PATENTED MEDICINE PRICES REVIEW BOARD

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

AND IN THE MATTER OF Janssen-Ortho Inc., (the "Respondent") and the medicine "Concerta"

STATEMENT OF ALLEGATIONS OF BOARD STAFF

INTRODUCTION

1. This Statement of Allegations results from an investigation by Board Staff into the price of Concerta (methylphenidate hydrochloride), a patented medicine sold in Canada by Janssen-Ortho Inc. ("Janssen-Ortho") in 18 mg, 27 mg, 36 mg, and 54 mg tablets (DINs 02247732, 02250241, 02247733, and 02247734). According to publicly available information in 2006, Janssen-Ortho sells Concerta at a price of $1.9800 for the 18 mg tablet, $2.2850 for the 27 mg tablet, $2.5900 for the 36 mg tablet, and $3.2000 for the 54 mg tablet. **(Attachment 1)**

THE MEDICINE

2. Concerta is a new formulation of an existing compound (methylphenidate hydrochloride) indicated for the treatment of Attention Deficit Hyperactivity Disorder ("ADHD"). **(Attachment 2)**

3. Health Canada issued a Notice of Compliance for the 18 mg, 36 mg, and 54 mg tablets of Concerta on June 26, 2003. Health Canada subsequently issued a Notice of Compliance for the 27 mg tablet of Concerta on June 30, 2004. **(Attachment 3)**

4. Janssen-Ortho began selling Concerta 18 mg, 36 mg, and 54 mg tablets in Canada on August 7, 2003, followed by the introduction of the 27 mg tablet on January 8, 2005.

THE PATENTS

5. Canadian Patent No.1, 222,950 pertained to Concerta, but expired on June 16, 2004. **(Attachment 4)** This patent was granted to Alza Corporation U.S.A. on June 16, 1987.

6. Canadian Patents No. 2,265,668 and No. 2,264,852 also pertain to Concerta. **(Attachment 5)** These patents were granted to Alza Corporation US. on August 23, 2005 and November 1, 2005 and will expire on November 12, 2017 and September 16, 2017 respectively.

7. Janssen-Ortho is, for purposes of the Patented Medicine Prices Review Board ("PMPRB"), considered the Canadian patentee.

THE REGULATORY FILINGS

8. In accordance with the *Patented Medicines Regulations, 1994* ("the Regulations"), Janssen-Ortho began filing price and sales information in September 2003 for the 18 mg, 36 mg, and 54 mg tablets and has since continued to file its price and sales data as per the Regulations.

9. As for the 27 mg tablet, Janssen-Ortho began filing price and sales information on July 30, 2005, which included information for the reporting period from January 1, 2005 to June 30, 2005 and has continued to file its price and sales data as per the Regulations.

APPLICABLE GUIDELINES

Category

10. Section 3 of Chapter 3 - Scientific Review Procedures ("Scientific Review Procedures") provides the following guidance with respect to determining categorization for a new drug product:

    3.1 A Category 1 drug product is a new DIN of an existing dosage form of an existing medicine, or a new DIN of another dosage form of the medicine that is comparable to the existing dosage form as per Schedule 7.

    3.2 A Category 2 drug product is one that provides a breakthrough or substantial improvement. It is a new DIN of a non-comparable dosage form of an existing medicine or the first DIN of a new chemical entity.

    3.3 A Category 3 drug product is a new DIN of a non-comparable dosage form of an existing medicine or the first DIN of a new chemical entity. These DINs provide moderate, little or no therapeutic advantage over comparable medicines. This group includes those new drug products that are not included in Category 2 above.

11. Based on the above Scientific Review Procedures, Board Staff categorized Concerta 18 mg, 36 mg, and 54 mg tablets as Category 1 new drug products as they represent new DINs of existing or comparable dosage forms of an existing medicine. **(Attachment 6)**

12. As the Concerta 27 mg tablet was introduced on the Canadian market in January 2005 (almost a year and a half after the introduction of the 18 mg, 36 mg, and 54 mg strengths), it was also classified as a Category 1 new drug product, as it represents a new DIN of an existing dosage form of an existing medicine.

