Expert peer review on application for whole blood and red blood cells

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes    No (if no, please provide reference and information)
      The applicant has cited a range of important publications. This range was widened by reviewer 1 and
   2. Due to the vast literature it is impossible to include all relevant studies

b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Major conditions for the use of whole blood or red blood cells are:
   - Severe hemorrhage, caused by injury or during surgery, and gastro-intestinal bleeding
   - Anemia (hereditary or induced by leukemia, lymphoma or non-hematological tumors)
   - Obstetric and gynecological conditions
   - Neonatal conditions (e.g. severe Rh incompatibility)

   In severe cases, transfusion of whole blood or red cell concentrates is lifesaving. There is no realistic alternative for the replacement of oxygen transport. However, the fine tuning, ie the definition of the borderline when transfusion becomes lifesaving, is still on-going and might depend on an ever changing environment (e.g. patient condition, health care level, doctor’s skill).

c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes    No (if no, please provide reference and information)
      The applicants have listed and commented the known side effects in Annex A of the application.

b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   As transfusions are routinely performed since appr. 60 years the side effects are well known. However, the focus changed during these years. In the beginning, hemolytic transfusion reactions were the greatest concern, later the transmission of viruses (Hepatitis B virus, HIV, hepatitis C virus and others e.g. West Nile virus, Chikungunya virus) and now immunological transfusion reactions (e.g. Transfusion-related acute lung injury (TRALI)). There are also papers pointing to the fact that under certain conditions transfusions are not always benefitting the recipient. There are differences in the interpretation of those results, and this is mainly due to the fact that classical randomized studies comparing transfusion against non-transfusion (and there is no realistic alternative) are ethically unacceptable.
c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
a. Have all relevant data on cost provided
   Yes   No (if no, please provide reference and information)
   The cost of the preparation of whole blood in specific settings is provided
b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
   While it is possible to calculate the costs of the preparation and the storage of a unit of whole blood or red blood cells, there are no data presented on cost effectiveness. This may due to the difficulty to define the value of a saved life.

c. Please provide any additional relevant information with reference

d. Is the product available in several low and middle income countries?
   Yes

4. Assessment of public health need
a. Please provide the public health need for this product (1-2 sentences)
   The public health need for the lifesaving effect of blood transfusions is obvious and well accepted.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable
   To my knowledge, there are no WHO guidelines recommending the use of whole blood and red blood cells, as their medical need is obvious. However, there are a number of WHO guidelines dealing with the preparation of whole blood and blood components:
   WHO requirements for the collection, processing and quality control of blood, blood components and plasma derivatives (1994).
   WHO good manufacturing practices for blood establishments (2011).
   World Health Assembly Resolution 28.72 Utilization and supply of human blood and blood products (1975) promoting voluntary non-remunerated blood donations
   World Health Assembly Resolution 63.12 on availability, safety and quality of blood products (2012).

5. Are there special requirements for use or training needed for safe/effective use?
   If yes, please provide details in 1-2 sentences
Yes, physicians have to be trained for correct administration of whole blood and red cell transfusions, for recognition and handling of adverse reactions and for the rational use of blood.

6. Is the proposed product registered by a stringent regulatory authority?
   Yes  No

7. Any other comments

In reviewing the comments to the application a wide range of opinions in favor and against the proposal becomes obvious. The arguments against are well summarized by reviewer 1. Serious, but yet unproven objections are:

- Increased commodification of blood/blood products
- The risk of undermining voluntary donations

In addition, there is concern that in some countries regulatory agencies are not well positioned to oversee the preparation of whole blood and red blood cells.

8. What is your recommendation to the committee (please provide the rationale)

A lay person might be surprised that whole blood is not yet on the list of essential medicines as it is common knowledge that blood transfusions save lives and are therefore essential for modern medicine. He would judge the discussion whether or not whole blood is a medicine or not as semantic, especially if he notices that condoms and diaphragms are also listed in EML.

Because of its lifesaving nature I recommend to put whole blood and red blood cells on EML and EMLc. However, to account for WHO’s advocacy for voluntary non-remunerated donations and the non-commercialization of human tissues I propose the addition of the following comment (as a comment was added to the listing of mifepristone):

“WHO (or WHA) strongly recommends to accept only voluntary non-remunerated blood donors and to prohibit commercialization of human cells and tissues”

To address the concerns regarding inadequate requirements by regulatory authorities the following comment could also be added:

“WHO (or WHA) reminds regulatory authorities to give due consideration to the specific nature of this product”