WHO

Public consultation

on the draft proposal

on

Principles for global consensus on the donation and management of blood, blood components and medical products of human origin

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January 2017

World Health Organization

WHO/HIS/SDS/2017.1

Contents

1. Background

Medical products of human origin (MPHO) are defined as substances derived wholly or in part from the human body and intended for clinical application. Source components in the human body include organs, tissues, blood, cells and gametes, secretions and excretions.

The World Health Assembly (WHA) has endorsed ethical principles and governance mechanisms [1] and the Secretariat, WHO collaborating centres and nongovernmental organizations have issued further guidance for facilitating implementation of these principles and mechanisms. Nevertheless, the available guidance is somewhat fragmented and generally oriented towards a number of specific products (e.g. blood and organs/tissues/cells).

Following a report by the WHO Secretariat, the Executive Board of the World Health Assembly, during its 136th session held in February 2015, requested "that the Director-General convene consultations with Member States and international partners, to support the development of global consensus on guiding ethical principles for the donation and management of medical products of human origin; good governance mechanisms; and common tools to ensure quality, safety and traceability, as well as equitable access and availability, as applicable, to result in a document to be submitted to the Seventieth World Health Assembly for its consideration."

Pursuant to the request in decision EB136(2), the Secretariat elaborated a framework of principles on donation and the management of medical products of human origin, in collaboration and consultation with a large and broad group of independent experts and scientific societies across the six WHO regions. The document was based on previous guidance, identifying ethical principles and governance mechanisms relevant to all types of medical products of human origin, and proposed a globally harmonized approach to governance, based on using shared tools. The goal was to foster more consistency of ethical practices in order to strengthen the overall safety, quality and availability of medical products of human origin.

That draft framework of principles, strategic approaches and policy options was opened on a dedicated web page on the WHO extranet for a public consultation between 22 September and 15 October 2016. Member States, WHO collaborating centres, non-State actors in official relations with WHO, as well as other institutions and stakeholders, such as scientific and professional societies, patients' associations and civil society members active in the field, were invited to provide comments. All the input provided through the consultative process was analysed and taken into consideration when drafting the latest version of the framework of principles.

The following report contains a summary of the consultative process, an overview of participation and the major issues that emerged from it.

Taking into account the suggestions made through this consultative process, the Secretariat has submitted its report on "Principles for global consensus on the donation and management of blood, blood components and medical products of human origin", for discussion at the 140th session of the Executive Board (23 January–1 February 2017).

[1] Resolutions WHA28.72 (1975), Utilization and supply of human blood and blood products; WHA58.13 (2005), Blood safety: proposal to establish World Blood Donor Day; WHA63.12 (2010), Availability, safety and quality of blood products; and WHA63.22 (2010) Human organ and tissue transplantation, in which the Health Assembly endorsed the WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation.

2. The public consultation process

The online consultation took place during a three-week period from 22 September to 15 October 2016 and was based on an online survey through a dedicated WHO website. The web page provided background on development of the framework, and included a link to the full draft and provided access to a questionnaire to be completed.
Participants were encouraged to focus on the following areas.

Section 1: Ethical common principles that apply to the donation and use of all medical products of human origin (MPHO)
Participants were requested to give their opinion on each of the 10 principles, through a 6-level Likert-type scale of agreement (I disagree strongly, I disagree, I slightly disagree, I agree slightly, I agree, I agree strongly) and provide comments in case of disagreement.

Section 2: Strategic approaches you would suggest adding to any of the ethical principles
Participants were invited to submit their suggestions on strategic approaches for each of the principles in addition to those already available within the framework document.

Section 3: Short description of how this framework could be useful to your specific areas of work
Participants were requested to state if the proposed framework would be of any value to their line of work and were also given the opportunity to upload any additional documentation that they felt was relevant and should be taken into consideration.

Section 4: About you (optional)
Participants were asked to provide information on their professional background and field of work, as well as their contact details if they wished (though this was not mandatory).

