28th February 2013

The Secretary
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
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Sir/Madam


An expert peer review of the application to place whole blood and red blood cells on the WHO Model Essential Medicine Lists (Reviewer 1) was posted on the website on 21 February 2013. A number of institutions, organizations and individuals had already submitted comments on this application. I refer you in particular to the earlier submission from a group of international experts in blood transfusion medicine which I represented: (http://www.who.int/entity/selection_medicines/committees/expert/19/applications/HongKong_Blood_Comment.pdf.

The publication of the expert review has stimulated rapid communication and broader discussion within the global blood community. I am therefore writing on behalf of those listed at the end of this letter, all of whom have given their express consent to its content, which they have reviewed and approved.

The organizations, institutions and experts listed below wish to express grave concern about the expert peer review (Reviewer 1) on the application for the placement of whole blood and red blood cells on the Essential Medicines Lists.

Applicability of EML application form to whole blood and red blood cells
Our comments follow the structure used in the expert review. However, the structure of the application form is designed to reflect key considerations in the review of manufactured pharmaceutical products. It does not encourage wider review of policy, legal, resource, ethical and societal implications of inclusion of a medicine or other therapeutic substance on the EML. These dimensions are, however, critical for a measured consideration of whole blood and red blood cells. The limitations of the application form should not permit them to be overlooked or undervalued.

Section 1: Assessment of efficacy
We strongly agree and affirm that whole blood and red blood cells are an essential therapy to which all patients requiring transfusion should have access. Indeed the reviewer identified that there is no comparator for whole blood and red cells thus confirming that whole blood and red cells are ‘essential’ in nature.
Section 2: Assessment of safety
Similarly in this section, the reviewer pointed out that there is no relevant comparator for whole blood and red cells on the EML, which we believe again support reiterate the 'essential' nature of whole blood and red cells. Furthermore, the safety of whole blood and red blood cells cannot be controlled in the same way as the production and use of pharmaceutical products. The safety of transfusion encompasses patient safety, blood donor health and safety and product safety as well as the safety of staff throughout the blood chain.

Patient safety
In addition to the transfusion-associated risks identified in the expert review, consideration should be given to the following factors which may affect the safety of blood supplies:

- Poor donor selection procedures resulting in the collection of blood from donors at high risk for transfusion-transmissible infections (including HIV, hepatitis viruses, syphilis, HTLV, malaria and Chagas disease) or medical conditions which may affect the safety or efficacy of the blood component
- Unreliable supplies of test kits and reagents for quality-assured blood screening
- Lack of quality systems and deficiencies in testing blood for TTI and blood group serology in blood centres, and in compatibility testing in hospital blood banks
- Weak blood cold chain systems for the storage and transportation of blood which may result in bacterial contamination, haemolysis or reduced efficacy
- Inappropriate or unnecessary prescribing of blood
- Poor blood administration procedures and inadequate patient monitoring during and after transfusion.

Blood donor safety
The potential risks to blood donors should also be taken into consideration:

- Failure to identify and defer individuals whose health might be jeopardized by blood donation: e.g. underweight donors, pregnant and lactating women and medical conditions including anaemia and other haematological disorders, hypertension, cardiovascular diseases, respiratory diseases, gastrointestinal diseases, metabolic and endocrine diseases, and immunological diseases
- Adverse donor reactions, including vasovagal episodes and soft tissue injuries
- Donation-induced iron depletion resulting from too-frequent donation intervals.

Waste management
Specific considerations apply to the management of infectious waste in blood transfusion services, hospital blood banks and clinical settings in which transfusion is performed. This includes devices, equipment and consumables used to collect, test, process, transport and administer blood, including discarded blood, sharps, non-sharps and effluents. Effective waste management systems are required to protect blood donors, patients, staff, the community and the environment.

