The Secretary of the 19th Expert Committee on Selection and Use of Essential Medicines
Office of the EML Secretariat
Medicine Access and Rational Use (MAR)
Department of Essential Medicines and Health Products
World Health Organization
20 Avenue Appia
CH-1211 Geneva 27
Switzerland
emlsecretariat@who.int

21 March 2013

Dear Sir/Madam

Subject: Comments on Expert Review No. 2 of the Application for the Addition of Whole Blood and Red Blood Cells to the WHO Model Essential Medicines List and the WHO Model Essential Medicines List for Children

We refer to the thorough and balanced analysis made by Expert Reviewer 2 on the application and responses to the application, which we broadly support, and wish to amplify some points further. We also refer to our previous comments dated 19 February 2013 and 28 February 2013. The following are some of the points that we would like to highlight:

1. First paragraph in page 1

The Expert reviewer 2 mentions this application follows the discussion in the European Committee on Blood Transfusion of the European Directorate for Quality of Medicines and Health Care (CD-P-TS/EDQM). However, we wish to bring attention to the personal comments by Dr Rut Norda, who at that time was serving as the Chair of the CD-P-TS/EDQM, at http://www.who.int/selection_medicines/committees/expert/19/applications/Norda_Blood_Comment.pdf, where she listed the major concerns that were raised during the meeting.

We therefore call upon the EML Expert Reviewers and WHO/EML Secretariat to review the official report of the CD-P-TS/EDQM meeting in November 2012 to get the full picture of the discussion pertaining to the application.

2. Second paragraph in page 1

We contend that the application from AABB does not make the case that whole blood and red cells meet the definition of “medicines”. We would also like to bring to attention that in the WHO Executive Board Document EB109/8: WHO Medicine Strategy: Revised procedure for updating WHO’s Model List of Essential Drugs available from http://www.who.int/selection_medicines/committees/en/index.html, which is the guidance document on the procedure for updating the WHO Model List of EML, the term “medicines” is defined as “pharmaceutical preparations used in clinical health practice”. Whole blood and red cells are therapeutic substances of human origin with inherent biological variability and having the potential for the transmission of known and unknown infections, including viruses (HIV, HBV, HCV), bacteria, parasites and prions, in contrast to pharmaceutically manufactured medicines and therefore do not fit the definition of medicines.
3. Assessment of safety, page 2

Expert reviewer 2 cites the quality and safety of blood and blood products is dependent on quality assurance processes (including GMPs) which ensure the safety of the final biological product for transfusion. However, ample evidence have shown that safety of whole blood and red cells is closely linked to the type of blood donations, and that voluntary non-remunerated blood donors are safer than paid donors. There is a real risk of commercialization and an almost inevitable shift away from voluntary non-remunerated blood donation if whole blood and red cells are placed on the EML, these cannot be ignored and require more extensive assessment.

Furthermore, we refer to our letter of 28 February 2013 in which we outlined the range of issues related to safety in every steps of blood transfusion chain particularly for patients and blood donors, as well as on staff, the community and the environment.

4. Assessment of public health need, page 4

Expert reviewer 2 provides links to WHO guidelines for the collection, processing and quality control of blood, blood components and plasma derivatives. We refer to our letter of 28 February 2013 in which we list numerous WHO guidelines, including on use of whole blood and red cells, available on: http://www.who.int/bloodsafety and WHO Regional Office blood safety websites.

5. Special requirements for use or training needed for safe/effective use, page 5

Indeed there are special requirements for safe and effective use of whole blood and red cells in hospital transfusion settings related to storage and transportation, inventory management including ABO and Rh group-specificities, prescription, compatibility testing and administration of whole blood and red blood cells and the identification and management of adverse transfusion events. These processes require highly specialized training of medical, paramedical and laboratory staff, including physicians, nurses, laboratory technicians, and support staff in safe and appropriate use of whole blood and red cells.

In addition, there are special requirements for training also for all other staff in the entire blood transfusion chain from donor selection and blood collection, testing, component preparation, processing and storage and transportation in blood donor centres, blood establishments and hospital transfusion laboratories/blood banks.