The draft framework and survey questionnaire are attached as Annexes 1 and 2.
The background document which was modified as a result of this consultation has been submitted to the Executive Board for its 140th session and is available here:
http://apps.who.int/gb/ebwha/pdf_files/EB140/B140_18-en.pdf

3. Participation

More than 400 individuals accessed and initiated the survey out of which 125 complete responses were finally submitted. The respondents came from 56 different countries (Table 1) covering all WHO regions, though with the majority (41%) based in Europe. (Figure 1)

Figure 1: Responses by WHO Region

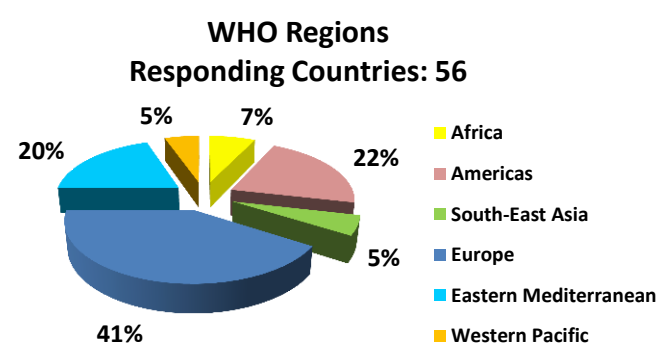


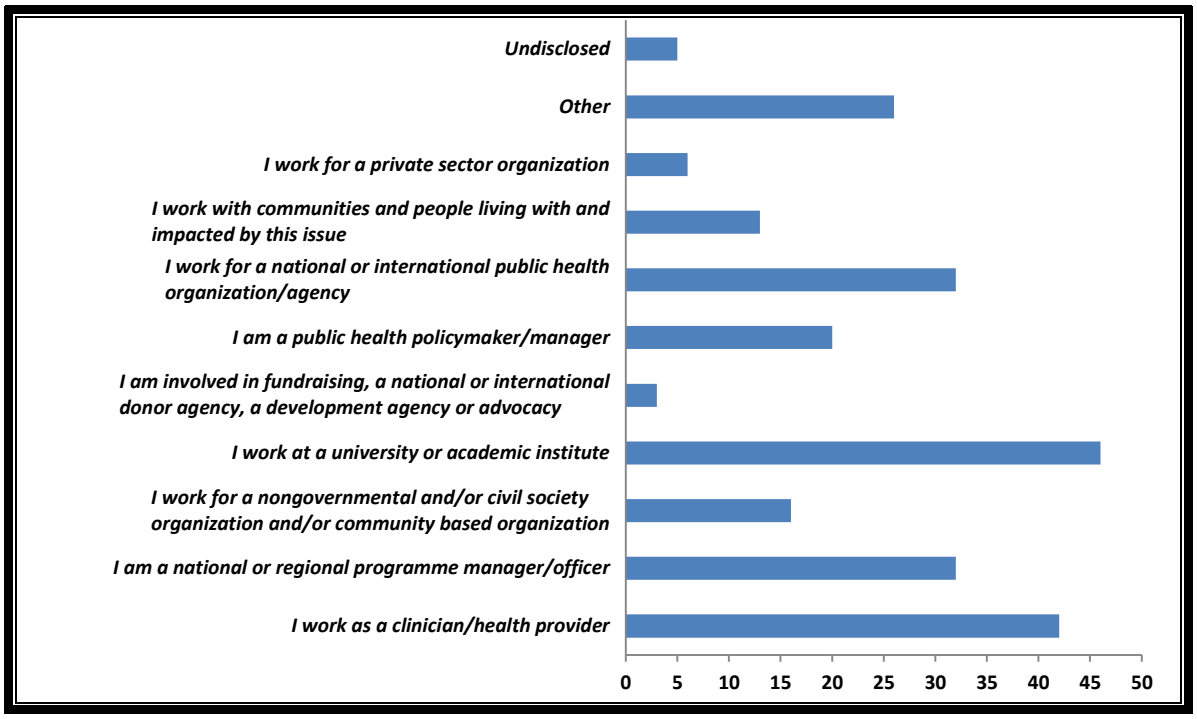
Table 1: Responses by country

Country	#	Region	Country	#	Region	Country	#	Region
Argentina	5	AMRO	Guinea	1	AFRO	Peru	1	AMRO
Australia	4	WPRO	Hungary	1	EURO	Poland	2	EURO
Austria	3	EURO	India	1	SEARO	Portugal	1	EURO
Belgium	2	EURO	Iran (Islamic Republic of)	4	EMRO	Romania	1	EURO
Bhutan	2	SEARO	Iraq	1	EMRO	Saint Vincent & the Grenadines	1	AMRO
Brazil	1	AMRO	Israel	1	EURO	Saudi Arabia	3	EMRO
Bulgaria	1	EURO	Italy	1	EURO	Slovakia	1	EURO
Canada	9	AMRO	Japan	1	WPRO	Slovenia	2	EURO
China	1	WPRO	Jordan	1	EMRO	South Africa	1	AFRO
Costa Rica	2	AMRO	Lebanon	2	EMRO	Spain	7	EURO
Cuba	2	AMRO	Malta	1	EURO	Sri Lanka	3	SEARO
Cyprus	2	EURO	Mexico	2	AMRO	Sweden	2	EURO
Egypt	2	EMRO	Namibia	3	AFRO	Switzerland	2	EURO
Eritrea	1	AFRO	Netherlands	6	EURO	Trinidad & Tobago	1	AMRO
Estonia	1	EURO	Norway	1	EURO	Tunisia	1	EMRO
Finland	2	EURO	Oman	3	EMRO	United Kingdom	2	EURO
France	1	EURO	Pakistan	2	EMRO	United States of America	7	AMRO
