April 27, 2009

Dr. Brien Benoit
Chairperson
Patented Medicine Prices Review Board
Box L40
Standard Life Centre
333 Laurier Avenue West, Suite 1400
Ottawa, Ontario K1P 1C1

Re: Response to Draft Revised Excessive Price Guidelines

Dear Dr. Benoit:

I am writing to you regarding the PMPRB's Draft Revised Excessive Price Guidelines released in March 2009 (the "Draft Guidelines"). AMGEN Canada Inc. ("AMGEN") appreciates the opportunity to provide comment on these matters. AMGEN's comments on each issue will be addressed individually.

Levels of Therapeutic Improvement

As noted in AMGEN's response to the Draft Guidelines released in August 2008, AMGEN is of the view that there is no need for different categories of drugs and that a single definition of excessive pricing should apply to all new patented medicines (see discussion below concerning introductory price tests).

Subject to the foregoing comment, AMGEN believes that the creation of four levels of therapeutic improvement for new patented medicines versus the three levels employed under the current Excessive Price Guidelines, represents a positive development recognizing incremental innovation.

Similar to our previous response to the August 2008 Draft Guidelines, the primary concern with the four categories of improvement is the lack of a clear definition of a "substantial improvement" versus a "moderate improvement". This will create uncertainty for patentees, particularly those like AMGEN that focus their research efforts on developing medicines for serious and grievous illnesses. One example of a new medicine that should represent a substantial therapeutic improvement is that of a new medicine that is being compared to therapies that lack efficacy and safety data from phase III clinical trials and/or are not approved for the primary indication of the new medicine.

Rather than providing clear definitions, the Draft Guidelines indicate that a variety of primary and secondary factors will be considered in categorizing drugs. It is also stated in the Draft Guidelines that secondary factors do not carry sufficient weight to move the

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level of therapeutic improvement from moderate to substantial improvement. The Working Group on Therapeutic Improvement organized by the PMPRB did not place such a limit on the value of other clinical and/or economic factors when determining if a new medicine is a substantial vs. moderate improvement. It should be clarified as to why the recommendations of the working group were not implemented, and such a restriction was placed in the Draft Guidelines.

To reduce the administrative burden on patentees, AMGEN believes there is no need for further scientific review by HDAP regarding the level of therapeutic improvement if Health Canada has already conducted its assessment and made the determination that a new therapy fulfills an unmet medical need and is granted a priority review. Any new therapy that is granted a priority review by Health Canada should automatically be categorized as a "substantial improvement" or "breakthrough".

Introductory Price Tests

It is AMGEN's position that the price of any new patented medicine should only be considered excessive if its price is higher than the prices of the same medicine in all comparator countries and is higher than the CPI-adjusted price of local comparator medicines. This single test would determine a level of excessive pricing that is simple and clear for patentees and all stakeholders to understand. AMGEN submits that prices of patented medicines are likely to be kept below this threshold, in any event, to ensure formulary inclusion, given the requirement that value for money be demonstrated to payers. Competitive pressures will also result in prices below this threshold.

With regards to conducting a Therapeutic Class Comparison (TCC) test to determine the Maximum Average Potential Price (MAPP) of a new medicine, the Draft Guidelines note that Board Staff will endeavour to find a publicly available price that is close to the Non-Excessive Average Price (NEAP) of the comparator medicines. Given the pending requirement to report and include a broad range of benefits into the average price calculations of a medicine, it is reasonable to expect a much higher degree of variability will exist between list price and the NEAP than was the case in the past. The fact that the NEAP is protected by Section 85 of the Patent Act, and is therefore not publicly disclosed, puts the patentee of a new medicine in the impossible position of having to make investment and other critical business decisions in the face of greatly increased uncertainty about its own MAPP. This will inevitably limit investment and potentially delay or discourage altogether manufacturers from launching new products in Canada.

AMGEN proposes that the MAPP be determined by the highest publicly available list price, and allow the patentee to work with its customers to determine what benefits should be offered. Limiting the price of the new medicine to the highest publicly available price would fulfill the mandate of PMPRB and would allow patentees the flexibility to work with its customers to define the value of new medicines.