Comparable Medicines and Dosage Regimens

13. Chapter 1 - Excessive Price Guidelines ("the Guidelines") sets out the tests applicable to the introductory price of Category 1 new drug products as follows:

> 8.3 Category 1 New Drug Products
>
> In addition to the Guideline applicable to all patented drug products detailed in Section 7, the introductory price of a Category 1 new drug product will be presumed to be excessive if it does not bear a reasonable relationship to the average price of other DINs of the same medicine in the same or comparable dosage forms (Schedule 1).
>
> When the above methodology is not considered adequate or appropriate, Board Staff may conduct a Therapeutic Class Comparison Test (Schedule 2) to determine if the introductory price of the new DIN is excessive. This could be relevant if, for example, the new DIN has a therapeutic use or dosage regimen that differs materially from the other DINs of the same or comparable dosage forms of the medicine.
>
> While the introductory price of a Category 1 DIN will normally be compared against DINs of the same patentee, Board Staff may consider it appropriate in some instances to include DINs of other patentees. (For example, another voluntary licensee of the same patent as that pertaining to the new drug product, or a patentee marketing a drug product containing the same active ingredient as the new drug product but for which a different patent pertains.) […]

14. As the dosage regimens of Concerta 18 mg, 36 mg, and 54 mg tablets differ materially from other methylphenidate containing drugs, Board Staff conducted a Therapeutic Class Comparison ("TCC") Test for each of

these strengths instead of a Reasonable Relationship (“RR”) Test.

15. With respect to the selection of comparable medicines, when conducting a TCC Test, Section 9 of the Scientific Review Procedures provides as follows:

    9.1 Comparable drug products are selected by identifying both comparable medicines and comparable dosage forms.

    9.2 Comparable medicines are clinically equivalent in addressing the approved indication that is anticipated to be the primary use of the new drug product under review. The PMPRB refers to the World Health Organization (WHO) Drug Utilization Research Group's Anatomical Therapeutic Chemical Classification System (ATC) as the starting point for the selection of comparable medicines.

    9.3 Comparable medicines will typically be those identified under the ATC classification system at the sub-class level above the single chemical substance. This will normally be the fourth sub-class level. If the appropriate comparable medicines are not identified at this level, then the PMPRB may choose from the next higher sub-class or another sub-class. In some instances, it may be appropriate to select from the fifth or single chemical substance level. Selection criteria will include the indication and therapeutic use, and could include other factors such as mode of action, spectrum of activity or chemical family.

    9.4 The PMPRB may omit from the comparison a chemical substance or a drug product of the same ATC therapeutic class as the drug product under review if, in the panel's or Board Staff's opinion, it is not clinically equivalent or is unsuitable for comparison. For example, drug products with primary uses other than to address the indication anticipated to be the primary use of the drug product under review may be omitted from the comparison. Similarly, the PMPRB may choose to add products from other ATC classes if they are clinically equivalent for the appropriate indication to the drug product under review.

16. With respect to the selection of comparable dosage regimens, when conducting a TCC Test, Section 10 of the Scientific Review Procedures provides:

    10.1 The dosage regimen recommended for comparison purposes will normally not be higher than the maximum of the usual recommended dosage taking into account relevant clinical

variables. The most appropriate strength of the medicine will be chosen for a particular dosage regimen.

10.2 Generally, a dosage regimen based on a course of treatment will be applicable to acute indications, while a per-day regimen (based on maintenance dose) will be applicable to chronic situations

10.3 Board Staff and the panels may rely on product monographs, credible scientific literature, expert advice or any combination thereof to facilitate their recommendation of the maximum of the usual recommended dosage, relevant clinical variables, clinically equivalent effects and other matters relating to price measurement.

17. Based on the above Scientific Review Procedures, the appropriate comparable medicines and comparable dosage regimens for the TCC Tests **(Attachment 6)** were as follows:

Concerta (methylphenidate hydrochloride)	**ratio-Methylphenidate (methylphenidate hydrochloride)**	**Ritalin (methylphenidate hydrochloride)**	**Ritalin SR (methylphenidate hydrochloride)**
18 mg once daily	5 mg TID		20 mg OD
36 mg once daily		10 mg TID	40 mg OD
54 mg once daily	5 mg TID +	10 mg TID	60 mg OD

* OD = once daily
* TID= three times a day

The Maximum Non-Excessive Prices for Concerta (18 mg, 36 mg, and 54 mg tablets)

18. The appropriate price tests for a Category 1 new drug product are set out in subsection 8.3 of the Guidelines, referred to above and subsection 7.1 of the Guidelines which provides that:

7.1 The price of a new or existing patented drug product will be presumed to be excessive if it exceeds the prices of the same medicine sold in all countries listed in the Regulations. These prices will be determined using the International Price Comparison Test described in *Schedule 3*.