Greece	1	EURO	Palestine	2	EMRO			
Guatemala	2	AMRO	Paraguay	2	AMRO			

AFRO=Regional Office for Africa, AMRO=Regional Office for the Americas, SEARO=Regional Office for South-East Asia, EURO=Regional Office for Europe, EMRO=Regional Office for the Eastern Mediterranean, WPRO=Regional Office for the Western Pacific

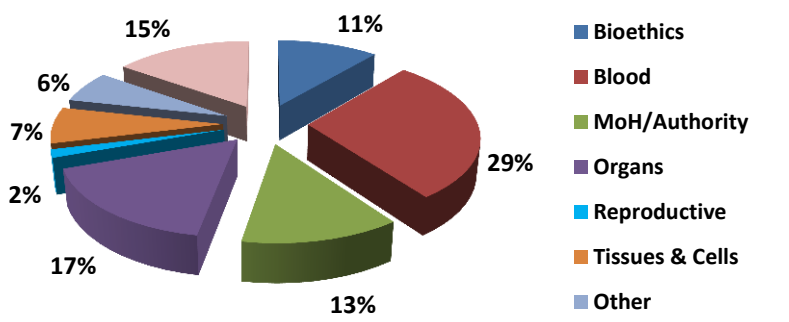
The consultation was successful in receiving input from a broad range of constituencies (see Figure 2), including ministries of health, health providers, civil society organizations, nongovernmental organizations, scientific and academic institutions, professional associations and networks.

Figure 2: Respondents' profiles



The respondents represented, in their majority, the field of blood (29%) but organs, haematopoietic progenitor cells (HPC), tissues and reproductive cells (gametes) were adequately represented, thus covering the entire spectrum of MPHO. In terms of background, participants were mainly from the clinical field and from regulatory authorities but there was also a high number representing the field of bioethics (see figure 3).

Figure 3: Respondents' background in terms of MPHO type



4. Summary of participants' input

All principles achieved a high level of acceptance ranging from 86,4% to 98,4% (see figure 4).

There were 69 disagreements in total, most of which concerning principles 3 (use only when of proven efficacy) and 5 (donor's financial neutrality). The majority of the opposing statements came from the blood and blood products sector (38%) (see figures 5 and 6).

