, the Guidelines apply the MIPC.

11. Thus it can be seen that, in determining the MNE price of a medicine, establishing the other medicines, if any, that are in the same therapeutic class as the medicine under review can be an important factor. Both Board Staff and sanofi-aventis agreed that the "threshold issue" in this case was whether or not Penlac could be put in a therapeutic class with Lamisil and Sporanox. In summary of the Parties' positions:

    a. sanofi-aventis argued that, for price comparison purposes, Penlac belongs in the same therapeutic class as Lamisil and Sporanox. During the relevant period, Lamisil and Sporanox were more expensive than Penlac. Accordingly, if the Panel were to agree with sanofi-aventis, Penlac would not have been the highest-priced medicine in its therapeutic class and thus would be presumed by the Guidelines not to have been excessively priced at any point between its introduction to the Canadian market and the expiry of the pertaining patent. sanofi-aventis would not be exposed to any remedy in relation to the excessive revenues alleged by Board Staff. Alternatively, sanofi-aventis argued for the same result if Penlac should not be considered to be in the same therapeutic class as Lamisil and Sporanox. The argument in broad terms is that the Board's Guidelines should not be applied to the pricing of Penlac and that other relevant considerations indicate that Penlac was not excessively priced;

    b. Board Staff argued that no other medicines were properly comparable to Penlac, and thus no other medicines were in the same therapeutic class as Penlac. Accordingly, Board Staff argued, the MIPC in the Board's Guidelines should be used. Penlac, having been sold in Canada at a price substantially above its median international price, was excessively priced. If the Panel were to agree with Board Staff, sanofi-aventis would be exposed to a substantial remedial order of the Board in relation to excessive revenues.

12. In terms of assessing the question of whether Penlac belongs in the same therapeutic class, the primary differences between the positions of sanofi-aventis and Board Staff were: (1) whether "clinical equivalence" was the appropriate criterion for the establishment of a therapeutic class for the price comparison purposes of the Act; and if so (2) what the proper indicia of clinical equivalence were; and (3) whether the data demonstrate that Penlac was clinically equivalent to Lamisil and Sporanox, such as to warrant Penlac's inclusion in a therapeutic class with those medicines.

13. As noted, Penlac is a topical medicine, whereas Lamisil and Sporanox are systemic medicines. Board Staff accepted that, in this particular case, this difference did not prevent the three medicines from potentially being in the same therapeutic class, provided that they were clinically equivalent. The Panel notes that in other cases, differing formulations between the medicine under review and other medicines for the same condition, or other relevant distinctions, could result in the exclusion of the medicine under review from the therapeutic class of the other medicines.

The Board's Regulatory Framework

14. In the assessment of the factors in subsection 85(1) of the Act, the starting point is the price at which the medicine is being sold [paragraph 85(1)(*a*)]. There are provisions in the Act and the Regulations that require a patentee to report the price at which its medicine is sold, so this information is on file with the Board. This price is then considered in light of:

    i. the prices of medicines in the same therapeutic class sold in Canada [paragraph 85(1)(*b*)];

    ii. the international pricing of the medicine [paragraph 85(1)(*c*)];

    iii. the price of medicines in the same therapeutic class outside of Canada [also paragraph 85(1)(*c*)]; and

    iv. changes in the CPI [paragraph 85(1)(*d*)].

15. The relationship between section 85 and the Board's Guidelines has been discussed in prior decisions of the Board, most particularly the decisions involving the medicines Dovobet and Adderall XR. The following extract from the case involving Adderall XR captures the important, but qualified, role of the Guidelines, and the Panel adopts the substance of this extract in these Reasons:

> 13. As the Board discussed in the *LEO Pharma* decision, it is evident that Parliament intentionally framed the factors in section 85 of the Act in very broad terms. The Act, in section 96, contemplates the Board establishing guidelines, and the Board did so with respect to the specific implementation of the general factors listed in section 85 (the "Guidelines").
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> 14. It is important to correctly characterize the significance of the Guidelines; their role should neither be understated nor overstated. As noted in the *LEO Pharma* decision, some guidelines are absolutely essential for the implementation of the general factors listed in section 85. In the *LEO Pharma* decision, articulating principles cited with agreement by the Federal Court on judicial review of that decision, the Board said:

...having directed the Board to the factors it must consider, section 85 does not stipulate how those factors must be used or weighed to assess whether or not the price of a medicine is excessive. In other words, section 85 does not provide a formula into which the Board can feed pricing information to calculate the MNE for a medicine.

In particular, two features of subsection 85(1) require the Board to exercise discretion, to apply judgment and expertise, and if appropriate to give consideration to the stakeholder input and compromise that went into the development of the Guidelines, when determining whether or not the factors in section 85 indicate that the price of a medicine is excessive.

First, performing a comparison does not dictate a conclusion that must result from that comparison. Section 85 leaves it within the discretion of the Board to determine the relevance of each comparison and of all of the comparisons taken together. For example, section 85 does not stipulate that if the price of a medicine is higher in Canada than in other countries it must be found to be excessive, nor that if it is lower in Canada than in other countries it must be found not to be excessive. The comparison of the price of the medicine in Canada with its price in other countries must be made, and then the relevance of that comparison must be assessed. So too with each of the other comparisons and then all of the comparisons taken together.

A second and related point is that each of the comparisons listed in section 85 could lead the Board towards a different conclusion. There are a number of permutations. For example, a medicine might be sold in Canada at a lower price than in other countries but at a higher price than comparable medicines sold in Canada, or vice versa. Each of the three comparisons must be considered, and then the weight to be given to each of them, and how they should relate to each other, must be determined.