With regards to price tests for slight to no improvement products the Draft Guidelines state, "It is possible that the HDAP may determine that a new patented drug providing slight or no improvement has no comparable drug products. In such exceptional cases, the introductory price(s) of the new drug product will be presumed to be excessive if the National Average Transaction Price or any Market-Specific Average Transaction Price exceeds the lower of:

(a) The lowest non-excessive price of the superior drug products identified pursuant to subsection 8.10 of Chapter 1 based on a TCC test (see Schedule 3), and
(b) The median international price determined by the Median International Price Comparison test (see Schedule 5)."

If HDAP can not identify a comparable drug product, it is then not appropriate to conduct a TCC test. For a TCC test to be conducted, there must be comparable drug products with the same indication, in which case using the highest priced comparator is reasonable as is stipulated in the current Guidelines. If no comparable drug products can be identified, AMGEN supports use of the median of the IPC test.

International Therapeutic Class Comparison Test

AMGEN supports the use of the International Therapeutic Class Comparison Test (ITCC) as a method of dispute resolution between patentees and the PMPRB, provided that it is applied using the same methodology as the TCC. Namely that the highest price comparator within the group be used as the reference for determining the MAPP. The PMPRB proposes to use the median price or median ratio in the ITCC while allowing the inclusion of the price of generic drugs is untenable. Although PMPRB has modified the test such that it includes only those generic products sold by the same manufacturer in Canada and the reference country, the test gives rise to enormous complexity related to significant year over year variations in this median reference that might result from isolated patent or other issues in foreign markets.

In addition, whether or not generic versions of the comparator are available in Canada should be an irrelevant consideration for the ITCC. A court decision that authorizes the grant of an NOC to a company that markets a generic or biosimilar (i.e., subsequent entry biologic) product under the *Patented Medicines (Notice of Compliance) Regulations* is not a final determination of whether that company's product will infringe an innovator's patent(s). There are now examples where generic companies are prohibited from marketing their products due to patent infringement even though they were previously granted NOCs. The temporary presence of generic or biosimilar versions of comparators in Canada will artificially reduce the comparator price in the ITCC analysis outlined in the Draft Guidelines. Innovators should not be penalized in setting a reasonable price for their products simply because generic companies may somehow obtain approval, if only temporary, for their versions of comparator products.

To address the concerns noted above, AMGEN advocates that the top of the ITCC be used rather than the median.

De-Linking of the ATP from the NEAP

The proposal for a de-linking methodology is a positive step forward compared to the current CPI-adjustment methodology. However, of concern with the DIP methodology as proposed is the threshold to which a price may return after demonstrating termination of a benefit. As proposed by the PMPRB, this is to be calculated based on market level pricing (i.e. the ATP may only rebound to the NEAP prior to a benefit being offered in that specific market excluding allowable CPI increases). This is particularly problematic

in markets (i.e. provinces) where a substantial proportion of the business is subject to a single tender. For example, if a vendor commits to a fixed price for the term of the contract in one province and at the end of that term, loses the contract to a competitor through a subsequent tender, they are unable to restore their price of the remaining business in that market to the level of other non-tender markets that have taken allowable price increases during that period. Subsequent to losing a tender, it is reasonable that a patentee be able to sell at the same price in the tender market as all other markets.

AMGEN recommends that the market specific ATP where benefits had been offered be allowed to increase up to the highest previous ATP with the inclusion of the increase in the Consumer Price Index in that market without being presumed to be excessive.

The proposed methodology still links the NEAP to a previous non-excessive net ATP. Instead, AMGEN proposes a true "de-linking" of the ATP from the maximum price a patentee may sell at. A true "de-linking" of the ATP and the maximum price a patentee may sell at requires a change in the CPI-Adjustment Methodology whereby the introductory maximum price is adjusted for changes in CPI annually without reference to the prior years ATP net of benefits.