Figure 4: Acceptance rate per principle

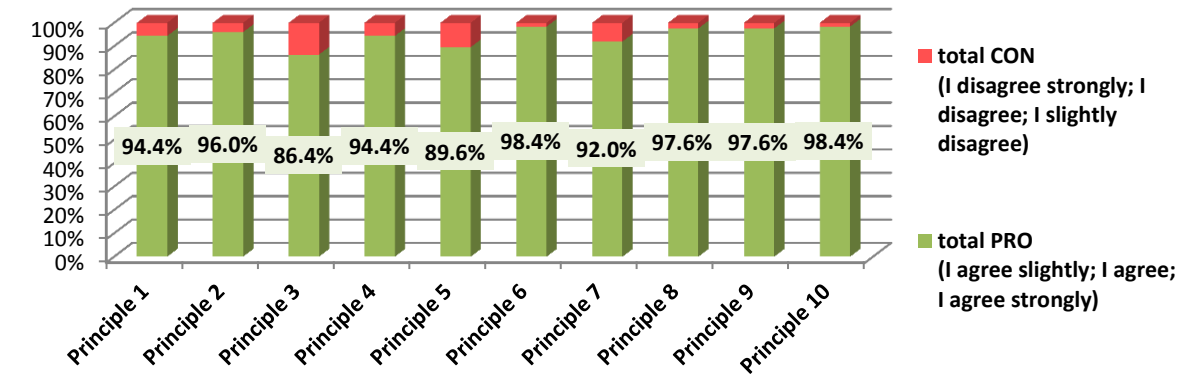


Figure 5: Disagreements per principle per professional background

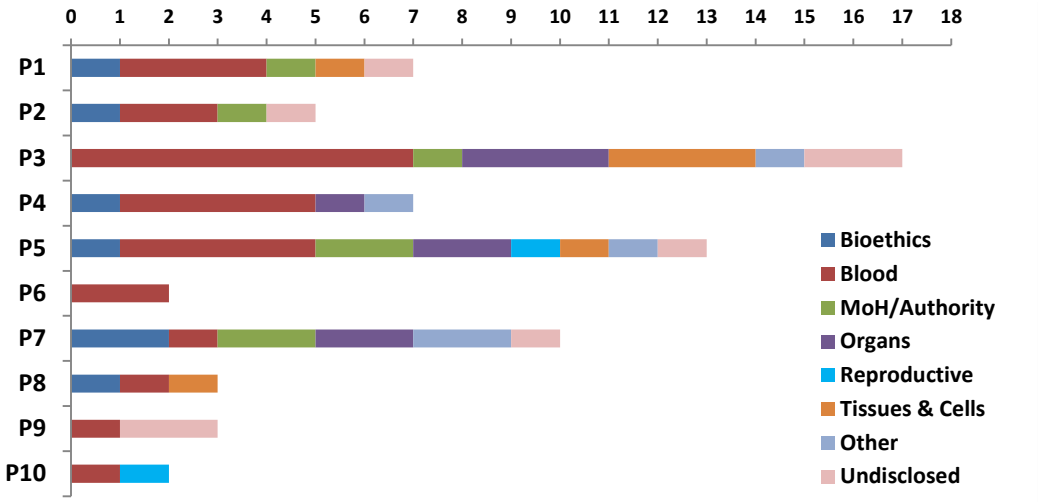
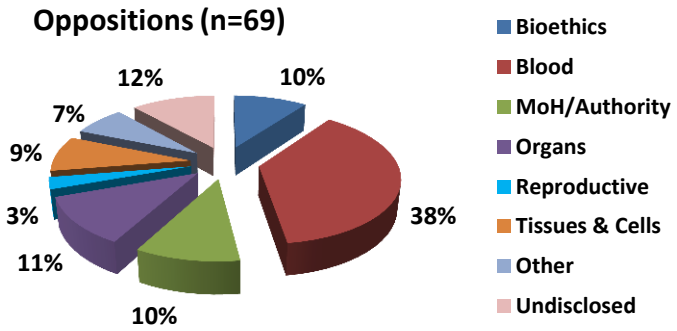


Figure 6: Acceptance rate per principle



4.1. Overview of consultation results and discussion per principle (section 1 of survey)

Principle 1: Governments are responsible for assuring the ethical and effective procurement, distribution and use of MPHOs. This responsibility includes the obligation to develop and enforce regulations to assure the maximum level of safety, quality and efficacy within and across national borders.

Acceptance rate: **94.4%**

Reactions & proposals: There were some minor reactions from the clinical field stating that safety and quality are the health professionals' responsibility and not to be imposed by policy-makers/regulators. The requirement for a maximum level of safety is *not* considered cost-effective and there should be a balanced risk assessment. This principle should also include the responsibility for long-term follow-up of donors and recipients.