…

The need for balancing is evident in the application of section 85 of the Act because each of the factors taken on its own does not merely pull directionally but, depending on the relevance of the comparison itself, could lead to a different conclusion. It could be logically impossible for the Board to give each of the factors equal weight, or it could be logical after consideration of all factors to give one or more factors primary or decisive weight, as otherwise there could be irreconcilable conflicts in the conclusions to be drawn from each of the factors.

In other words, the Board must come to a single specific price that is the MNE for a medicine, and, needless to say, the three different factors stipulated by subsection 85(1) do not generate that single figure, for both of the reasons mentioned: the act of comparing does not entail any specific

conclusion, and for a given medicine each of the three factors could suggest an MNE that is different in direction and/or degree.

15. The Guidelines were established after consultation with stakeholders, as mandated by subsection 96(5) of the Act. The Guidelines aim to provide a structure for the necessary particularization and integration of the general factors listed in section 85, to provide fairness through consistent treatment among patentees, and to give patentees guidance on the process that will be used in establishing the MNE for their medicines, both when the medicines are first introduced to a market in Canada and each year thereafter that they are sold in Canada.

16. On the other hand, the Guidelines are not binding on the Board. Furthermore, situations could arise that are not contemplated by the Guidelines, or changes in medicine or the marketing of medicines in Canada could give rise to situations that are no longer covered appropriately by the Guidelines. In each case where the review of the pricing of a medicine comes before a panel of the Board, the panel must determine whether the medicine is priced excessively within the terms of section 85 of the Act. To the extent that the Guidelines speak to this issue, the panel must determine whether the Guidelines provide for an appropriate and reasonable implementation of the factors in section 85 of the Act before establishing an MNE by the terms of the Guidelines. If the Guidelines do not result in an appropriate implementation of section 85 of the Act, the panel must depart from the Guidelines.

Therapeutic Class

17. A necessary starting point in the Panel's analysis is a description of what constitutes a "therapeutic class" as that expression is used in paragraphs 85(1)(*b*) and (*c*) of the Act. The Guidelines use the concept of therapeutic equivalence (termed "clinical equivalence") to define a therapeutic class. There was general agreement among the expert witnesses that clinical equivalence is determined primarily by an assessment of how well the medicine works, or can be expected to work, to treat the condition for which it is indicated (effectiveness or efficacy[2]) and what side-effects and contra-indications the medicine has (safety). The relationship between effectiveness and safety in this analysis was an issue in this case and is discussed later in these Reasons.

18. The Panel concludes that clinical equivalence is the appropriate concept to use when defining a therapeutic class for the purposes of implementing paragraphs 85(1)(*b*) and (*c*) of the Act. It reflects the wording of the Act, in that a therapeutic "class" connotes a group of medicines that share a common feature or features. As to what that

[2] Efficacy is demonstrated in a trial by establishing that a medicine can achieve its intended effect in the particular conditions of the trial and thus might be expected to do so in a clinical (that is, real life) setting. Effectiveness is demonstrated by observational studies that examine how well the medicine achieves its intended effect in a clinical setting. Depending on the data available, either or both concepts could be used to measure clinical equivalence.

commonality should be, therapeutic (clinical) equivalence captures the intent of the Act, in that paragraphs 85(1)(*b*) and (*c*) deal with price comparisons, and the principal factors in that regard are the relative effectiveness and safety of the medicines being compared; that is, their relative therapeutic/clinical equivalence.

19. Broadly speaking, and as reflected in the Guidelines:

    a. if the new medicine is comparable in effectiveness and safety to other medicines already on the market, its manufacturer should be entitled to sell it at a price as high as the most expensive of those medicines; and

    b. if the new medicine is materially less effective and/or safe relative to the other medicines already on the market, its manufacturer should not (at least by reason of that comparison) be entitled to sell it at a price as high as the most expensive of those medicines.

20. The converse is also embodied in the Board's approach to setting the MNE price of a new medicine. If 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. Reference then must be had to the criteria in paragraphs 85(1) (*c*): the price of the medicine outside Canada and (in the event that, unlike the situation in Canada, there are comparable medicines sold outside Canada) the price outside Canada of other medicines in the same therapeutic class. As the Board has noted in other decisions, more weight is likely to be put on the first of those two factors, because the comparison is more direct (same medicine, different countries vs. different medicine, different countries) though whether this weighting is appropriate in any given case would have to be considered on the facts of that case.

21. If, as in Canada, there is no other medicine outside Canada in the same therapeutic class, then the only factors left in subsection 85(1) that the Board can consider (assuming changes in the CPI are not in issue) are the price of the medicine (under review) in Canada and outside Canada. Still, in this situation the Board would have to be satisfied that the determination of whether or not the medicine was being sold at an excessive price could be made under those factors such that it was not necessary to have resort to the factors in subsection 85(2).

22. Medicines in the same therapeutic class, for the purposes of paragraphs 85(1)(*b*) and (*c*), are not merely medicines used to treat the same condition. To use an extreme example for illustration, it would not be logical, when grouping medicines for the purpose of assessing the appropriateness of the price of one of them, to include in the group medicines that are barely effective and others that are 100% effective, nor medicines that have a high risk of serious side effects and others that have no side effects. Such a class could result in setting a price cap for a barely effective, very risky medicine by reference to the prices of completely effective, completely safe medicines.

This would make no sense in relation to the objectives of the Act. This is why clinical equivalence is the appropriate criterion for a therapeutic class as that term is used in paragraphs 85(1)(*b*) and (*c*) of the Act.

23. It is the position of sanofi-aventis that a relative deficiency in the effectiveness of a medicine (compared to other medicines in the proposed therapeutic class) could be compensated for by superior safety characteristics of the medicine. There is some logic to this position, because it is consistent with the notion that comparably priced medicines should have equal value to the patient, and this might be the case, for example, with a medicine that is less effective but safer than alternatives.