6. Proposed product registered by a stringent regulatory authority, page 5

The reviewer refers to licensing requirements in seven developed countries in the application. It is important to note that about 100 countries have special legislation and regulatory requirements in which blood is regulated separately from medicines. A regulatory model adopted in few countries with well-developed health system and sufficient resources cannot just be imposed on other countries with different health systems and level of resources.

Even countries with well-regulated systems are vulnerable to insidious commercial pressures as seen recently in Canada, one of the countries given as an example in this section, in which a commercial company is planning to open three for-profit plasma collection facilities and pay individuals for their plasma. It may be significant that one of the plasma collection
centres will be sited near to a university and hostel for homeless people. Concerns expressed by a provincial health minister and professional medical organizations have been mirrored by a public outcry at the prospect of a for-profit blood sector that will encourage blood collection from “donors” whose primary motivation is payment and which may steadily undermine voluntary blood donation.


7. Any other comment, page 5

The reviewer mentions some arguments in favour of the application citing the objectives which the applicant proposes to achieve with the inclusion of whole blood and red blood cells on the EMLs. However, no evidence has been provided to support the contention that these will in fact be achieved by their inclusion on the EMLs.

The reviewer summarizes some arguments against this application and identifies two dimensions of the decision. We wish to point that the only source of whole blood and red blood cells are from blood donors and in addition to the moral and ethical dimensions, there are other important aspects including safety of blood donors and the sustainability of the supply of safe and quality whole blood and red cells that are likely be impacted by the decision to include whole blood and red blood cells on the EML. There is an urgent need to examine the possibility that the good intention of putting these on the EML is not exploited for profit-making in some countries.

We therefore strongly agree with the expert reviewer 2 in recommending “to postpone the decision to allow more time to identify additional clinical evidence and to allow for a broader, more comprehensive discussion among all the stakeholders to reach an informed decision” with the caveat that the identification of evidence should not be confined to clinical evidence but should include a systematic assessment and analysis of both the presumed benefits and the potential negative impact of such a decision.

We reiterate that the decision to include whole blood and red blood cells on the EML should not be rushed and should not simply be based on an assessment of efficacy, product safety, cost-effectiveness and regulation, as for pharmaceutically manufactured medicines. The major differences between whole blood and red cells (therapeutic substance of human origin) and medicines must be considered related to community participation, blood donor motivation and recruitment, careful selection to assess of donor suitability to donate, special requirement for the blood donation process, safety and health of donors, care of donated blood unit, handling, testing, processing, correct storage and transportation. All these processes are highly specialized and are extremely important to ensure improved patient access to adequate supplies of safe and quality whole blood and red cells.

The decision-making process should look beyond the standard criteria for the review of medicines and include an in-depth examination of the complexities of systems and requirements for providing safe, self-sufficient and accessible supplies of therapeutic substances of human origin which extend far beyond their pharmacological properties, and for their safe and appropriate use.

In conclusion, we reaffirm that whole blood and red blood cells are essential therapeutic substances for patient care, and this has been recognized in numerous World Health Assembly resolution and guidelines. However, as national blood programme managers and practising blood transfusion physicians and scientists from different countries, we are acutely
aware of far-reaching implications of this application and reiterate our concerns that the inclusion of whole blood and red blood cells on the EML and EML(c) will have the opposite effect, as in the case of plasma-derived medicinal products where there is a rapidly growing disparity in access between high- and low-income countries. We again express our strong concerns that the decision to include whole blood and red cells on EML can have major negative effects on national blood systems in majority of the countries.

Sincerely yours

[Signature]

Dr Che Kit Lin (signed on behalf of the following experts)
Chief Executive and Medical Director
Hong Kong Red Cross Blood Transfusion Service
15 King's Park Rise, Yaumatei
Kowloon
Hong Kong SAR, China

On behalf of the following international experts in Blood Transfusion Medicine:

1. **Australia**: Mr Peter Carolan, International Consultant, Voluntary non-remunerated Blood Donation (VNRBD), formerly Senior Officer (Blood), Health and Care Dept, IFRC, Geneva, Switzerland; Member, WHO-IFRC task force for ‘A global framework for action towards 100 per cent VNRBD’.