As noted by AMGEN previously, there are several operational issues associated with the methodology proposed by the PMPRB. Fluctuations in ATPs due to the granting and expiry of multiple benefit programs offered to different classes of trade customers in different markets will further tax the resources of patentees who will need to justify these fluctuations and the PMPRB that will need to investigate them. As noted in AMGEN's response to the Draft Guidelines released in August 2008, many benefits are not offered on a DIN or even single product level basis and that the realization of a benefit often does not correspond to PMPRB reporting periods, which further complicates the application of the de-linking methodology. Clarification is required as to how such benefits are to be handled to provide patentees with greater certainty in the price review process.

If the Draft Guidelines are implemented as proposed AMGEN will be required to employ significant incremental resources solely for PMPRB reporting purposes. These will include additional human resources as well as financial reporting system changes. Furthermore, it is expected that the PMPRB will be required to conduct more investigations and hearings, due to the complexity of what has been proposed.

"Any" Market Price Review

AMGEN's position is that the current policy of the PMPRB is sufficient with respect to reviewing prices in "any market", as there does not appear to have been excessive pricing when prices were reviewed in this manner in PMPRB's Discussion Guide released in May 2006. It was communicated by Board Staff in a teleconference with patentees on April 8, 2009 that introductory price reviews will be done by class of trade and by province, but not by class of trade and province combined (i.e. hospitals in Alberta). However, on page 18 paragraph 2.2 of the Draft Guidelines it states "The PMPRB may review the price of any new patented drug product in any market in Canada (including for class of customer in a province/territory)". This appears to contradict what was communicated during the teleconference. AMGEN proposes that

language clarifying the PMPRB's position noted in the teleconference be included in the Guidelines.

AMGEN supports the change from the Draft Guidelines released in August 2008 in which the calculation of excess revenues is based on the average price across all markets in Canada.

Re-Setting of the NEAP

The provision in the Draft Guidelines that the NEAP for medicines sold through a Special Access Program (SAP) can only be reset based on "cost of making and marketing" arguments upon receiving NOC from Health Canada is too restrictive. As has been noted in AMGEN's past submission, patentees often receive requests from health care providers and patients to make drugs available under a SAP at little or no charge prior to drug approval. The Draft Guidelines will force patentees to sell medicines requested through SAP at full price. Given that public and private insurers are highly unlikely to pay for medicines prior to issuance of a NOC from Health Canada, this will ultimately limit patient access to medicines through SAP. AMGEN believes it is not the intent of PMPRB to limit patient access to new medicines, and therefore recommends that the Draft Guidelines be revised to allow re-setting the NEAP for medicines sold under SAP upon receiving an NOC.

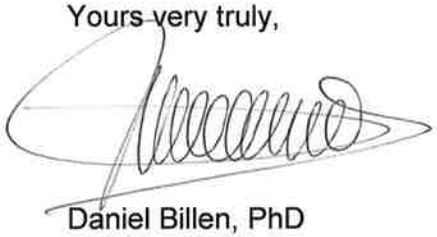
Conclusion

AMGEN appreciates the opportunity to comment on the Draft Guidelines. In summary, while we believe that some of the modifications clarify and improve upon the previous version, we remain deeply concerned about specific provisions of the Draft Guidelines which will greatly increase the level of business uncertainty facing our industry and add substantially to the resource burden on individual patentees. Most troublesome is the proposal that PMPRB will use information available only to itself in determining the MAPP for a new patented medicine, making it virtually impossible for the patentee to perform the most basic commercial assessments in advance of investment decisions. Of particular concern for patients is the provision that products sold through SAP cannot have their NEAP re-set due to the issuance of an NOC by Health Canada, which will limit access to medicines provided at little or no cost for patients who may have few therapeutic options left.

We trust that our comments will be carefully considered and will have a positive influence on the final guidance document. We would urge the PMPRB to extend significantly the timeline for implementation to allow patentees the opportunity to make the adjustments necessary to comply with any changes that are ultimately adopted. AMGEN recommends implementation of the Draft Guidelines in mid to late 2010.

We hope to work with the PMPRB to ensure that changes to the Draft Guidelines respect the PMPRB's mandate under the *Patent Act*, that foster innovation, and do not inhibit the biotechnology industry's ability to bring innovations to market in Canada and ensure patients have access to important new medicines.

Yours very truly,



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