24. However, the Panel considers this to be a very difficult, if not impossible, analysis to undertake, and one that misapprehends the concept of clinical equivalence. While compromising safety for efficacy or vice versa is an analysis that must be undertaken in clinical practice, it is a highly subjective and individual decision. It is not a principle that is suitable for broadly-based analysis in the context of establishing non-excessive prices. Different scientists, clinicians and patients could have widely differing views on the balance between risk and effectiveness, depending on their individual perceptions of the severity of the condition, the impact it is having, or could have, on the patient's life, and each patient's aversion to risk. The matter is further complicated by the possibility of relatively poor-quality data on effectiveness having to be weighed against good-quality data on risk, or vice versa.

25. Furthermore, a different safety profile will tend to make a medicine less, not more, clinically equivalent to its comparators. The evidence of sanofi-aventis was that Penlac was appropriate for certain patients who might not tolerate the systemic medicines, which, as Dr. Mitchell Levine (called by Board Staff) noted, indicates that Penlac was less like the systemic medicines. Indeed, on their own, differences in safety and appropriateness for different patient populations, if substantial enough, could put a medicine into a different therapeutic class than others for the same indication.

26. Accordingly, the Panel does not consider it practical or appropriate to consider the two concepts to be additive. Rather, clinical equivalence requires comparable efficacy and comparable safety.

27. The Guidelines provide a potential reward to patentees of safer medicines. A substantial improvement in safety can be reflected in the Guidelines by the categorization of a medicine that offers such an improvement as a Category 2 medicine, which allows the patentee to introduce the medicine to the Canadian market at its median international price. This is often an advantage to patentees, as the median international price can be higher than the price of domestic comparators. In this particular case, with Penlac's median international price lower than its domestic price, access to the median international price would not present a domestic pricing advantage for sanofi-aventis. That, however, is the result of the international pricing decisions of

sanofi-aventis, not the operation of the Guidelines. This point is addressed in further detail later in these Reasons.

28. Finally, even if the Panel were to attempt to weigh together the effectiveness and safety of Penlac with those of Lamisil and Sporanox, the conclusion would be that Penlac's reduced risk of serious but quite rare side effects, and its indication in certain patient populations, is not a sufficient advantage over Lamisil and Sporanox to compensate for its markedly inferior effectiveness relative to those medicines. The concept behind Penlac – focusing the medication on the affected part of the body and thus sparing the rest of the body from potential interactions or side effects – was unquestionably a good one. However, the effectiveness of the attempt is so much lower than the systemic medicines that the improved safety is not likely to be seen as an appropriate trade-off by many of the patients who are informed of the data. The Panel accepted the evidence of Dr. Vincent Ho, a practicing dermatologist and a professor of dermatologic pharmacology called by Board Staff, to the effect that patients who could not or did not want to take the systemic medicines, when informed of the efficacy data, generally opted to do nothing rather than use Penlac.

29. sanofi-aventis observed that Lamisil has been consistently assessed as being more efficacious than Sporanox. In one study and on one measure of treatment success the difference in efficacy between Lamisil and Sporanox was as great as the difference between Sporanox and Penlac. sanofi-aventis argued that if one considers Lamisil and Sporanox to be in the same therapeutic class despite their different levels of efficacy (as the witnesses for sanofi-aventis and Dr. Ho did), then arguably Penlac should be in that therapeutic class.

30. The argument of sanofi-aventis on this point is premised on an interpretation of the data (widely disparate efficacy of Lamisil and Sporanox) that the Panel does not accept. It is clear that the evidence demonstrates that Lamisil is more effective than Sporanox, but the preponderance of the evidence (particularly the more reliable evidence) indicates that Lamisil and Sporanox are both reasonably effective at treating the symptoms of onychomicosis, whereas Penlac is not particularly effective.

New Medicine Categorization

31. At this point it is useful to describe an element of the Board's Guidelines that does not arise directly in this case but was used in evidence and argument to discuss relative clinical equivalence and the formation of therapeutic classes for the purposes of paragraphs 85(1)(*b*) and (*c*).

32. When a new medicine is introduced to the market, the Guidelines require that it be categorized depending on several factors, including its performance relative to existing medicines. This is the first point at which relative effectiveness and safety are considered. A medicine that demonstrates "moderate, little or no therapeutic

improvement" over existing medicines is deemed a "Category 3" medicine that must be priced no higher than the most expensive of the existing medicines for the same condition sold in Canada.

33. A medicine that is a "breakthrough" or provides a "substantial improvement" over comparable existing medicines is deemed a "Category 2" medicine, in which category (as noted earlier) it has the potential, depending on its international prices, to be priced higher than a Category 3 medicine.

34. Dr. Neil Shear, called by sanofi-aventis, argued that this should end the analysis of the relative therapeutic merits of the medicine, and that once this categorization is complete, therapeutic classes should be composed of any medicine that treats a condition, regardless of relative effectiveness, as long as each medicine has some efficacy (i.e. greater than placebo).

35. The Panel does not agree. For the reasons noted earlier, the Board must consider therapeutic classes when determining the MNE price of a medicine, and clinical equivalence is central to the concept of a therapeutic class that is established for pricing purposes. As noted earlier in these Reasons, on the approach advocated by sanofi-aventis and Dr. Shear, a risky medicine that arrives on the market providing barely any benefit to patients would be put in the same therapeutic class and could be priced as high as an existing safe medicine that provides a complete cure. This would not be a reasonable way to implement paragraphs 85(1)(*b*) and (*c*) of the Act.

36. In the Guidelines, categorization serves a different purpose than the determination of a therapeutic class. Categorization, in the context of this discussion, allows a new medicine that provides a breakthrough or a substantial improvement over existing medicines potentially to break out of the therapeutic class comparison completely and have resort to its international median price as the cap on the price of the medicine in Canada. Medicines that do not meet that high threshold of therapeutic improvement have their price cap set by the domestic therapeutic class comparison. But within the group of medicines that treat a given condition, there must also be an alignment of effectiveness and safety, so that reference to prices of comparable medicines continues the objective of rewarding superior medicines.