Decision taken: It was agreed that the safety level should be the highest possible and to include the development of follow-up registries in the explanatory text.

Principle 2: Equity in donation should be promoted by engaging all members of society in efforts to meet needs for MPHOs.

Acceptance rate: **96.0%**

Reactions & proposals: Comments were related to the fact that not all members of society might be eligible donors due to various health or social reasons. It is necessary to reflect this in the principle.

Decision taken: It was agreed to take this into account and rephrase accordingly.

Principle 3: MPHOs should be used only when of proven efficacy and in the absence of alternative therapies of comparable or superior efficacy.

Acceptance rate: **86.4%**

Reactions & proposals: MPHOs are likely to be increasingly used in advanced therapy product drug development, and this should be allowed. This principle could block future developments and research trials in innovative treatments of unproved efficiency. It is also necessary to consider cost-effectiveness and not only efficacy when comparing MPHO to alternative products.

Decision taken: It was agreed that there should be a balance between risks, benefits and costs. The point regarding clinical trials and innovative medicines is critical and should be taken into consideration. This section was revised accordingly.

Principle 4: Donation of components of the human body for use in medical products should be conditional upon informed and voluntary decision-making by donors or their relatives.

Acceptance rate: **94.4%**

Reactions & proposals: It is also necessary to take into account presumed consent systems. There is a need to distinguish between living and deceased donors because of the different procedures related to procurement. The proposed concept of the donor advocate might generate a need for new staff and will increase costs to health systems.

Decision taken: There was agreement on the point of presumed consent that applies only to deceased donations. This section was revisited to address the issue.

Principle 5: Financial neutrality: In order to guard against the exploitation of vulnerable individuals and promote equity in donation, persons who provide their biological materials for use in MPHOs should not benefit or lose financially as a result of the donation.

Acceptance rate: **89.6%**

Reactions & proposals: The opposing comments were related to the fact that there are instances where donors of biological material (i.e. plasma for fractionation and gametes) are compensated beyond expenses incurred. The respondents believe that donor payment should continue for these types of MPHO because there will be a major impact on the supply (i.e. plasma derivatives) if this changes, thus putting patients/users of these vital products at risk. The argument for donor payment is also related to the fact that these products are repeatedly donated thus the degree of donor effort, psychological, physical impact should be compensated but not in such a remunerative way as to result in coercion. Thus a one-size-fits-all principle should not apply.

Contrary to the wish of maintaining donor remuneration, there were other comments (mainly from the field of organs, tissues and bioethics) which support the concept of financial neutrality and its application to all MPHOs, thus ensuring that there should be no exceptions and ethical deductions that could compromise the solidity of the donation process and the fight against organ trafficking.

Furthermore, there were proposals regarding the aim of this principle which should be extended to cover inappropriate or unethical financial gain not only from the donation processes, but also from manufacturing and distribution for transplantation. Organizations which collect whole blood or blood components from voluntary and unpaid donors might sell products gained from this source in a commercial manner. In order to avoid ethical imbalances or problems, such practices should at least be made fully transparent and public.

Decision taken: The concept of financial neutrality that WHO introduced has been praised by many and it should therefore definitely be maintained. Nevertheless, it is necessary to address the strong reactions related to certain specific types of MPHO and to assess the impact that such a proposal would have. It has been agreed not to modify the core essence of the principle but to acknowledge that some sectors have developed their systems along the lines of donor compensation. Member States and institutions which are not currently applying the voluntary non-remunerated donation principle for specific products are urged to explore the possibility of a future transition and it is suggested that they should, as a priority, develop policies requiring financial neutrality in order to minimize the risk that the burdens of donation fall primarily on economically disadvantaged populations. These safeguards could include tracking systems to monitor the frequency and localisation of an individual donor, and adequate insurance coverage for donors, irrespective of any payments made to them. The wording of the principle was revisited accordingly.

Principle 6: Prospective and actual donors of human biological materials for use in medical products should be protected against physical and psychosocial risks to the fullest extent possible.

