Submission from Amgen Australia to the Senate Standing Committee for Community Affairs' Inquiry into the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2007*
13 June 2007

The purpose of this submission is to further clarify Medicines Australia's submission to the Senate Standing Committee for Community Affairs' Inquiry into the *National Health Act (Pharmaceutical Benefits Scheme) Bill 2007* ("the PBS Reform Bill") at Section 4 relating to Biopharmaceutical Products. We support Medicines Australia's submission, and the purpose of this submission is to complement and provide further clarification of it in one part only.

Amgen Australia ("Amgen") is the world's largest biotechnology company and one of a small number of global companies focused on pioneering the development of biological medicines to treat rare and serious illnesses. Amgen has a strong presence in Australia and this year alone will invest approximately $41 million in Australia in researching and developing medicines for grievous illness including cancer, osteoporosis and kidney disease.

Like Medicines Australia, Amgen is concerned to clearly establish to the Committee that due to the complexities inherent in the manufacture of biopharmaceutical products, the relatively simple processes governing approval of generic small molecule drugs are inadequate to be applied to biosimilars. This has implications not only for the safety of patients using biotechnology products but also for the remuneration of biotechnology products.

As stated in Section 4 of Medicines Australia's submission, biopharmaceutical products (biologics) have unique characteristics because of their high molecular weights, their complex three-dimensional structures, the complexity of their manufacturing processes by living organisms and the dependence of biological activity on reproducibility of the production process.

The reference in the PBS Reform Bill to "bioequivalent" is critical to the fundamental operation of the proposed reforms given the reference pricing links proposed, as it dictates movement of a drug from F1 to F2 (with the exception of combination products). The PBS Reforms propose that:

- There will be no ongoing price link across medicines listed on F1 and those listed on F2;
- Reference pricing will continue to apply between medicines that are linked within reference pricing groups on F1.

It is critical that at no stage is "biosimilar" assumed to equal "bioequivalence" in the movement of a drug from F1 to F2.

There is currently no agreed simple definition globally of the term "biosimilar", it is not yet well understood and it has not been explicitly defined in the PBS Reform Bill. The word "biosimilar" has different interpretations by different groups. While some would use this word to state that two products have the same biological action, others may inappropriately use this word to define two products that have both the same biological action and are also substitutable at the individual patient level.

The application of the PBS Reform legislation needs to ensure that:

- a new biosimilar product is both biosimilar and deemed by the TGA to be substitutable before this is used as the basis for determining whether it would be interchangeable at pharmacy level; or
- that the triggering of price reductions on entry of a biosimilar, ie, its movement from F1 to F2, only applies to the biosimilar and its reference innovator if not deemed substitutable by the TGA, and not to the other products in the therapeutic class. This is why the use of the word biosimilar requires clear definition.

The TGA has complex guidelines for the evaluation and registration of biosimilar products, in contrast with the more straightforward bioequivalence required to be demonstrated in relation to generic products involving small molecules. It is critical to understand that TGA registration of biosimilar products only implies that the product is safe and effective compared to the innovator biological product, not that it is likely to be "interchangeable" with the innovator product.

In this regard, the TGA has adopted European (EMEA) Guidelines for the evaluation of similar biological medicinal products. The relevant EMEA Guideline on Similar Biological Medicinal Products (CHMP/437/04) states, in the last paragraph of section 2.1,"It should be recognised that, by definition, similar biological medicinal products are not generic medicinal products, since it could be expected that there may be subtle differences between similar biological medicinal products from different manufacturers or compared with reference products, which may not be fully apparent until greater experience in their use has been established."

Amgen accepts that the registration of biosimilar products should be used as a trigger for the cost savings identified in the PBS Reform Bill. It is entirely appropriate that cost savings should be applied between a biosimilar and its reference product. Inappropriate interchangeability/substitution driven by cost mechanisms, however, should be avoided due to risks to patient safety. This would align with PBS reforms, TGA and global guidelines. The abovementioned EMEA guideline, for instance, specifically cautions against assuming therapeutic interchangeability where, for example, two biosimilar products would be placed in F2.

While the Government has already proposed sensible amendments to the legislation with regard to biosimilars, Amgen believes there is need for further clarification in relation to this issue to ensure the implementation of the legislation is consistent with the TGA's regulatory processes in determining if a second biological product is 'biosimilar' to an original biological product.

Amgen therefore recommends that, rather than suggesting actual amendments in the PBS Reform Bill at this late stage in the Bill's passage through Parliament, to instead clarify this issue through regulation. This could be done by a deeming provision being included in the regulations to assist in linking the existing TGA regulatory framework for biosimilar products with the PBS reform legislation.

Recommendations

1. That a deeming provision be included in the regulations to assist to link the existing regulatory framework for biosimilar products with the PBS reform legislation, and that, to this effect, the following wording be adopted as a Regulation:

   "(1) For the purposes of Part VII of the *National Health Act,* a pharmaceutical item may be regarded as bioequivalent or biosimilar to another pharmaceutical item if

it meets the requirements of bioequivalence or biosimilarity as specified in guidelines relating to the approval of therapeutic goods for marketing in Australia applicable to, whether generally or specifically, the kind of drug contained in the pharmaceutical items.

(2) In determining whether two pharmaceutical items meet the requirements of bioequivalence or biosimilarity, the Pharmaceutical Benefits Advisory Committee may seek and have regard to the advice, if any, of the Therapeutic Goods Administration or any of its committees.

2. That the TGA is defined as the authority with responsibility for evaluating and deciding on interchangeability/substitutability in the case of biosimilars, as it currently does for small molecule generic medicines.