37. The issue of categorization also came up when it was used to indicate the differences between the therapeutic characteristics (effectiveness and safety) of Penlac, on the one hand, and Lamisil and Sporanox on the other. The evidence of experts called by both parties was that if Penlac had been the first medicine on the market and either Lamisil or Sporanox was introduced, the efficacy of either systemic medicine is so much better than that of Penlac that there would be a case to be made that the systemic medicine would be a "substantial improvement" and should be categorized by the Board as a Category 2 medicine. On this evidence, if Lamisil or Sporanox came on the market after

Penlac, they would not likely be tied to a therapeutic class with Penlac and thus limited in price to that of Penlac.

38. The converse is implicit in this observation, because nothing pertaining to a therapeutic class should turn on the sequence in which medicines are introduced to the market. If Lamisil and Sporanox, with their superior efficacy, would not be tied to Penlac's price, then Penlac, with its inferior efficacy, should not be entitled to be priced by comparison with Lamisil and Sporanox.

39. While it is difficult to conclude definitively that Lamisil and Sporanox belong in the same therapeutic class when that was not the direct subject of this proceeding, the weight of evidence, both in the literature and from the expert witnesses, is that they should be in the same therapeutic class. Considering all of the literature, they both have comparable and reasonable efficacy and Penlac does not. The Panel concludes that if the systemic medicines do belong in the same therapeutic class, Penlac does not belong in that therapeutic class with them.

The Board's Dovobet Decision

40. sanofi-aventis has also relied on the Board's decision regarding the medicine Dovobet, where the Board discussed the process of creating a therapeutic class. The patentee of Dovobet had developed a compound medicine that combined two separate medicines that, before Dovobet, had to be applied separately to treat psoriasis. The question was whether the compound medicine belonged in the same therapeutic class as the two separate medicines that were its constituent elements. This is a different question than the one that is before this Panel.

41. That said, the Panel believes that its decision in this case is consistent with the decision in the Dovobet case because, on the weight of all of the evidence, adding Penlac to a therapeutic class consisting of Lamisil and Sporanox would (to use the language of the Dovobet decision) "compromise the homogeneity of the class to a degree that, as a matter of scientific and practical judgment, is inappropriate." Indeed, the Dovobet panel (at pages 15-17 of that decision) specifically rejected the proposition that "therapeutic class" was equivalent to "therapeutic options" and noted that its therapeutic class decision would have been different if there had not been clinical equivalence:

> The use of separate active-ingredient medicine comparators for combination medicines is always, of course, subject to the caveat that it will not be appropriate if there is reliable evidence that the separate medicines used in a combination therapy have a materially different clinical effect than the combination medicine.

Other positions allegedly taken by the HDAP regarding relative efficacy

42. Dr. Shear testified on behalf of sanofi-aventis to the effect that, during his tenure on the Human Drug Advisory Panel[3] (from 1998 to 2003), the HDAP would not consider comparable efficacy to be a requirement for inclusion in a therapeutic class. sanofi-aventis also presented evidence that, with respect to the medicine Champix, the HDAP recommended a therapeutic class that included smoking cessation therapies with efficacies as divergent as those of Penlac and the systemic medicines.

43. The Panel is unable to draw any conclusions from these allegations that are pertinent to the case before it. This is for both doctrinal and evidentiary reasons. First, for the reasons cited earlier in these Reasons, the Panel considers comparable effectiveness to be an important factor in the assessment of clinical equivalence. Should the HDAP have departed from this principle, the Panel would consider the HDAP to have departed from the Guidelines and require an explanation. That said, effectiveness will be measured by different factors depending on the disease, the medicines available to treat it and the standards by which success is measured. Accordingly, it is not at all apparent that the HDAP did depart from this principle in the Champix case.

44. As for the practice of the HDAP during Dr. Shear's tenure, the proposition that, for example, a medicine that is barely effective should be included with medicines that provide complete cures in the same therapeutic class for price comparison purposes is so inherently inconsistent with the Act and the Guidelines that the Panel would be surprised to have this alleged practice confirmed with specific examples. In any event, as noted, it is the Board that decides such matters, and the Board's Guidelines make it clear that a therapeutic class is established on the basis of clinical equivalence. Clinical equivalence is established by comparable effectiveness and comparable safety. As noted, the Panel considers this feature of the Guidelines to be the appropriate implementation of the expression "therapeutic class" in paragraphs 85(1)(*b*) and (*c*) of the Act.

45. Second, it is not possible to judge what the HDAP did or why they did it in the circumstances cited by sanofi-aventis because those cases were not before the Panel and the record is not otherwise adequate to support a conclusion on the point. Also, much of the information relied on by sanofi-aventis in relation to the Champix VCU was not introduced during the hearing (but rather in final argument) and Board Staff did not have an opportunity to test the material during the hearing or call its own evidence in response to it.

46. In conclusion on this point, the Panel is not persuaded that the HDAP has taken a different approach to the establishment of a therapeutic class in this case than in other cases that have been brought before it, and the Panel would not be swayed from the

[3] The HDAP is an independent expert panel of scientists who provide advice to Board Staff regarding the application of the Board's Guidelines to specific medicines under review.

concept of clinical equivalence endorsed in these Reasons if the HDAP had taken a different approach in other cases.

The Expert Witnesses

47. Both parties filed multiple expert reports on the topics of dispute between them. This material was reviewed by the Panel in advance of the hearing. At the hearing, the evidence of each expert was outlined in an examination-in-chief and tested in thorough cross-examination by the opposing party. This evidence, and the parties' submissions on the weight that should be given to it by the Panel, was then summarized in comprehensive and very helpful oral, and then written, submissions. The Panel has considered the evidence thoroughly and, except for the salient points and findings, will not reproduce it in detail in these Reasons.