19. By letter dated April 28, 2004, Board Staff advised Janssen-Ortho that the introductory prices of the 18 mg, 36 mg and 54 mg strengths of Concerta appeared to exceed the Guidelines during the introductory period, August

2003 to December 2003, based on an International Price Comparison ("IPC") Test and a TCC Test conducted for each strength. As a result an investigation was commenced into the introductory prices for these three strengths of Concerta. **(Attachment 7)**

20. By letters dated May 28, 2004 and November 29, 2004 and in response to Board Staff's investigation letter, Janssen-Ortho maintained its position that the prices of the 18 mg, 36 mg, and 54 mg strengths of Concerta were not excessive. **(Attachment 8)**

21. By letter dated November 14, 2005, Board Staff advised Janssen-Ortho that it had completed its investigation and that the price of Concerta continued to be excessive for the 18 mg, 36 mg, and 54 mg strengths. **(Attachment 9)**

22. In response, Janssen-Ortho filed additional material on January 18, 2006 with the Chairperson of the PMPRB, requesting an Advance Ruling Certificate ("ARC") pursuant to subsection 98(4) of the *Patent Act*.

23. The Chairperson denied Janssen-Ortho's request for an ARC.

24. In light of the additional material filed by Janssen-Ortho in support of its request for an ARC, and following the Chairperson's refusal of this request, Board Staff referred the medicine, Concerta (18 mg, 36 mg, and 54 mg), to the Human Drug Advisory Panel ("HDAP") for its review during a meeting held on June 26, 2006. The HDAP was asked for its recommendation as to categorization and the appropriate comparable medicines and comparable dosage regimens for Concerta (18 mg, 36 mg, and 54 mg) and for each of the recommended comparable medicines.

25. In a report dated June 26, 2006, in accordance with subsection 3.1 of the Scientific Review Procedures referred to above, the HDAP recommended that Concerta (18 mg, 36 mg, and 54 mg) be classified as Category 1 new drug products as they represent new DINs of existing or comparable dosage forms of an existing medicine (methylphenidate). **(Attachment 10)**

26. Based on the scientific information available to the HDAP at the time of its review, and in accordance with subsection 8.3 of the Guidelines and section 9 of the Scientific Review Procedures above, the HDAP recommended the expansion of the therapeutic class to include Dexedrine and Adderall XR, in addition to Ritalin and Ritalin SR as appropriate comparators for the conduct of a TCC to Concerta, as all these medicines are in the same 4th level in the Anatomical Therapeutic Chemical ("ATC") Classification System and share the same indication as Concerta. **(Attachment 10)**

27. The HDAP recommended the following once daily comparable dosage regimens for Concerta (18 mg, 36 mg, and 54 mg) and the comparable medicines: **(Attachment 10)**

Concerta (methyl-phenidate) (mg)	**Ritalin (methyl-phenidate) (mg)**	**Ritalin SR (methyl-phenidate) (mg)**	**Dexedrine (dextro-amphetamine) (mg)**	**Adderall XR (mixed salts amphetamine) (mg)**
18	20	20	15	10
36	40	40	30	20
54	60	60	45	30

28. The HDAP selected comparable dosage regimens based on the available comparative clinical trials, product monographs, guidelines and review literature in accordance with subsection 10.3 of the Scientific Review Procedures referred to above.

29. Following the recommendations of the HDAP, Board Staff conducted IPC Tests for the 18 mg, 36 mg, and 54 mg strengths of Concerta, as per subsection 7.1 of the Guidelines, and the results, based on Janssen-Ortho's regulatory filings, indicated that during the introductory period, the prices of the 18 mg, 36 mg, and 54 mg strengths in Canada were below the highest price of the comparator countries listed in the Regulations. **(Attachment 11)**