Haemovigilance
Haemovigilance systems for the monitoring, investigation and reporting of adverse events associated with blood donation and transfusion are critical in preventing the occurrence or recurrence of adverse events resulting from the donation of blood and its components, and from the transfusion of blood products. Haemovigilance should encompass the entire blood chain, from blood donors to patients.
Section 3: Assessment of cost and availability
The cost of the collection, production and use of a unit of whole blood or red cells cannot be standardized. The cost depends on a wide range of variables in each country that affect capital and recurrent costs, including infrastructure, labour costs, fuel for blood collection and distribution, and the procurement of equipment, reagents and other consumables. Again in this section the reviewer make the distinction that there is no relevant comparator on the EML which make the case of the ‘essential’ nature of whole blood and red cells. Furthermore, the essential role of whole blood and red cells are proven as these are available in all low, middle and high income countries.

Section 4: Assessment of public health need
WHO has produced extensive policy guidance documents and guidelines on clinical transfusion and other components of the blood chain, supported by training programmes and materials:
http://www.who.int/bloodsafety/en/

Specifically, we would like to highlight that WHO has produced the module on 'The clinical use of blood in obstetrics, paediatrics, surgery and anaesthesia, trauma and burns' to guide the safe and appropriate prescribing and administration of blood and blood products at http://www.who.int/bloodsafety/clinical_use/en/Manual_EN.pdf.

And the use of whole blood and red cells was also covered in Volume 2 of WHO IMAI district clinician manual: Hospital care for adolescents and adults: Guidelines for the management of common illnesses with limited resources at http://apps.who.int/iris/bitstream/10665/77751/3/9789241548290_Vol2_eng.pdf

Other WHO links include
http://www.emro.who.int/entity/blood-safety/
http://www.euro.who.int/en/what-we-do/health-topics/Health-systems/blood-safety
http://www.wpro.who.int/topics/blood_safety/en/index.html

5. Are there special requirements for use or training needed for safe/effective use?
The special requirements for use and training are much wider than suggested by the reviewer. They extend throughout the blood chain including the education and recruitment of blood donors, donor selection and counselling, blood collection, haematological and virological testing, component preparation, inventory management, waste management, storage and distribution, clinical use and blood administration.

6. Is the proposed product registered by a stringent regulatory authority?
The review indicates that many countries ‘manage’ blood products through the national medicines regulatory authority. We believe that the use of the word ‘manage’ here is inaccurate as the mandate of NMRA is mostly to ‘regulate’ the safety and quality of blood products instead of ‘managing’. While the application list 7 countries in which whole blood and blood products are classified as ‘medicine’, almost 100 countries, including countries in the European Union, have legislative and regulatory frameworks through the NMRA for whole blood and red blood cells due to the specialized nature of these therapeutic substances of human origin and the risk of transmission of HIV, hepatitis B, hepatitis C and
other life-threatening infections through transfusion separate from legislative and regulatory framework of medicine.

7. Any other comments
In Section 7, the reviewer notes that there are strong views both for and against including whole blood and red blood cells on the EMLs. The arguments against the inclusion are summarized briefly as reflecting 'the values and preferences of some national groups and authorities'. However, extensive comments have been submitted to the EML Secretariat, and posted on the website, by national blood services, international organizations and professional societies including the Asia Pacific Blood Network (10 countries), European Blood Alliance (23 countries) and the South Asian Association of Blood Transfusion Medicine (8 countries). In addition, twelve submissions have been made by directors of national blood services, national/regional blood transfusion societies and other stakeholders, and our own comments have been agreed by 22 international experts in blood transfusion from 19 countries, the majority of whom are also directors of national blood services and members of the WHO Expert Panel on Blood Transfusion Medicine. Many of those who have expressed their views represent developing countries and are together responsible for managing a significant proportion of the world's blood supply. Their comments explicitly reflect their professional concerns about the wider impact of the inclusion of whole blood and red blood cells on the EMLs.

It is vital that the Expert Reviewers, and the Expert Committee on the Selection and Use of Essential Medicines, recognize the importance of the issues raised by these contributors, their expertise and experience in the field of blood transfusion particular in the developing countries and their requests for wider consultation before a decision is reached.