48. All of the witnesses had impressive credentials and no serious challenge was taken to their qualification to testify as expert witnesses. Also, it was evident that each of the witnesses made a considerable effort to prepare their reports and testify before the Panel. Board Staff submitted in final argument that the evidence of the sanofi-aventis expert witnesses must be considered in light of their connections (in varying degrees) to the pharmaceutical industry and (in some cases) sanofi-aventis itself.

49. The Panel agrees with the proposition that relative independence is a critical factor in the weight to be given to the evidence of any witness, both as to relationships that could give rise to bias or the demonstration of bias in the evidence of the witness. If it had been necessary to do so – for example to decide between two bare opinions in a vacuum of literature – the Panel would have had to consider the relative independence of the expert witnesses called by both parties.

50. However, the Panel did not need to discount the evidence of any of the witnesses on this particular account in order to reach the conclusions in these Reasons. The Panel was able to reach conclusions on the points in issue and determine the weight to be given to the various witnesses' evidence through an assessment of their affidavits, the substance and manner of their *viva voce* testimony and the extent of the consistency of their opinions with the literature.

The Evidence

51. This matter came before the Panel as a result of a disagreement between sanofi-aventis and Board Staff, the latter acting on the advice of the HDAP.

52. The members of the HDAP are experienced in the application of the Board's Guidelines but have no other connection to the Board. The members of the HDAP are not given any pricing information concerning the medicine under review or the potential comparators, or the potential financial implications of their scientific advice.

They examine the scientific literature pertinent to their task in each case and review any submissions that the patentee may make on the literature and issues that may bear on the application of the Guidelines to the medicine under review. Evidence concerning the conclusions reached by the HDAP has some weight, being an independent expert review of the literature and the patentee's submissions with the Board's Guidelines in mind. However, as its conclusions are stated without much elaboration, they alone cannot be relied on by Board Staff in a pricing hearing, where expert witnesses are called to give detailed opinions.

53. The HDAP reviewed the scientific literature pertinent to Penlac and the submissions that had been made by sanofi-aventis to Board Staff. In summary, sanofi-aventis put much the same case to Board Staff that was presented to the Panel: that Penlac was sufficiently comparable in effectiveness to Lamisil and Sporanox[4] that it should be considered to be clinically equivalent and thus in the same therapeutic class as those medicines. sanofi-aventis also argued that, to counter the arguably poorer efficacy of Penlac relative to Lamisil and Sporanox, Penlac was safer and provided better value than those medicines. Detailed submissions and references to the scientific literature were submitted to support these positions.

54. In attempting to establish a therapeutic class for Penlac, the HDAP followed the process, stipulated by the Guidelines, of considering the agents in the fourth sub-class level of the World Health Organization's Anatomical Therapeutic Chemical Classification System (the "ATC") to identify medicines for the treatment of onychomicosis. There were no such medicines. The HDAP then looked at other levels of the ATC for medicines that treat onychomicosis, and found Lamisil and Sporanox. Board Staff pointed out that this was unusual, because the HDAP normally looks for potential comparators that are in the same formulation, whereas Penlac is a topical medicine and Lamisil and Sporanox are oral systemic medicines. However, the HDAP did consider the systemic medicines to be potential comparators providing, as stipulated in the Guidelines, they were clinically equivalent.

55. The HDAP then reviewed the submissions of sanofi-aventis and the scientific literature to assess clinical equivalence. The three members of the HDAP concluded unanimously that, because of the degree to which Penlac was less effective than Lamisil and Sporanox, Penlac was not clinically equivalent to those medicines. Dr. Levine, who was on the HDAP panel that came to this conclusion, expanded on this point in his evidence by noting that normally the HDAP permits a 10%-15% variance in effectiveness when establishing a therapeutic class, whereas the differences in the case of Penlac and the systemic medicines were much greater: "off the scale", as Dr. Levine put it.

[4] sanofi-aventis also suggested to the HDAP that Fulvicin (griseofulvin) was a comparable medicine, but given that Fulvicin is so rarely prescribed for onychomicosis, that position was not pursued in this proceeding.

56. On the point that is relevant to this hearing, the HDAP concluded that there were no medicines that were comparable to Penlac; that is to say, the only potential comparators were Lamisil and Sporanox and Penlac was not in a therapeutic class with those medicines. Penlac, HDAP concluded, does not have a therapeutic class. One might also phrase the conclusion to the effect that there are no other medicines in the same therapeutic class as Penlac.

57. After the conclusions of the HDAP were communicated to sanofi-aventis, the company provided further submissions and literature in an effort to persuade Board Staff of its position. Dr. Levine was engaged by Board Staff to review these submissions. He provided two reports in which he analyzed the supplementary submissions and indicated that he still considered the conclusions that the HDAP had reached to be sound.

58. Dr. Ho presented expert evidence to the same effect in this proceeding, on behalf of Board Staff. The substance of his evidence was that Penlac was so ineffective that he and his colleagues seldom, if ever, prescribe it. He said that most of his patients who do not want to take the systemic medicines, when informed of Penlac's efficacy rates, made what he considered to be the sensible choice not to bother with Penlac. Onychomicosis is primarily a cosmetic problem and evidently not worth the bother of daily applications of a medicine that is, on Dr. Ho's experience and as he interprets the literature, marginally, if at all, effective.

59. sanofi-aventis presented the evidence of Drs. Aditya Gupta, Charles Lynde, Kirk Barber and Neil Shear, researchers and medical doctors with expertise in dermatology, to support the position of sanofi-aventis concerning the efficacy and safety of Penlac. Dr. Shear also presented evidence specifically concerning the appropriate way to establish a therapeutic class for the purposes of the Guidelines.