30. Based on the recommendations of the HDAP, Board Staff also conducted TCC Tests, as per subsection 8.3 of the Guidelines, comparing each of the three strengths of Concerta (18 mg, 36 mg, and 54 mg) to Ritalin, Ritalin SR, and Dexedrine. Adderall XR (mixed salts amphetamine), one of the comparable medicines recommended by HDAP, was excluded from the TCC Tests, in accordance with Schedule 2- Therapeutic Class Comparison Test, as the 10 mg, 20 mg and 30 mg strengths of Adderall XR are being sold in Canada at prices Board Staff considers to be excessive and as such, these prices are the subject of an ongoing hearing before the Board. The results of the TCC Tests conducted by Board Staff **(Attachment 12)** were as follows:

    i) For the 18 mg strength, the introductory price exceeded the maximum non-excessive ("MNE") price of $0.5048 per tablet by more than 285% in 2003;

    ii) For the 36 mg strength, the introductory price exceeded the MNE price of $0.9672 per tablet by more than 165% in 2003;

iii) For the 54 mg strength, the introductory price exceeded the MNE price of $1.4508 per tablet by more than 115% in 2003.

The Maximum Non-Excessive Price for Concerta (27 mg tablet)

31. As per subsection 7.1 of the Guidelines, Board Staff conducted an IPC Test on the 27 mg strength of Concerta. The result indicated that, during the introductory period, the 27 mg strength was sold in only one country listed in the Regulations and the price in Canada was lower than the price in its sole comparator country. **(Attachment 13)**

32. As per subsection 8.3 of the Guidelines, Board Staff also conducted a RR Test comparing the 27 mg strength of Concerta to the 18 mg, 36 mg, and 54 mg strengths of Concerta. The results of the RR Test indicated that the introductory price exceeded the MNE price of $0.7772 per tablet by more than 190% in 2005. **(Attachment 14)**

Completion of the Investigation

33. By letter dated July 10, 2006, Board Staff advised Janssen-Ortho of the HDAP recommendations regarding Concerta (18 mg, 36 mg, and 54 mg). Board Staff also advised Jansen-Ortho that it had completed its investigation and the prices of the 18 mg, 36 mg, and 54 mg strengths of Concerta were excessive in the introductory period (August 2003 to December 2003) and continued to exceed the Guidelines in subsequent reporting periods. The price of the 27 mg strength of Concerta was also excessive in the introductory period (January 2005 to June 2005) and continued to exceed the Guidelines in subsequent reporting periods. **(Attachment 15)**

OTHER

34. Board Staff reserves the right to make such other allegations and submissions and introduce other additional documents as Board Staff may advise and the Board may permit.

35. Pursuant to section 86 of the *Patent Act*, a hearing shall be held in public unless the Board orders otherwise. Board Staff submits that any hearing conducted by the Board into the prices of Concerta should be held in public and, subject to orders of the Board, all information and documents filed should form part of the public record.

ORDER REQUESTED

36. It is respectfully submitted that there are grounds for the Board to conclude, pursuant to section 83 of the *Patent Act,* that Janssen-Ortho is selling or has sold the medicine known as Concerta in any market in Canada at prices which are or were excessive.

37. Board Staff seeks the issuance of an Order as against Janssen-Ortho, the terms of which would be as follows:

a) The MNE prices of Concerta (18 mg, 36 mg, and 54 mg tablets) in Canada for the period August 7, 2003 to December 31, 2006 inclusive shall be as follows:

Concerta 18 mg	Price/Unit
Reporting Period	MNE
Aug03-Dec03	$0.5048
Jan04-Dec04	$0.5139
Jan05-Dec05	$0.5255
Jan06-Dec06	$0.5341

Concerta 36 mg	Price/Unit
Reporting Period	MNE
Aug03-Dec03	$0.9672
Jan04-Dec04	$0.9846
Jan05-Dec05	$1.0069
Jan06-Dec06	$1.0233

Concerta 54 mg	Price/Unit
Reporting Period	MNE
Aug03-Dec03	$1.4508
Jan04-Dec04	$1.4769
Jan05-Dec05	$1.5103
Jan06-Dec06	$1.5349

b) The MNE price of Concerta (27 mg tablet) in Canada for the period January 8, 2005 to December 31, 2006 inclusive shall be as follows:

Concerta 27 mg	Price/Unit
Reporting Period	MNE
Jan05-Jun05	$0.7772
Jan05-Dec05	$0.7772
Jan06-Dec06	$0.7927

c) The MNE prices of Concerta (18 mg, 27 mg, 36 mg, and 54 mg tablets) in Canada in future years shall be calculated in accordance with the Guidelines.

d) In accordance with subsection 83(1) of the *Patent Act*, Janssen-Ortho shall cause the maximum prices at which it sells

Concerta in Canada to be reduced to the MNE prices effective on or before 30 days from the date of the Board's Order.