2. **Bhutan**: Dr Mahrukh Getshen, Transfusion Medicine Specialist, Blood Bank, JDW, NR Hospital, Thimphu.

3. **Cameroon**: Dr Jean-Baptiste Tapko, former Regional Adviser, Blood Safety and Laboratories, WHO/AFRO; President Elect, African Society of Blood Transfusion, Yaoundé.

4. **France**: Dr Gilles Follea, Executive Director, European Blood Alliance.

5. **Ghana**: Dr. Justina Kordai Ansah, Director, National Blood Service Ghana; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

6. **Honduras**: Dr Elizabeth Vinelli, Medical Director, National Blood Program, Honduras Red Cross, Comayaguela; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

7. **India**: Dr Zarin Bharucha, International Consultant Transfusion Medicine; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.
8. **India**: Dr Nabajyoti Choudhury, Additional Director, Department of Transfusion Medicine, Fortis Memorial Research Institute, Haryana; Secretary General, South Asian Association of Transfusion Medicine; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

9. **India**: Dr Sanjay Kumar Jadhav, Assistant Director (Blood Transfusion), Maharashtra State Blood Transfusion Council, Government of Maharashtra, Mumbai; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

10. **Italy**: Dr Giuliano Grazzini, Director, Italian National Blood Centre, Istituto Superiore di Sanità, Rome; Member, European Committee on Blood Transfusion (Partial Agreement) (CD-P-TS), Council of Europe; Italian Representative, Competent Authorities on Blood and Blood Components, European Commission.

11. **Macao SAR, China**: Dr Crystal Ping Hui, Director, Blood Transfusion Service, Macao Health Bureau; Member, Asia Pacific Blood Network.

12. **Malaysia**: Dr Yasmin Ayob, Medical Consultant to the National Blood Centre and National Heart Institute, Kuala Lumpur; President of the Malaysian Blood Transfusion Society; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

13. **Malawi**: Dr Bridon Mbaya, Medical Director, Malawi Blood Transfusion Service, Blantyre; President, African Society for Blood Transfusion.

14. **Mauritius**: Dr Janaki Sonoo, Pathologist, Laboratory and Transfusion Medicine, National Blood Transfusion Service, Quatre Bornes; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

15. **Nigeria**: Prof. Banji Adewuyi, Professor of Haematology, University of Ilorin Teaching Hospital, Kwara; Vice President (ECOWAS), African Society for Blood Transfusion.

16. **Norway**: Dr Hans Erik Heier, Professor Emeritus (Transfusion Medicine), Institute of Clinical Medicine, University of Oslo.

17. **Oman**: Dr Shahnaz Al-Balushi, Director, Department of Blood Services, Ministry of Health.

18. **Pakistan**: Prof. Hasan Abbas Zaheer, Project Director, Safe Blood Transfusion Services Programme, Pakistan; Founding President, Pakistan Society of Blood Transfusion; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

19. **Singapore**: Dr Diana Teo, Senior Director, Blood Services Group, Health Sciences Authority.

20. **Sweden**: Dr Rut Norda, Regional Medical Director, Dept. Clinical Immunology and Transfusion Medicine, Uppsala University Hospital, Uppsala.

21. **United Arab Emirates**: Dr Amin Hussain Al Amiri, Assistant Undersecretary, Medical Practice and License; Chairman of Supreme National Blood Transfusion Committee, Ministry of Health, Sharjah; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.
22. **United Arab Emirates**: Dr May Raouf, Medical Director, Sharjah Blood Transfusion and Research Centre, Ministry of Health, Sharjah; WHO Expert Advisory Panel on Blood Transfusion Medicine.

23. **United Kingdom**: Dr Alan Kitchen, Head, National Health Service Blood and Transplant, National Transfusion Microbiology Reference Laboratory, London; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.