60. The witnesses for sanofi-aventis presented quite a different view of the efficacy of Penlac from those of Board Staff. As practicing dermatologists, their position was that Penlac, though plainly less effective than the systemic medicines, had some efficacy and was more appropriate or the only option in a number of situations where the systemic medicines were not suitable. They considered it one of the tools in the tool chest of a dermatologist treating onychomicosis, albeit not as effective as the systemic medicines.

61. The Panel considered the evidence of the witnesses and had reference to the scientific literature to resolve the differences between the witnesses called by sanofi-aventis and Board Staff. In assessing the efficacy of a medicine, scientists, clinicians and the Board look to the available evidence. There is a hierarchy of reliability in the evidence that is available concerning the efficacy and safety of medicines. The most reliable evidence comes from well-designed, randomized double-blind controlled trials (RCTs) and the least reliable evidence comes from the general knowledge of an expert clinician, with a

range of forms of evidence with intermediate reliability between the top and bottom of the hierarchy.

62. The conclusions that can be reliably drawn from the different types of evidence concerning the efficacy or effectiveness of medicines have been the subject of discussion in scientific circles and in hearings before the Board. This is an important topic for the Board, because the Board must look at various forms of evidence in order to categorize the performance of new medicines relative to the performance of other existing medicines. The fact that expert opinions are the least reliable form of evidence does not render such evidence worthless, but such evidence is not likely to sustain a finding (for or against) clinical equivalence by the Board, and in all events the Board gives the greatest weight to the most reliable evidence available.

63. There is then the question of what conclusions can be drawn from RCTs. The Panel concludes that, while any trial must be well designed, implemented and analyzed if it is to produce reliable information, the most reliable trials comparing the relative effectiveness and safety of medicines are those in which the medicines to be compared are administered in a single trial; that is, a "head-to-head" trial. A head-to-head trial is designed, implemented and analyzed in a manner that aims to ensure that the medicines under review are compared in identical circumstances, so that a comparison of their relative effectiveness and safety is not compromised by variations in the manner in which the data were gathered or analyzed.

64. When head-to-head trials are not available, scientists may conduct a meta-analysis, in which the results of multiple separate trials assessing the effectiveness of the medicines under review are compared. For example, one might compare the results of a trial in which the efficacy of medicine "A" was assessed with the results of another trial in which the efficacy of medicine "B" was assessed, and attempt to draw conclusions about the relative efficacy of the two medicines. Likewise, one might assess the efficacy of medicines "A" "B" and "C" by comparing the results of a trial in which the relative efficacy of medicines "A" and "B" were assessed with the results of another trial in which the relative efficacy of medicines "B" and "C" were assessed. The most reliable meta-analyses are those in which comparably high quality trials (RCTs) are assembled and analyzed.

65. However, in studies that gather data from multiple trials – even high-quality trials – there could be variations among the trials in design, patient population, implementation, and analysis. As a result, it is likely that a comparison of their results will not be as informative as a large, well-designed head-to-head trial in which the performance of medicine "A" is compared directly with the performance of medicine "B" in identical circumstances. Accordingly, while a meta-analysis can be useful (and sometimes all that is available), all other factors being equal, such a comparison would generate less reliable – and potentially significantly less reliable – information than the results of a good head-to-head trial.

66. There are no head-to-head trials comparing the effectiveness of Penlac with Lamisil and Sporanox. sanofi-aventis had no obligation to conduct head-to-head trials for the benefit of the Board, though the absence of them makes it more difficult for sanofi-aventis to counter the evidence to the effect that Penlac is not particularly effective relative to those medicines.

67. Dr. Gupta, called as an expert by sanofi-aventis, recognized the value of head-to-head trials and testified that, in his work as a consultant for sanofi-aventis, he had urged sanofi-aventis in the strongest terms to undertake head-to-head RCTs with Penlac and the systemic medications. He testified that he implored sanofi-aventis to do these trials because the existing trials (the trials relied on by sanofi-aventis in this proceeding) were insufficient to establish the efficacy of Penlac relative to the systemic medicines. He testified that, despite his pleas, sanofi-aventis did not undertake the head-to-head trials.

68. sanofi-aventis did not call a company witness to testify to these matters. Board Staff asked the Panel to draw an adverse inference from this fact.

69. sanofi-aventis responded to Board Staff's position by noting correctly that the onus is on Board Staff to establish that Penlac was excessively priced: sanofi-aventis had no obligation to call any evidence. Nonetheless, it is peculiar that no representative of sanofi-aventis appeared to testify before the Panel. The persuasive quality of the evidence concerning the relative efficacy of Penlac and the systemic medicines has been an issue in the dialogue between sanofi-aventis and Board Staff for some time, including, of course, in this hearing. Dr. Gupta testified that there were "always issues about the efficacy" of Penlac – hence his insistence to sanofi-aventis to do head-to-head RCTs with the systemic medicines.

70. It is not necessary for the Panel to draw an adverse inference from the failure of sanofi-aventis to present a company witness. It is not necessary to reach a conclusion as to why sanofi-aventis did not conduct the trials that would have provided good-quality evidence as to the efficacy of Penlac relative to the systemic medicines. There is simply a gap in the evidence on this point – a gap of which sanofi-aventis was aware, was advised by its expert consultant to fill, but chose not to fill.

71. In this case, the position of Board Staff was that (1) the trials and studies relied on by sanofi-aventis to place Penlac in the same therapeutic class as Lamisil and Sporanox were not of the quality (in terms of scientific method and rigour) that is necessary to draw reliable conclusions regarding the relative effectiveness of Penlac, Lamisil and Sporanox, and (2) the most reliable of the trials comparing these medicines showed that Penlac was significantly less effective than Lamisil and Sporanox.