Acceptance rate: **98.4%**

Reactions & proposals: Almost full agreement and the respondents' proposals were related to enhancing the protection of the donor by including long-term monitoring (e.g. 10 years after hematopoietic progenitor cell mobilization by granulocyte-colony stimulating factor (G-CSF), and lifelong after kidney donation). It was also suggested adding protection from psychological pressure (including financial pressure).

Decision taken: It was decided not to modify the wording of the principle, since the proposals were mainly related to the strategic approach and that the "fullest extent possible" actually covers a lifetime period.

Principle 7: Information about the relevant product, including its human origin, should be routinely provided when offering MPHOs to prospective recipients.

Acceptance rate: **92.0%**

Reactions & proposals: Most comments related to protecting the identity of the donor and opposed disclosure of such information to the recipient. Other respondents believed that this should apply only to certain types of MPHO (e.g. solid organs), as it is more difficult to apply to tissues (e.g. bone). Furthermore it was suggested that recipients should be informed about the donation-related policy in the country or health care jurisdiction in which the MPHO was procured and not only in their own country, as the document states.

Decision taken: There has obviously been some confusion and misunderstanding generated regarding the type of information (human origin of the product) that should be provided to the recipients. It is not intended to disclose the donor's identity which must remain protected (see principle 10). It was agreed to rephrase and clarify this point to avoid further misinterpretation.

Principle 8: Equity in access to the benefits of MPHOs should be promoted by sustained efforts to remove barriers to access, and to establish and implement waiting lists and allocation systems for MPHOs that are based on clinical criteria and ethical norms, not considerations of financial or social status.

Acceptance rate: **97.6%**

Reactions & proposals: The principle is sound and well accepted. However, waiting lists may not always be applicable (e.g. related to musculoskeletal tissues, blood and gametes). It is suggested to reedit it so that it considers waiting lists and allocation criteria, where appropriate.

Decision taken: The comments were considered valuable and going in the right direction, but there was a need to acknowledge the differences in the allocation/distribution of various types of MPHO and to avoid setting a requirement for a common system (waiting lists, allocation criteria). The text was revisited accordingly.

Principle 9: In order to minimize the risk of harm to donors and recipients and to protect the stability and sustainability of MPHO services, all steps in the development and use of MPHOs should be fully traceable and subject to rigorous quality management systems and vigilance and surveillance programs.

Acceptance rate: **97.6%**

Reactions & proposals: Overall consensus with just one comment received drawing attention to the fact that having these rigorous management systems in place can sometimes be obstructive and costly. Rules regarding sharing information might get in the way of good sense and patient care.

Decision taken: The requirement for complicated quality systems could indeed have a negative financial impact and it was therefore decided to "soften" their status from "rigorous" to "effective".

Principle 10: The organization and delivery of MPHO-related activities, as well as their clinical results, must be transparent and open to scrutiny, while ensuring that the personal anonymity and privacy of donors and recipients are always protected.

Acceptance rate: **98.4%**

Reactions & proposals: Most comments are related to anonymity which may not always apply (in the case of directed living donation). There are also cases of gamete donation where anonymity could be lifted for reasons of familial ties.

Other concerns related to the transparency of the procedures, essentially in situations where there is a financial gain made by the institutions which process and distribute MPHOs (e.g. plasma derivatives).

Decision taken: There was agreement that "anonymity" and "privacy" might be understood differently across different languages and cultures, therefore it was decided to replace the terms with "confidentiality".

As regards transparency, it was also agreed that the comments were indeed valid and that the issue should be addressed, but perhaps not in the main text of the principle but in the form of an explanatory note.

4.2. Overview of suggested strategic approaches (section 2 of survey)

There were a total of 265 additional comments and proposals (see Table 2) related to the strategic approaches already described in the draft document. Most of the comments were simple agreements with the proposed principle or, for those opposing the principle, further elaboration on the reasons for disagreement. There were some new ideas related to the strategic approach and implementation, but often based on a similar strategy already in place in the participant's country.