The reviewer notes that no evidence is provided to support claims. In fact, while there are evidence to support these claims, we have actually asked for more time to review the evidence given the complexity of the issue and the short time available since the application was put up on WHO website. We therefore refer to our earlier comments in which we specifically recommended that a systematic assessment and review of evidence should be conducted on the potential impact of the inclusion of whole blood and red blood cells on the EMLs before a decision is taken.

The reviewer concludes that 'It is not therefore not at all clear that adding whole blood and red blood cells to the EML will achieve any significant public health or clinical gains and WHO should be prepared to undertake an evaluation of the impact if the additions are made.'

If it is uncertain that any public health or clinical gains will be achieved, it is incumbent on the Expert Committee to defer a decision until a systematic assessment of the possible impact has been made. We feel strongly that it would be inappropriate for the Expert Committee to make a decision to include whole blood and red cells on the EMLs at its forthcoming meeting in April 2013 meeting without addressing the need for further assessment and consultation of the issues and in the face of such strong divergent views.

Section 8: What is your recommendation to the committee (please provide rationale)
In the opinion of Reviewer 1, the application has made the case that (1) whole blood and red blood cells meet the general definition of a 'medicine' (2) that they meet the criteria for the WHO Essential Medicines List.
We contend that the application does not make the case in relation to these two points and make the following observations:

- The reviewer has made a point on the essential nature of whole blood and red cells but does not provide a rationale for the recommendations that these are 'medicine'. Although the application from AABB has proposed that whole blood and red cells meet the definition of "medicine", we would like to bring to your attention that in WHO Executive Board Document EB109/8: WHO Medicine Strategy: Revised procedure for updating WHO's Model List of Essential Drugs at http://www.who.int/selection_medicines/committees/en/index.html and http://apps.who.int/gb/archive/pdf_files/EB109/eeb1098.pdf, the term "medicines" is used to describe pharmaceutical preparations used in clinical health practice. Similarly, this is also used in the WHO Essential Medicines Selection webpage at http://www.who.int/selection_medicines/en/ (accessed on 28/02/2013) in which it is stated "...Selection of medicines follows market approval of a pharmaceutical product which defines the availability of a medicine in a country...."

- The reviewer has made a point on the essential nature of whole blood and red cells but does not provide a rationale for the recommendations that these are 'medicine'.

- In our earlier comments, we have already highlighted the significant differences between medicines, which are chemically synthesized pharmaceutical products, and whole blood and red cells, which are therapeutic substances of human origin, donated by individuals, with inherent variability because of their biological nature and risk of transfusion-transmissible infection.

- Reviewer 1 notes that there is no relevant comparator on the EML. Whole blood and red blood cells are collected, tested, processed and used in a different way from pharmaceutically manufactured products. It is precisely because of this that the wider repercussions of adding whole blood and red blood cells to the EMLs necessitate broader consultation in order to determine whether the consequences may result in more harm than good.

Therefore the recommendation of Reviewer 1 that 'whole blood and red cells should be added to Section 11, Blood Products and Plasma Substitutes' actually contradicts the his/her conclusion in Section 7.

Need for systematic assessment, review of evidence and analysis

- We reiterate our recommendation that a systematic assessment, review of evidence and analysis should be conducted on the potential impact of the inclusion of whole blood and red blood cells on the EMLs, with particular reference to the capacity of countries to ensure universal access and safe and appropriate use. This assessment should be wide-ranging and address all dimensions of the issue.

- We and others who have commented on this application would be pleased to contribute to this process.

- We assert that this assessment and analysis should take place prior to a decision being made on whether to place these blood components on the EMLs, not subsequently.

Need for wider consultation

- We, and a number of other stakeholders who have commented on the application, also called for a full consultative process with governments, national blood services and other stakeholders.
• We believe that the potential negative repercussions for the countries we represent are so great that a structured consultation with Member States is vital.