72. sanofi-aventis defended the quality of the trials and studies on which it relied, arguing that these studies demonstrated that Penlac had efficacy that was similar enough to that of Lamisil and Sporanox to warrant the inclusion of Penlac in the same therapeutic class as those medicines. sanofi-aventis noted that, by one measure and using certain data,

it could be observed that Penlac, while the least effective of the three medicines, was no less effective relative to Lamisil than Lamisil was relative to Sporanox.

Measuring Effectiveness and Efficacy

73. For the treatment of onychomicosis, there are different measures of success. One measure is "mycological cure", which occurs when testing indicates that there is no fungus present on the nail. Another measure is "clinical cure", which occurs when the nail shows no deformity or visible signs of infection. Finally, "complete cure" is present when there is both mycological cure and clinical cure.

74. "Complete cure" was described in the evidence as the "gold standard" for assessing the efficacy of treatments for onychomicosis. The evidence indicated two primary reasons for this. First, the manner in which mycological cure is tested leads to a consistent over-reporting of cures. Second, given that onychomicosis is primarily a cosmetic disease, a return to relative normalcy in the appearance of the nail is the objective of the treatment, so clinical cure is an important part of the success of the treatment. This is not to say that mycological cure is not a useful and common measure of treatment success, nor that the subjectivity of the assessment of clinical cure is immaterial to the analysis. However, on balance, the evidence made it clear that mycological cure is not as significant a measure as complete cure when assessing the efficacy of medicines for the treatment of onychomicosis. Accordingly, the Panel gave the most weight to findings of complete cure when assessing the relative efficacy of Penlac and the systemic medicines.

75. Board Staff and sanofi-aventis debated the relevance of less central matters in the significance of the literature, such as relapse rates and the significance of placebo success. The Panel found that it was able to accept the positions of sanofi-aventis on these topics and still come to the conclusions recommended by Board Staff as to the relative efficacy of Penlac and the systemic medicines.

The Scientific Literature

76. Weighing the varying data and conclusions in scientific literature in order to find the best conclusion regarding the efficacy of a medicine requires careful consideration. Having read the reports and supporting literature of the experts called by both parties, and having heard their evidence in chief and under cross-examination, the Panel concludes that the weight of evidence establishes conclusively that Penlac is substantially less effective than Lamisil or Sporanox.

77. The only double-blind randomized control trials involving Penlac were referred to as the "312 and 313 studies". These were not head-to-head trials, but rather Penlac vs. placebo trials. The complete cure rate for Penlac in these studies, after 48 weeks of treatment, was 5.5% in the 312 study and 8.5% in the 313 study. Even though onychomicosis is a difficult disease to cure, these are low success rates, especially

considering that success rates in trials – where clinicians and patients are usually more assiduous in maintaining the proper treatment regimen – are typically higher than in normal use.

78. In contrast to the Penlac complete cure rates in the 312 and 313 studies, the LION study, which was a well-conducted head-to-head study involving Lamisil and Sporanox, found complete cure rates of 50% and 30% respectively.

79. Of the meta-analyses in the evidence, the Panel found the Casciano/Shear study to be the most reliable and informative. It found mycological cure rates of 32% for ciclopirox (Penlac), 81% for terbinafine (Lamisil) and 65% for itraconazole (Sporanox). Allowing for the higher reported cure rates in assessments of mycological cure, these figures are in line with the complete cure rates in the individual trials of the medicines.

80. The Panel did not find helpful the pharmacoeconomic meta-analysis of Penlac, supported by an educational grant from Dermik Laboratories (the predecessor to sanofi-aventis) and published by Dr. Gupta in 2000. Unlike the Casciano/Shear meta-analysis, it considered mostly open trials involving Penlac, but mostly RCTs of the systemic medicines, resulting in a predictable and acknowledged bias. Its results are not in line with the more reliable trials and studies. The HDAP did not consider it reliable. Dr. Gupta acknowledged some of its limitations in the study itself and on cross-examination. Accordingly, the Panel did not ascribe much weight to this meta-analysis.

Conclusion Regarding Clinical Equivalence

81. Having concluded that Penlac is substantially less effective than Lamisil or Sporanox, and that the advantages of Penlac do not offset this inferior efficacy, the Panel concludes that Penlac is not clinically equivalent to Lamisil and Sporanox, and does not belong in a therapeutic class with those medicines for the purposes of consideration under paragraphs 85(1)(*b*) and (*c*) of the Act.

The Onus of Proof and the Guidelines

82. It is clear from the jurisprudence of the Board and was agreed by the parties that (1) the onus is on Board Staff to prove on a balance of probabilities that Penlac was excessively priced as that expression is used in the Act; and (2) Board Staff cannot meet that onus simply by showing that the price of Penlac was higher than the MNE price that results from the application of the Guidelines.

83. sanofi-aventis argued that Board Staff simply relied on the Guidelines to prove its case. The Panel disagrees. The relevant provision of the Guidelines in this case is the requirement for clinical equivalence in a therapeutic class as that term is used in paragraphs 85(1)(*b*) and (*c*). This is largely a matter of argument, and for the reasons given earlier, the Panel agrees with the position of Board Staff that clinical equivalence is the essence of a therapeutic class established pursuant to those provisions of the Act.

The Panel's decision on this point is not based simply on a finding that the price of Penlac exceeded the MNE price that results from the application of the Guidelines, but rather on a finding that the Guidelines, in this case, provide an appropriate implementation of the Act. As a result, the price of Penlac was excessive within the meaning of the Act.

Other arguments Relating to the Requirement of Clinical Equivalence

84. sanofi-aventis disagreed with this rationale for the requirement of clinical equivalence for three particular reasons.

85. sanofi-aventis argued that, in this particular case, where Penlac is less expensive than Lamisil and Sporanox, even if Penlac were determined to be in the same therapeutic class as those medicines, Penlac's price could not have risen to the prices of those medicines because its price was constrained to increases in CPI following its introduction to the market at a price lower than the systemic medicines.

