

**WMDA Policy Statement for the Utility of
Autologous or Family Cord Blood Unit Storage**
*(This policy statement has been approved and adopted
by the WMDA board on the 25th of May 2006)*

The Cord Blood Registries Subcommittee, a joint collaboration of the Ethics and Donor Registries Working Groups, of the WMDA has discussed the EU recommendations, policy statements of several professional organizations in the US, Europe and Asia and considered the public interest and the interests of its member organizations in public and autologous cord blood banking. It is recommending the following policy statement.

1. The World Marrow Donor Association supports the establishment of public cord blood banks that are based on altruistic and voluntary cord blood donation. These units should be available for any patient who needs an allogeneic transplant and for related research. A large, diverse inventory of cord blood units and an effective ability to exchange units internationally offers the most benefit for all populations and is the most cost effective strategy. Public cord blood banking should be supported by national governments.
2. Collection and storage of cord blood units from family members of patients affected with, or at risk for, diseases that may be treatable by transplantation have a documented value. The storage of cord blood units where there is a clear medical indication should be supported.
3. Today the likelihood that an autologous cord blood unit will be used for transplantation is very low. There is currently no clear proof that these cells will be able to be used for regenerative medicine or to treat other diseases in the future. However, at the present time it is impossible to predict the results of research that may affect the future potential use of these cells.
4. Storing cord blood for autologous use is an option in many countries. Cord blood collection and storage is a medical procedure done at a critical time for the mother and baby. For this reason, in these countries, national governments must ensure that the family receive impartial and accurate information about the potential risks and benefits of private storage and sign an informed consent document.
5. All cord blood banks should be subject to the same standards, regulations and accreditation requirements.
6. Promotion or general funding of autologous or related cord blood storage in the absence of a medical indication for directed donation should not be supported by national governments.

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EXPLANATORY REPORT OF THE
CORD BLOOD REGISTRIES SUBCOMMITTEE**

The World Marrow Donor Association (WMDA) mission statement is: WMDA is a voluntary organisation of representatives of blood stem cell donor registries, cord blood banks, other organisations and individuals, with an interest in hematopoietic stem cell transplantation. It provides a forum for mutual discussion of all issues regarding the clinical use of hematopoietic stem cells from unrelated donors across international boundaries. These discussions, which take place in working groups, make it possible to formulate guidelines on for example logistics, quality control, accreditation, ethics, finances, information technology and registry accreditation.

Background

Many WMDA member organizations facilitate transplants of umbilical cord blood units (CBUs) as well as adult donor marrow and peripheral blood stem cells (PBSC) in their own country and internationally. Approximately 70% of patients with blood disorders such as leukemia, severe aplastic anemia and congenital or other acquired disorders will not have a suitable family donor. These patients rely on public donor registries around the world to provide the adult or umbilical cord hematopoietic cells needed to restore their immune system after receiving the chemotherapy and/or radiation treatment that may cure their disease. The world-wide exchange of adult donor cells and CBUs for transplantation has functioned efficiently and relies on the altruistic donation of these cells from donors who do not know who their recipient is.

There are three different types of Cord Blood Storage.

1. Public Cord Blood Banking
2. Medically Indicated, Directed Family Cord Blood Storage
3. Autologous or Family Storage (Private Cord Blood Banking)

Public Cord Blood Banking

Cord blood unit donation and storage for public unrelated, *allogeneic (cells come from a person other than the patient)* use is a newer and growing donation option. Today, there are a number of countries that offer public programs for collection and storage of these cells by cord blood banks. These banks store cells for use by patients who need a transplant from an unrelated donor. Many registry members of the WMDA list these CBUs and make them available for their domestic patients and other patients throughout the world.

More than 1,500 transplants occur annually world-wide with unrelated CBUs. This number is growing each year.

Public CBU storage is supported by many professional organisations and national governments, and there is extensive medical and scientific documentation of usage of unrelated CBUs for transplantation. Some governments also provide funding to support public CBU storage.

Medically Indicated, Directed Family Cord Blood Storage

A number of cord blood banks offer CBU storage to families who are expecting another baby and already have a sibling with a disease that is potentially treatable with an allogeneic cord blood transplant. The rationale is that if the new baby's HLA type is compatible with the affected sibling, cord blood has the potential to be a good source of cells for transplant for the donor's sibling. The likelihood that a sibling will share both HLA haplotypes is 25%.