• The majority of letters that oppose this application call for a longer period of time before a decision is reached by the Expert Committee to enable wider consultation and full discussion of the implications for countries.

• We note that although the International Society of Blood Transfusion was included by AABB in its application letter, its position identified on its website identifies the importance of its Code of Ethics and a belief that a more considered consultation on the issues raised by this will be of value. Similarly, the Chinese Society for Transfusion Medicine has, subsequent to its original letter of support, clarified its position and requested that before a final decision was reached, further full consultation with member states, international/national blood services/organizations should be considered, all possible negative consequences should be anticipated and effective preventing measures should be identified.

• We propose to bring this matter to the attention of the Governing Bodies of WHO to allow for full consultation and proper debate.

Summary
We believe that to classify whole blood and red blood cells as medicines will seriously endanger national blood systems, particularly in low-income countries. We fear that it will have far-reaching negative consequences on the safety, quality, availability, self-sufficiency and sustainability of national blood supplies and will result in less patient access in many countries.

We expect due consideration to be given to the views and comments on the application from institutions, organizations and individual experts that have been posted on the website.

Recommendations
In view of the gravity of this matter and the potentially dangerous repercussions for the blood supply in many countries*:

1 We request the Expert Committee to facilitate a systematic assessment, review of evidence and analysis of the potential impact of the inclusion of whole blood and red blood cells on the EMLs.

2 We request the Expert Committee to engage in a broader, structured consultation with governments, national blood services, international and regional blood alliances and networks, non-governmental organizations, national regulatory authorities, professional societies, international and intergovernmental organizations and developmental partners, including PEPFAR, World Bank and other agencies providing financial support for the strengthening of national blood systems.

3 We strongly recommend that the consultative process should fully involve developing countries, which were not represented among the organizations submitting the application but which are likely to be most adversely affected.
4 We urge the Expert Committee to defer any decision on the addition of whole blood and red blood cells to the EMLs until a fuller assessment and wider consultation have been completed.

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

**International Organization in Blood Transfusion Medicine**

**Member countries of the European Blood Alliance (EBA) including:**
1. Austrian Red Cross Blood Transfusion Services  
2. Belgian Red Cross French Speaking - Blood Service  
3. Belgian Red Cross Flanders - Blood Service  
4. Croatian Institute of Transfusion Medicine  
5. Organization of Transfusion Centres in Denmark  
6. Estonian Blood Centers  
7. Finnish Red Cross Blood Service  
8. Etablissement Français du Sang  
9. German Red Cross Blood Transfusion Services  
10. Irish Blood Service  
11. Icelander Blódbankinn  
12. Centro Nazionale Sangue - Istituto Superiore di Sanità (Italian National Institute of Health)  
13. Latvian Blood Centre  
14. Blood Transfusion Service of the Luxembourg Red Cross  
15. National Blood Centre - Lithuania  
16. Maltese National Blood Transfusion Service  
17. Sanquin Blood Supply Foundation - the Netherlands  
18. Portuguese Blood Institute (Instituto Português Do Sangue)  
19. National Institute of Transfusion Hematology – Romania  
20. Blood Transfusion Centre of Slovenia  
21. Comité Científico para la Seguridad Transfusional – Spain  
22. Swedish Blood Alliance  
23. Swiss Transfusion SRC Ltd.  
24. NHS Blood and Transplant - United Kingdom  
25. Welsh Blood Service
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. **Ghana**: Dr. Justina Kordai Ansah, Director, National Blood Service Ghana; Member, WHO Expert Advisory Panel on Blood Transfusion Medicine.

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

6. **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.

7. **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.

8. **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.

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

10. **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.

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

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

13. **Norway**: Dr Hans Erik Heier, Professor Emeritus (Transfusion Medicine), Institute of Clinical Medicine, University of Oslo.
14. **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.

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

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

17. **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.

18. **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.