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 "Risperdal Consta"

STATEMENT OF ALLEGATIONS OF BOARD STAFF

INTRODUCTION

1. This Statement of Allegations results from an investigation by Board Staff into the prices of Risperdal Consta, a patented medicine sold in Canada by Janssen-Ortho Inc. ("Janssen-Ortho") in 25 mg, 37.5 mg, and 50 mg vials (DINs 02255707, 02255723, and 02255758). According to publicly available information in 2005, Janssen-Ortho sells Risperdal Consta at a price of $243.00 for the 25 mg vial, $364.50 for the 37.5 mg vial and $486.00 for the 50 mg vial. **(Attachment 1)**

THE MEDICINE

2. Risperdal Consta is a new formulation of an existing compound (risperidone) indicated for the management of the manifestations of schizophrenia and related psychotic disorders. **(Attachment 2)** It is a prolonged release suspension for intramuscular injection. Risperidone is in the 4th level N05AX of the Anatomical Therapeutic Chemical ("ATC") Classification System known as: Nervous System; Psycholeptics; Antipsychotics; Other antipsychotics. It is the 1st entry in this 4th level ATC class to be introduced in Canada.

3. Health Canada issued a Notice of Compliance for Risperdal Consta (25 mg, 37.5 mg, and 50 mg) on July 16, 2004. **(Attachment 3)**

4. Janssen-Ortho began selling Risperdal Consta (25 mg, 37.5 mg, and 50 mg) in Canada on September 21, 2004.

THE PATENTS

5. Canadian Patent No. 1,256,867 pertains to Risperdal Consta. **(Attachment 4)** This patent was granted to Janssen Pharmaceutica, naamloze vennootschap, Belgium, on July 4, 1989 and will expire on July 4, 2006.

6. Canadian Patent No. 2,251,987 also pertains to Risperdal Consta. **(Attachment 5)** This patent was granted to Alkermes Controlled Therapeutics Inc. II, US and Janssen Pharmaceutica, naamloze vennootschap, Belgium, on May 10, 2005 and will expire on May 6, 2017.

7. Janssen-Ortho is the licensee of the patents referred to above and as such is, for the purposes of the Patented Medicine Prices Review Board ("PMPRB"), considered as the Canadian patentee.

THE REGULATORY FILINGS

8. In accordance with the *Patented Medicines Regulations, 1994* ("Regulations"), Janssen-Ortho filed price and sales information for Risperdal Consta on November 19, 2004, for the first 30 days of sales of Risperdal Consta (25 mg, 37.5 mg, and 50 mg) in Canada, namely the period from September 21, 2004 to October 20, 2004 and has since continued to file its price and sales information as per the Regulations.

APPLICABLE GUIDELINES

9. Following the procedures outlined in the PMPRB's Compendium of Guidelines, Policies and Procedures for new medicines, Board Staff referred the medicine Risperdal Consta to the Human Drug Advisory Panel ("HDAP") for its review during a meeting held on February 17, 2005. The HDAP was asked for its recommendation as to the categorization of the medicine, the appropriate comparable medicines, and comparable dosage regimens for the comparable medicines.

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. In a report dated February 17, 2005, the HDAP recommended that Risperdal Consta (25 mg, 37.5 mg, and 50 mg) be classified as Category 3 new drug products as they represent new DINs of a non-comparable dosage form of an existing medicine that provide moderate, little or no therapeutic advantage over other comparable therapies for the management of the manifestations of schizophrenia and related psychotic disorders. **(Attachment 6)**

Comparable Medicines and Dosage Regimens

12. With respect to the selection of comparable medicines, 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.

13. Based on the scientific information available to the HDAP at the time of its review, the HDAP recommended the following comparable medicines and dosage regimens:

Drug	Comparable Dosage Regimens	
Risperdal Consta	25 mg q 2 weeks	50 mg q 2 weeks
Risperdal oral (risperidone)	3 daily	6 daily
Zyprexa/Zyprexa Zydis oral (olanzapine)	10 daily	20 daily
Seroquel oral (quetiapine)	300 daily	600 daily
Fluxanol injection (flupentixol decanoate)	40 q 2 weeks	80 q 2 weeks
Modecate injection (fluphenazine enanthate)	50 q 2 weeks	100 q 2 weeks
Haloperidol injection	200 q 4 weeks	400 q 4 weeks
Piportil L4 injection (pipotiazine palmitate)	125 q 4 weeks	250 q 4 weeks
Clopixol depot (zuclopenthixol)	200 q 2 weeks	400 q 2 weeks

14. The HDAP recommended the exclusion of Clozaril (clozapine) for the purpose of this review as this drug product is reserved for patients who do not respond to other anti-psychotics and its use has been related to significantly higher risks in terms of side effects.

15. Due to the difficulty in establishing a comparable dosage regimen for the 25 mg and 37.5 mg dose of Risperdal Consta, the HDAP recommended that the comparable dosages for the 25 mg be derived on a proportional equivalence basis to the 50 mg dose and the 37.5 mg dose be compared on a mg to mg basis to the 25 mg and 50 mg doses.

The Maximum Non-Excessive Price

16. Chapter 1 - Excessive Price Guidelines ("the Guidelines") sets out the appropriate price tests for a Category 3 new drug product as follows:

    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.

8.5 Category 3 New Drug Products

In addition to the Guideline applicable to all patented drug products detailed in Section 7, the introductory price of a Category 3 new drug product will be presumed to be excessive if it exceeds the prices of all of the comparable drug products based on a Therapeutic Class Comparison Test (Schedule 2).