Table 2: Strategic approach suggestions

Principle	Total comments & proposals
P1	39
P2	27
P3	28
P4	27
P5	39

Principle	Total comments & proposals
P6	24
P7	21
P8	24
P9	17
P10	19

4.3. Overview of impact and added value (section 3 of survey)

The framework proposal was well received overall, with 93 out of the 125 respondents acknowledging the importance of this WHO initiative. For many countries where legal frameworks do not exist or where they are undergoing amendments, this proposal comes as a guarantee and a valuable reference for their future development.

The document has further added value, not only as an ethical framework, but also as a practical tool for guidance. The positive impact can be spread to all levels of involvement from central government to regional/local health administration and to health care facilities and professionals.

It has been acknowledged, even from those opposing some of the principles, such as the necessity of financial neutrality of the donor, that this framework should lead to more efficient, safe and medically sound collection of substances for MPHOs.

Below are some of the original comments submitted through the consultation.

"This framework will be important for advocacy with our authorities on the importance of appropriate legislation. These principles complement existing legislation properly in our country."

"Having such documents in hand will help us to look for strategies, initiatives or regulations to fulfil these needs."

"Broadly shared and discussed principles for the donation and management of MPHOs are the cornerstone for the sustainable supply of these."

"It should be a permanent reminder in front of the tendency to treat MPHOs as any other good, focussing on the economic benefit and commercialization with the argument of free market."

"Transparency in the process, extremely high quality control and audit, and the ability to track donations, improves confidence and relieves anxiety in the recipients of MPHOs."

"This framework will be useful in the training of health workers (nurses, medical students, pharmacists and allied health professionals). It is a fact that this concept of donation of the product of human origin will be new to most of our communities, especially to African cultures".

5. Comments/suggestions of key stakeholders

Additionally to the online web consultation there were a number of interventions and commentaries provided by key stakeholders (Member State authorities, NGOs in official relations with WHO, scientific and professional societies, patient associations and civil society organizations), via letters and email correspondence, in response to the Secretariat's invitation. These were more institutional positions rather than individual comments as in the web-based survey. These came from:

- Australian Government – Department of Health
- German Federal Ministry of Health
- European Commission – Directorate General for Health and Food Safety
- Kingdom of Saudi Arabia – National Committee of Bioethics
- Principality of Monaco – Directorate of Health Action
- Ministry of Health of the Slovak Republic
- The World Federation of Haemophilia (WFH)
- The Platform of Plasma Protein Users (PLUS)
- The Transplantation Society (TTS)
- The European Blood Alliance (EBA)
- The Nuffield Council on Bioethics (NCOB)

Furthermore, the draft framework was presented and discussed at a number of high-level meetings taking place during that period of time, with Secretariat staff members invited to attend. These meetings included:

- Meeting of the European Committee on Organ Transplantation (CD-P-TO) of the Council of Europe – Strasbourg, France;

- Meeting of the Council of Europe Committee on Bioethics (DH-BIO) ad hoc Working Group on the Prohibition of Financial Gain – Paris, France;
- Council of Europe First Workshop for National Focal Points on Transplant-Related Crimes – Madrid, Spain;
- NOTIFY Project on Global Vigilance and Surveillance for MPHOs – Second Technical Meeting – Rome, Italy;
- Workshop to Advance Organ Donation and Transplantation – Beijing, China;
- The Iberoamerican Council of Donation and Transplantation [Red Consejo Iberoamericano de Donación y Trasplante (RCIDT)] 16th annual meeting – San José, Costa Rica;
- Meeting of the National Transplant Institute of Argentina [Instituto Nacional Central Único Coordinador de Ablación e Implante (INCUCAI)] – Buenos Aires, Argentina;
- Seventh Annual Congress of the Latin American Association of Tissue Banks (ALABAT) – Buenos Aires, Argentina;
- European Commission Meeting of the Competent Authorities for Blood and Blood Components – Brussels, Belgium;
- Ad hoc meeting between stakeholders and representatives of members of the Competent Authorities on Substances of Human Origin Expert Group (CASoHO) – Brussels, Belgium;
- French National Institute of Blood Transfusion (Institut National de la Transfusion Sanguine) Seminar on the ethics of transfusion "The non-profit" – Paris, France.

The feedback received through these different communication channels largely followed the same direction as the web-based consultation and input was also taken into account during the redrafting of the background document.