June 2006 INOtherapy – manufactured by INO Therapeutics Inc.

This Advisory Note provides information on the PMPRB's price review process and the patented medicine INOtherapy.

The mandate of the Patented Medicine Prices Review Board (PMPRB) is two-fold:

Regulatory – To protect consumer interests and contribute to Canadian health care by ensuring that prices charged by manufacturers for all patented medicines sold in Canada, under prescription or over the counter, are not excessive.

Reporting – To contribute to informed decisions and policy making by reporting on pharmaceutical trends and on the R&D spending by pharmaceutical patentees.

The PMPRB is a quasi-judicial tribunal that carries out its mandate independently of other bodies such as Health Canada, which approves drugs for safety and efficacy, and public drug plans, which approve the listing of drugs on their respective formularies for reimbursement purposes.

It is mandated to review the prices being charged by manufacturers of patented drugs for compliance with the *Patent Act*. If, following a public hearing, the Board finds that a price is excessive it may order a reduction in the price to a non-excessive level and the offset of excessive reveues.

Price Review Process
In accordance with the *Patent Act*, the Board has established excessive price guidelines in consultation with provincial ministers of health, consumer groups, the pharmaceutical industry and other stakeholders. The determination of whether a price is "excessive" is based on the factors listed in the *Patent Act*, which include prices of other drugs within the therapeutic class and prices at which the drug is sold in other countries.

The general effect of the Guidelines is to limit the prices of most new patented drugs to the highest price of comparable drugs on the Canadian market that treat the same condition or disease; in the case of a breakthrough drug, that provides substantial improvement over existing available therapies. the price in Canada may not exceed the median of the prices for the same drug in seven other industrialized countries specified in the *Patented Medicines Regulations, 1994* (Règlement).

The PMPRB also reviews any subsequent price increases, to ensure that prices of patented medicines are, at no time, excessive. The PMPRB reviews the price of every patented medicine for the duration of any patent that pertains to the medicine.

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INOtherapy

The price of INOtherapy has been under the Board's jurisdiction since September 2004, when it was first sold under Health Canada's Special Access Program (SAP).

Indication

- INOtherapy treats infants who suffer from respiratory failure and is administered in hospitals exclusively.

Drug approval (Health Canada)

- INOtherapy is a complete delivery system, comprised of several components: 1) the ingredient – nitric oxide; 2) the ventilator to deliver the product; 3) the services of a therapist to administer the product; and, 4) other related services.

- INOtherapy received its Notice of Compliance (NOC) from Health Canada on September 23, 2005.

Patent issuance (Canadian Intellectual Property Office; Industry Canada)

- INOtherapy is a patented drug product. The first patent on INOtherapy was issued in June 1999 relating to the indication of nitric oxide for infants in respiratory failure and to the delivery system. INO Therapeutics is the Canadian patentee.

Price Review

- At the time of introduction of INOtherapy, nitric oxide (the drug component) was already being sold for the same indication. INO Therapeutics did not prevent such sales from the time of the issuance of the patent until the issuance of the Notice of Compliance (NOC). The PMPRB was informed that hospitals were notified that nitric oxide for respiratory failure in infants, as sold to hospitals by other manufacturers would no longer be offered on the Canadian market once the NOC for INOtherapy was issued.

- The PMPRB reviewed the price of INOtherapy at the time of its first sale (i.e. 2004) and determined that the price was within the Guidelines. The Canadian price was the lowest of the seven comparator countries in which it was sold.

- INO Therapeutics filed its 2005 price and sale information pursuant to the Regulations. The data were examined and the price continued to be within the Guidelines. The Canadian price remains the lowest in the seven comparator countries in which it is sold.

- At the end of July, INO Therapeutics, as all other patentees, will next submit price and sale information for the review by the PMPRB to ensure that the prices remain within the Board's Excessive Price Guidelines.

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