86. This, however, is not a factor in the Panel's analysis. The Panel does not put weight on the fact, in isolation, that Penlac is less expensive than the systemic medicines. The prices of medicines that are not in the same therapeutic class as a medicine under review is not a factor for consideration in subsection 85(1) of the Act. It would, in any event, be very difficult and somewhat arbitrary to establish a non-excessive price for a medicine by reference to the prices of non-comparable medicines that treat the same condition. While generally speaking (as provided for in the Act) non-excessive prices of medicines can logically be established by reference to the prices of comparable medicines, there is no obvious metric, or even set of principles, for the appropriate relationship between of the prices of non-comparable medicines that treat the same condition.

87. Accordingly, even if the Act permitted the Panel to assess the price of Penlac by reference to the prices of medicines that are not in its therapeutic class, the Panel has no way (and none was suggested by sanofi-aventis) to assess whether the price of Penlac was appropriately lower than the prices of the systemic medicines. The international prices of Penlac, on the other hand, are stipulated by the Act as a relevant factor for comparison and provide a logical and objective basis for comparison.

88. On a second point, sanofi-aventis notes, correctly in the Panel's view, that strict criteria for inclusion in a therapeutic class will tend to leave more medicines without a therapeutic class, with the result that the MNE prices of those medicines will be determined by the MIPC. Often, given that patented medicines (especially in the United States) are more expensive internationally than in Canada, the effect of this could be to generate higher MNE prices. The MIPC is normally seen as a "premium" price, made available by the Guidelines for medicines that represent a breakthrough or substantial improvement relative to existing medicines.

89. While this is true, the result is not unreasonable. The Guidelines implement subsection 85(1) of the Act, and that subsection lists only two factors (other than CPI changes, which are not relevant here[5]) for comparison with the price of a medicine in Canada for the determination of whether that price is excessive: the prices of the medicine outside of Canada and the prices of other medicines in the same therapeutic class. Where there is no therapeutic class for a medicine, the remaining factor is its international pricing.

90. As noted, the MIPC is disadvantageous to sanofi-aventis in the particular case of Penlac. That, however, is a consequence of the pricing decisions made by sanofi-aventis. The logic of the MIPC itself is, as outlined immediately below, a fair and reasonable implementation of the requirement to consider international prices when determining if a medicine has been sold at an excessive price in Canada. There are two tests set out in the Guidelines for the implementation of paragraph 85(1)(c): the Highest International Price Comparison and the MIPC. The former provides that the price of a patented medicine will be presumed to be excessive if it is sold in Canada at a price that is higher than its price in the comparator countries. (This has never been alleged with respect to Penlac). The latter provides that the price in Canada of a breakthrough or substantial improvement medicine, or a medicine for which there is no therapeutic class, will be presumed not to be excessive if the price is not higher than the median of its international prices.

91. The MIPC test does not oblige the patentee to sell the medicine in Canada at the lowest price at which it is sold in the designated countries, nor does it entitle the patentee to sell the medicine in Canada at the highest price at which it is sold in the designated countries. The Panel considers the Median International Price Comparison to be a fair compromise that will typically reward patentees for improvements and breakthroughs in the medicines they manufacture, and the test has the advantage for patentees of being clear and objective. Accordingly, the Panel concludes the MIPC is an appropriate implementation of paragraph 85(1)(*c*) of the Act.

92. In this case, the conclusion is that the MIPC is disadvantageous to sanofi-aventis as a result of its pricing decisions. The Guidelines could be further refined to address the point raised by sanofi-aventis by providing, for example, that where the MIPC test is required because there is no therapeutic class, and where there is no therapeutic class because the new medicine under review is either significantly less effective or less safe than existing medicines for the same condition, then the MNE price in Canada is the lowest of the international prices of the medicine. Alternatively, the Panel could depart from the Guidelines and stipulate such an MNE price for Penlac in this decision, presumably to the disadvantage of sanofi-aventis. Again, where the price of the medicine in Canada and internationally are the only pertinent factors in subsection 85(1), the Panel might conclude that it is unable to assess whether Penlac has been

[5] Other than in the indirect manner described in paragraph 85.

sold at excessive prices, which would require resort to the factors in subsection 85(2) (the costs of making and marketing the medicine). However, as these points were not canvassed during the hearing, the Panel will leave that matter to the consideration of the full Board for future cases. In any event, the Panel concludes that, using the domestic and international prices of Penlac, and applying the MIPC, it is able to determine that Penlac was sold in Canada at excessive prices.

93. On this topic, the Panel can clarify the Guidelines by observing that when applying section 8.4 of the *Excessive Price Guidelines*, in which it is stated that a Category 2 medicine should be priced by reference to "comparable drug products, based on a Therapeutic Class Comparison Test and the median of the international prices identified in an International Price Comparison Test", the comparable medicines in the Therapeutic Class Comparison Test will typically be those that, but for the novel or improved efficacy or safety of the medicine, would be in the same therapeutic class as the medicine under review.

94. The third disagreement of sanofi-aventis with the requirement of clinical equivalence was that it did not accommodate improved safety in conjunction with relative efficacy. The Panel has explained, earlier in these Reasons, why differences in safety do not offset inferior effectiveness in the establishment of a therapeutic class.

Order

95. The Panel has reviewed the draft order submitted with Board Staff's written final argument and considers it appropriate in form and content. It is based on evidence that was filed during the hearing and accepted by the Panel as to the various prices at which Penlac was sold in Canada and in the comparator countries and the volume of sales in Canada during the relevant reporting periods. These data are used to establish the MNE prices of Penlac during the relevant period and the corresponding excessive revenues for each period, the cumulative amount of which is $9,409,074.36. A corresponding Order accompanies these Reasons.

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Mary Catherine Lindberg
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Original signed by

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