e) In accordance with subsection 83(2) of the *Patent Act*, Janssen-Ortho shall offset the amount of excess revenues estimated to have been derived by Janssen-Ortho from the sale of Concerta (18 mg, 36 mg, and 54 mg tablets) at excessive prices from August 7, 2003 until the date on which the price reductions referred to in paragraph d) above come into effect:

   i) With respect to the period from August 7, 2003 to December 31, 2005, Janssen-Ortho shall pay to Her Majesty in right of Canada, within 30 days of the date of the Board's Order, an amount equal to the amount set out in **Attachment 16**; and

   ii) With respect to the period from January 1, 2006 to the date on which the price reductions referred to in paragraph d) come into effect, Janssen-Ortho shall pay to Her Majesty in right of Canada, a further amount equal to the amount of the excess revenues estimated by the Board to have been derived by Janssen-Ortho from the sale of Concerta (18 mg, 36 mg, and 54 mg tablets) at excessive prices and make the payment within 30 days of receipt of a notification from the Board of its estimate of excess revenues based on the information filed in response to paragraph g) below;

f) In accordance with subsection 83(2) of the *Patent Act*, Janssen-Ortho shall offset the amount of excess revenues estimated to have been derived by Janssen-Ortho from the sale of Concerta (27 mg tablet) at an excessive price from January 8, 2005 until the date on which the price reduction referred to in paragraph d) above comes into effect:

   i) With respect to the period from January 8, 2005 to December 31, 2005, Janssen-Ortho shall pay to Her Majesty in right of Canada, within 30 days of the date of the Board's Order, an amount equal to the amount set out in **Attachment 16**; and

   ii) With respect to the period from January 1, 2006 to the date on which the price reduction referred to in paragraph d) comes into effect, Janssen-Ortho shall pay to Her Majesty in right of Canada, a further amount equal to the amount of the excess revenues estimated by the Board to have been derived by Janssen-Ortho from the sale of Concerta (27 mg

tablet) at an excessive price and make the payment within 30 days of receipt of a notification from the Board of its estimate of excess revenues based on the information filed in response to paragraph g) below;

g) Janssen-Ortho shall, within 30 days of the date of the Board's Order:

i) Notify federal/provincial/territorial ministers of health or their representatives and all customers of the price decreases as required by the Board's Order (a copy of which shall be included in such notifications) and the effective date of such price decreases;

ii) Submit copies of the above-noted notifications and any other notice to the Board; and

iii) Provide to the Board information concerning the quantity of Concerta (18 mg, 27 mg, 36 mg, and 54 mg tablets) sold and either the average price per package or the net revenue from sales of all four strengths of Concerta in Canada, in the same form as required by subsection 4(1) of the Regulations for the period January 1, 2006 to the date on which the price reductions referred to in paragraph d) come into effect.

Dated at Ottawa this 14th day of July 2006.

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LIST OF ATTACHMENTS

Attachment 1	AQPP- Guide du pharmacien propriétaire
Attachment 2	Product Monograph for Concerta dated June 18, 2003
Attachment 3	Notices of Compliance for Concerta – June 26, 2003 and June 30, 2004
Attachment 4	Canadian Patent No. 1,222,950 granted June 16, 1987 (abstract)
Attachment 5	Canadian Patent No. 2,265,668 granted August 23, 2005 and Canadian Patent No. 2, 264,852 granted November 1, 2005 (abstract)
Attachment 6	New Medicine Scientific Review and Review Sheets for New Medicines dated January 19, 2004
Attachment 7	Letter from Board Staff to Janssen-Ortho dated April 28, 2004
Attachment 8	Letters from Janssen-Ortho to Board Staff dated May 28, 2004 and November 29, 2004
Attachment 9	Letter from Board Staff to Janssen-Ortho dated November 14, 2005
Attachment 10	HDAP New Medicine Review dated June 26, 2006
Attachment 11	Concerta – International Prices (18 mg, 36 mg, 54 mg tablets)
Attachment 12	Concerta 18 mg, 36 mg, 54 mg-Therapeutic Class Comparison Tests
Attachment 13	Concerta- International Prices (27 mg tablet)
Attachment 14	Concerta 27 mg- Reasonable Relationship Test
Attachment 15	Letter from Board Staff to Janssen-Ortho dated July 10, 2006
Attachment 16	Concerta - Calculation of Excess Revenues