When there is a clear medical indication for the storage of directed CBUs there is a significant probability of using those stored units. This is especially likely in siblings that are affected by malignant, genetic or immune disorders. The Children's Hospital Oakland Research Institute, Sibling Donor Program carefully screens families before storing a unit for potential family use. In late 2004, it reported having shipped 41 of 1,266 (1:31) units that were used for transplantation¹. Other hospitals may have higher use rates, particularly if the original indication for transplantation is clear.

Some transplant centers don't strongly recommend this donation option because the hematopoietic stem cells could be collected from the sibling at a later time if they were actually needed. However, storage of cord blood from a sibling of an affected child may provide a valuable source of cells with quite a high likelihood of use. They are also collected at no risk to the infant donor.

Autologous or Family Storage (Private Cord Blood Banking)

Private cord blood storage companies have developed in many countries to sell cord blood storage to families for potential future *autologous* (*patient's own cells*) or family use. This is called "private storage" because the units are collected and stored solely to be available for the individual donor or the immediate family. These companies charge a collection fee, generally between \$1000-\$1500 USD and an annual storage fee, often approximately \$100. Some companies also provide financial incentives to health care professionals who recruit their potential customers and bonuses based on the number of successfully collected units.

Companies advertise and promote their programs to pregnant women. Some companies have used sales approaches that appear focused on making the

family feel that they are not being good parents if they don't store their baby's cord blood for future use.

The European Commission Recommendations

The European Group on Ethics in Science and New Technologies to the European Commission issued an opinion paper on the Ethical Aspects of Umbilical Cord Blood Banking on 16 March 2004. The paper summarized issues related to characteristics of cord blood, autologous transplantation, current research, and other information about cord blood banking and registries. Members of the Cord Blood Registries Subcommittee and Ethics Working Group have discussed the EU Group policy statement and generally agree with the conclusions and statements.

The Council of Europe Committee of Ministers adopted the following five recommendations on 19 May 2004².

1. "If cord blood banks are established, they should be based on altruistic and voluntary cord blood donation and used for allogeneic transplantation and related research;
2. The promotion of donation for autologous use and the establishment of cord blood banks for autologous use should not be supported by member states or their health services;
3. Accurate information should be provided to the population about the advantages and disadvantages of cord blood banks;
4. Where autologous cord blood banks are being established, the promotional material or information provided to families must be accurate, and fully informed consent to cord blood storage must be obtained;
5. Autologous cord blood banks that are being established must meet the quality and safety standards set out in the Council of Europe's Guide to safety and quality assurance for organs, tissues and cells".

Likelihood of Using an Autologous Cord Blood Unit Today

Several governing bodies, notably the European Union and individual members of the Union and some professional organizations, such as the American Academy of Pediatrics³ and the American College of Obstetricians and Gynecologists⁴ have adopted policy statements about the ethics and utility of private and public storage of umbilical cord blood. The general conclusion is that because of the very low probability of autologous use for diseases treatable by transplantation today, and for lack of medical and scientific documentation of autologous cord blood usage, storing cord blood is not recommended and families should not feel pressured to store autologous cord blood.

One important question for families to consider is how likely it is that a privately stored cord blood unit will ever be used. It is important to recognize

that for many of the diseases for which cord blood is used today, a physician would not use autologous cord blood for several reasons.

1. Unrelated HSC transplantation in hematopoietic malignancies is not just a replacement therapy where the malignant bone marrow is replaced by that of a healthy donor. It is also a form of immunotherapy where the donor's immune system acts against the patient's residual malignant cells in a phenomenon called graft-versus-leukemia effect. This effect cannot be found in autologous hematopoietic stem cell transplantation.
2. Numerous studies have shown that preleukemic and leukemic cells may be found in the cord blood of children who later develop childhood leukemia. The use of autologous cord blood cells for the treatment of childhood leukemia is therefore contraindicated because preleukemic cells already present at birth could cause a re-occurrence of the disease being treated.
3. Unrelated hematopoietic stem cell (HSC) transplantation can be used to treat a number of genetic diseases that affect the hematopoietic system, such as hemoglobinopathies, inherited immunodeficiencies, storage disorders etc. The HSCs found in CB carry the same genetic information or, in this case, the same genetic defects as the donor. For this reason, autologous cord blood transplantation cannot be used to treat any genetic diseases.