8.6 When it is inappropriate or impossible to conduct a Therapeutic Class Comparison Test, Board Staff will give primary weight to the median of the international prices identified in an International Price Comparison Test (Schedule 3) to determine if the introductory price of the new DIN is excessive.

8.7 Unless the introductory price of the new DIN is outside the Guidelines, it will establish the benchmark price. If the introductory price exceeds the Guidelines, the maximum non-excessive price will establish the benchmark price. Thereafter, the price will be reviewed using the test applicable to existing DINs.

17. As per the above Guidelines, Board Staff conducted International Price Comparison ("IPC") Tests on the 25 mg, 37.5 mg, and 50 mg vials of Risperdal Consta and the results indicated that during the introductory period, September 2004 to December 2004, the 25 mg, 37.5 mg, and 50 mg vials were sold in 5 countries (Germany, Sweden, Switzerland, UK and US) and Canada ranked 2nd highest above the median. **(Attachment 7)**

18. Board Staff also conducted Therapeutic Class Comparison ("TCC") Tests **(Attachment 8)** on Risperdal Consta 25 mg and 50 mg vials and a Reasonable Relationship ("RR") Test **(Attachment 9)** on Risperdal Consta 37.5 mg vial. The results of these tests were as follows:

i) For the 25 mg strength of Risperdal Consta, the results of the TCC Test indicated that the introductory price exceeded the maximum non-excessive ("MNE") price of $94.5000 per vial by more than 155% for the period September 2004 to December 2004.

ii) For the 50 mg strength of Risperdal Consta, the results of the TCC Test indicated that the introductory price exceeded the MNE price of $189.0000 per vial by more than 155% for the period September 2004 to December 2004.

iii) For the 37.5 mg strength of Risperdal Consta, the results of the RR Test indicated that the introductory price exceeded the MNE price of $141.7500 per vial by more than 155% for the period September 2004 to December 2004.

19. By letter dated April 13, 2005, Board Staff advised Janssen-Ortho of the results of the price review of Risperdal Consta (25 mg, 37.5 mg, and 50 mg) and that an investigation was commenced into the introductory price of Risperdal Consta. **(Attachment 10)**

20. In response, Janssen-Ortho filed additional materials on May 6, 2005 with Board Staff, reiterating its position that the prices of Risperdal Consta are not excessive. **(Attachment 11)**

21. Following its review of Janssen-Ortho's submission, Board Staff advised Janssen-Ortho by letter November 16, 2005 that it had completed its investigation and that the prices of Risperdal Consta continued to be excessive. **(Attachment 12)** In fact, based on publicly available information in 2005, the prices of Risperdal Consta for all three DINs remain 2nd highest of the comparator countries listed in the Regulations and exceed the Median International Prices.

OTHER

22. 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.

23. 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 price of Risperdal Consta 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

24. 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 Risperdal Consta in any market in Canada at prices which are or were excessive.

25. 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 Risperdal Consta in Canada for the period September 21, 2004 to December 31, 2005 inclusive shall be as follows:

Risperdal Consta 25 mg	Price/Unit	Risperdal Consta 37.5 mg	Price/Unit	Risperdal Consta 50 mg	Price/Unit
Reporting Period	MNE	Reporting Period	MNE	Reporting Period	MNE
Sep04-Dec04	$94.5000	Sep04-Dec04	$141.7500	Sep04-Dec04	$189.0000
Jan05-Dec05	$96.2010	Jan05-Dec05	$144.3015	Jan05-Dec05	$192.4020

b) The MNE prices of Risperdal Consta in Canada in future years shall be calculated in accordance with the Guidelines;

c) In accordance with subsection 83(1) of the *Patent Act*, Janssen-Ortho shall cause the maximum prices at which it sells Risperdal Consta in Canada to be reduced to the MNE prices effective on or before 30 days from the date of the Board's Order;

d) 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 Riserdal Consta at excessive prices from September 21, 2004 until the date on which the price reductions referred to in paragraph c) above come into effect:

i) With respect to the period from September 21, 2004 to June 30, 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 13**; and

ii) With respect to the period from July 1, 2005, to the date on which the price reductions referred to in paragraph c) 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 Risperdal Consta 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 e) below.

e) 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 Risperdal Consta sold and either the average price per package or the net revenue from sales of Risperdal Consta in Canada, in the same form as required by subsection 4(1) of the Regulations for the period July 1, 2005, to the date on which the price reductions referred to in paragraph c) come into effect.

Dated at Ottawa this 18th day of January 2006.

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LIST OF ATTACHMENTS

Attachment 1	AQPP - Guide du pharmacien propriétaire October 2005
Attachment 2	Product monograph for Risperdal Consta
Attachment 3	Notice of Compliance for Risperdal Consta – July 16, 2004
Attachment 4	Canadian Patent No. 1,256,867 granted July 4, 1989
Attachment 5	Canadian Patent No. 2,251,987 granted May 10, 2005
Attachment 6	HDAP New Medicine Review dated February 17, 2005
Attachment 7	Risperdal Consta - International Prices
Attachment 8	Risperdal Consta - Therapeutic Class Comparison Tests
Attachment 9	Risperdal Consta - Reasonable Relationship Test
Attachment 10	Letter dated April 13, 2005 from Board Staff to Janssen-Ortho Inc.
Attachment 11	Letter and supplementary information dated May 6, 2005 from Janssen-Ortho Inc. to Board Staff
Attachment 12	Letter dated November 16, 2005 from Board Staff to Janssen-Ortho Inc.
Attachment 13	Risperdal Consta - Calculation of Excess Revenues