MEMORANDUM

From: A. Padilla, QSD

To: Secretary, Expert Committee on the Selection and Use of Essential Medicines

Date: 20 February 2007

Our ref:

Attention:

20/02/2007

Your ref: E/19/81/15

Through: Acting Coordinator, QSD
Director, PSM 21/2/07 seen/

Originator:

Subject: RE-INSTATEMENT OF POLYVALENT HUMAN IMMUNOGLOBULINS IN THE WHO MODEL LIST OF ESSENTIAL MEDICINES

In response to your memorandum requesting comments to the Application for the Inclusion of Polyvalent Human Immunoglobulins in the WHO Model List of Essential Medicines, please find attached PSM's comments.

With our apologies for the delay.

ENCL. (1)

Comments to support the "Application for the re-instatement of Polyvalent Human Immunoglobulin in the WHO Model List of Essential Medicines"

The following are the comments from the Department of Medicines Policy and Standards (PSM) in support of the addition of the Polyvalent Human Immunoglobulin to the WHO Model List of Essential Medicines:

Polyvalent human immunoglobulins, the topic of this application, are prepared by fractionation of human plasma pools derived from at least one thousand healthy whole blood donors or plasmapheresis donors. The immunoglobulin fractions contain antibody specificities, which mostly belong to the class of Immunoglobulin G, covering the entire range of infectious pathogens to which the donor populations have been exposed.

During the past years the use of immunoglobulin therapy in patients with primary immunodeficiency (PID) syndromes has been reviewed quite extensively. The general opinion of these reviews is that, although for ethical reasons no randomised clinical trials have been performed, the administration of polyvalent human immunoglobulin is standard treatment of primary immunodeficiences. No alternative treatment to polyvalent immunoglobulin is available for most, if not all, of these diseases. The evidence that such treatment is able to reduce the incidence and severity of bacterial and viral infections in these disorders is derived from studies comparing different dosage schemes. The studies in which the efficacy and safety of polyvalent immunoglobulin has been evaluated include children and adults, both sexes and various populations around the world. Stringent regulatory authorities have approved primary immunodeficiency as an indication for polyvalent human immunoglobulins.

The re-instatement of the Polyvalent Human Immunoglobulin to the WHO Model List of Essential Medicines, would not only facilitate the possibilities of diagnosis and treatment of immunodeficient patients in developing countries but, in addition, would contribute to improving access of developing countries to a range of blood derived medicinal products, already on the Model List, which are used for replacement therapy in a variety of life-threatening diseases. The following are reasons in support of this consideration:

1. Interdependence of the manufacturing processes for blood derived medicinal products.

Several blood derived medicinal products are already on the Essential Medicines List: e.g. blood coagulation factors and specific immunoglobulins. Each of these medicinal products is obtained from the fractionation of plasma pools, as is the proposed polyvalent human immunoglobulin, and the production processes are therefore interdependent. The availability of such interrelated products will be improved when immunoglobulin will be reinstated to the list, providing further justification to improving quality and safety of plasma for fractionation worldwide.

2. Cost-effective preparation of a range of essential blood derived products

The addition of the polyvalent human immunoglobulin, a product considered to be in shortage worldwide, would stimulate to increase the fractionation of plasma available from developing countries (as a by-product of the collection of whole blood needed to ensure the local supply of red cell concentrates), either through existing local or regional plants or through contract-fractionation programs, provided this plasma can meet the WHO Recommendations (1) for the production, control and regulation of plasma for fractionation.

Furthermore, the use of local plasmas would allow the preparation of the best suited human polyvalent immunoglobulins, able to fight the local pathogens affecting immunodeficient patients. In addition, the availability of locally collected plasma that would meet GMP principles for fractionation, will also contribute to enhance the quality of safety of the other blood-derived products such as red cell, platelets and plasma for transfusion. When sustained demand from the developing world would be assured, Member States would b stimulated to improve the quality of blood establishments in their countries.

3. Global safety regulations for the manufacture of blood derived products

In spite of what is mentioned in the application, a WHO batch release system for blood products does not exist. The inclusion of the Polyvalent Human Immunoglobulin would certainly help the WHO plans of action when having this preparation in the Essential Medicines List.

The inclusion of this product under the category of blood products within the WHO Model List would draw the attention of Member States to the need for improving safety regulations in the manufacturing of blood products and the regulation of blood establishments. Since several years manufacturers need to comply with a number of regulatory guidelines for the collection and control of starting materials, testing of viral markers, and the manufacture of plasma derivatives, including the implementation of virus inactivation and removal procedures. Since 1994, no virus transmissions have been reported, following treatment with licensed virally-inactivated Immunoglobulins.

Pharmacovigilance systems should however be implemented in developing countries and progress in the implementation of viral inactivation and removal technologies need to be ensured in all fractionation facilities at global level. WHO Guidelines (2) on viral inactivation and removal procedures have been published to help manufacturers and regulators with their implementation and enforcement.

4. Diagnosis of PIDs

PIDs are often not diagnosed in most of the developing world. The awareness about a well established therapy that can save lives and prevent morbidity can have a significant

impact on public health. Re-instatement on the list, with the likely associated increase in affordable availability of immunoglobulin, as described above, will encourage diagnosis.

In summary, the inclusion of this product to the WHO Model List of Essential Medicines will undoubtedly contribute to increasing the standard and safety of care to patients and, to improving manufacturing technologies and quality and safety of blood products worldwide.

References:

(1) WHO Recommendations for the Production, Control and Regulation of Human Plasma for Fractionation , Geneva Switzerland. October 2005. Available on the internet at http://www.who.int/bloodproducts

(2) WHO Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products. Technical Report Series (TRS) No. 924, Annex 4