Overall, there is general agreement that the likelihood of autologous cord blood transplantation is extremely remote. Similarly, the possibility that another family member will use the stored CBU for HSC transplantation for a potential future illness is very low for the following reasons.

1. First, the incidence of HSC transplantation treatable disorders in the first two decades of life is rather low.
2. In 25% of these cases the stored CBU will be a full mismatch and therefore unsuitable for use.
3. In 25% of the cases the sibling itself will be full matched and, since there is no documented advantage of the use of a stored CBU, freshly collected HSCs may be a better choice of graft.
4. In 50% of the cases the CBU will be a partial match and the stored CBU will be of potential use. However, in approximately 40% of the cases a suitable matched unrelated donor will be available and would be the preferred choice of a donor. In many cases, especially if the patient is older, the CBU cell content may be insufficient for use.

Future CBU Use

Today, no one really knows how cord blood cells might in all aspects be useful in the future and how they will compare to future use of other cell types that are also being used in research today. Private cord blood banks claim that these cells may be used for many diseases in the future. Some private banks

indicate these cells can be stored for any member of the family, downplaying the role HLA matching plays in cells used for transplantation.

Many private cord blood banks advertise that autologous cord blood stem cells might be used in the (near) future in reparative or replacement stem cell therapy protocols for various kinds of severe diseases. Although the field of basic stem cell research is rapidly moving forward, there is at present no known protocol where autologous cord blood stem cells are used in therapy. Indeed, the future role of autologous stem cells in new treatment protocols is still very unclear.

Further, if autologous stem cell therapies should become reality in the future, these protocols will probably rely on generally and easily accessible stem cells, and requirements for standards concerning collection, manipulation, storage, quality assessment etc. would be defined in detail to comply with criteria for good manufacturing practice (GMP). It would therefore probably be difficult to accept cord blood cells cryopreserved several years ago under conditions not in compliance with GMP standards and a given protocol. Thus, stem cell therapy protocols should be developed before cell sources are defined and collection methods developed for these treatment modules.

Failure to Inform

One of the major issues raised in many of the existing policy statements regarding autologous cord blood storage is that of false or misleading advertisement. Advertising materials often fail to differentiate between unrelated and autologous hematopoietic stem cell (HSC) transplantation, and there is a strong tendency to over-interpret data from basic stem cell research. Advertisements imply that the indications for unrelated transplantation also hold true for autologous transplants as well, which is not the case.

Many marketing materials make exaggerated claims about how likely the units are to be used in the future. They use advances in embryonic stem cell (ESC) research as an argument to promote autologous cord blood storage. The progress made in ESC research is very promising and may hold the key to the future treatment of many serious diseases. Yet, what advertising materials fail to clarify is that ESCs are *pluripotent (capable of becoming any type of cell)* stem cells derived from early embryos and data from ESC research cannot be transferred to HSC or other stem cell populations found in the CBU. Stem cells from embryos are not used for marrow or peripheral blood or umbilical cord blood transplants.

Furthermore, many companies fail to clarify that HSC or other stem cell populations used in many studies, such as those where stem cells are tested for treatment of adult diseases such as cardiovascular disorders, are collected from the patient's own bone marrow. It is thus very important that families and individuals receive accurate information that distinguishes between the

potential for use of currently accepted medical therapies using CBUs and possible future uses, which have not yet been proven or tested in humans.

The European Union (EU) Group in its opinion paper published 16 March, 2004 and titled "Ethical Aspects of Umbilical Cord Blood Banking"⁵ based the following statements on such considerations.

1. "Research is taking place into differentiation of pluripotent stem cells into specific cell types which could be used for the treatment of chronic diseases such as Parkinson's, diabetes, cancer, or cardiac infarcts by means of human stem cells but no clear proof of utility of stem cells has been shown". The opinion also states that, "The possibility of using one's own cord blood stem cells for regenerative medicine is currently purely hypothetical. Research in this field is only at a very early stage." The conclusion of the section on current research is, "It is therefore highly hypothetical that cord blood cells kept for autologous use will be of any value in the future".
2. A portion of the opinion that discusses the ethical aspects of cord blood banking states that, "The legitimacy of commercial cord blood banks for autologous use should be questioned as they sell a service which has presently no real use regarding therapeutic options. Thus they promise more than they can deliver."

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