OECD workshop consensus report: Ethical considerations with respect to human derived products, specifically human serum, in OECD TGs

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What are the issues ?

The ethical needs and concerns with use and sourcing of human materials, particularly serum, in OECD in vitro Test Guidelines (TGs) were explored in a dedicated international workshop held in 2019.

The health-related aspects of the donation procedure, including tissue screening, donor health, laboratory work health protection, permission from the donor for commercial use, payment of the donors and the potential for exploitation of low-income populations and data protection of the donors; supply, availability, and competition with clinical needs; traceability of the serum and auditability/GLP needs for the OECD TG Programme, were examined.

Here we provide the **recommendations** of the workshop with respect to the use of human serum, and potentially other human reagents, specifically with regard to test method development for OECD TG utility as part of the Mutual Acceptance of Data requirement across all OECD member countries.

These include

1. **Informed donor consent terminology,**

2. **Suitable sources for human serum to ensure waste supplies are used**, that can no longer be used for medical purposes, ensuring no competition of supply for essential medical use.

3. **A checklist of human serum information requirements** to be included with the Good Laboratory Practise report

Terminology

Blood: Whole blood collected from a human donor and processed either for transfusion or for manufacturing uses.

Blood Components: Therapeutic constituents of human blood (red cells, white cells, platelets and plasma) that can be prepared by various methods.

Human Serum: The fluid portion of the blood obtained after removing of fibrinogen and other clotting factors. Used for many important applications, including human cell culture, drug testing, tissue typing, and cell therapy research. Human blood serum does not contain white blood cells, red blood cells, or platelets.

Human Plasma: The fluid portion of blood that can be separated from whole blood or collected through plasmapheresis, contains clotting factors. Intended either for transfusion purposes or for the manufacture of plasma derived medicinal products (PDMPs) or other manufacturing uses, such as in vitro medical devices.

Recovered Plasma: Plasma recovered from a whole blood donation and used for manufacturing.

Source Plasma: Plasma obtained by plasmapheresis intended for further manufacturing.

Plasmapheresis: A process where human plasma is obtained either for transfusion or for manufacturing purposes and cellular blood components are returned to the donor during or at the end of the donation.

1. Informed Consent Terminology

UK National Health Service Blood and Transplant

'*In some cases, we are unable to use your donation for direct transfusion to patients. This may be for a number of reasons including test results, processing issues or information we receive after donation.*
As part of our commitment to a high-quality service, we sometimes use donations for laboratory work, education, training, research and development, which may include DNA studies and export. Donations may also be used in the preparation of healthcare related medicinal products, within NHSBT or by other organisations which could be outside the UK. These are essential for effective patient care. If we use your donation for any of these purposes, we will ensure that:

- *ethical approval is obtained where appropriate*
- *there are no implications for your health or welfare*
- *you cannot be identified; this includes any work involving DNA studies*
- *any income generated is used for the benefit of NHSBT and the wider NHS. NHSBT is a non-profit organisation*
- *no DNA analysis is performed that may identify you without your specific/explicit consent …*

…. meeting our responsibilities under the Data Protection Act 2018, which constitutes the UK implementation of the General Data Protection Regulation (GDPR).'

The information provided to donors also explains that using expired blood for non-medical purposes **reduces disposal and waste expenses** for the National Health Service.

2. Suitable sources for human serum to ensure waste supplies are used

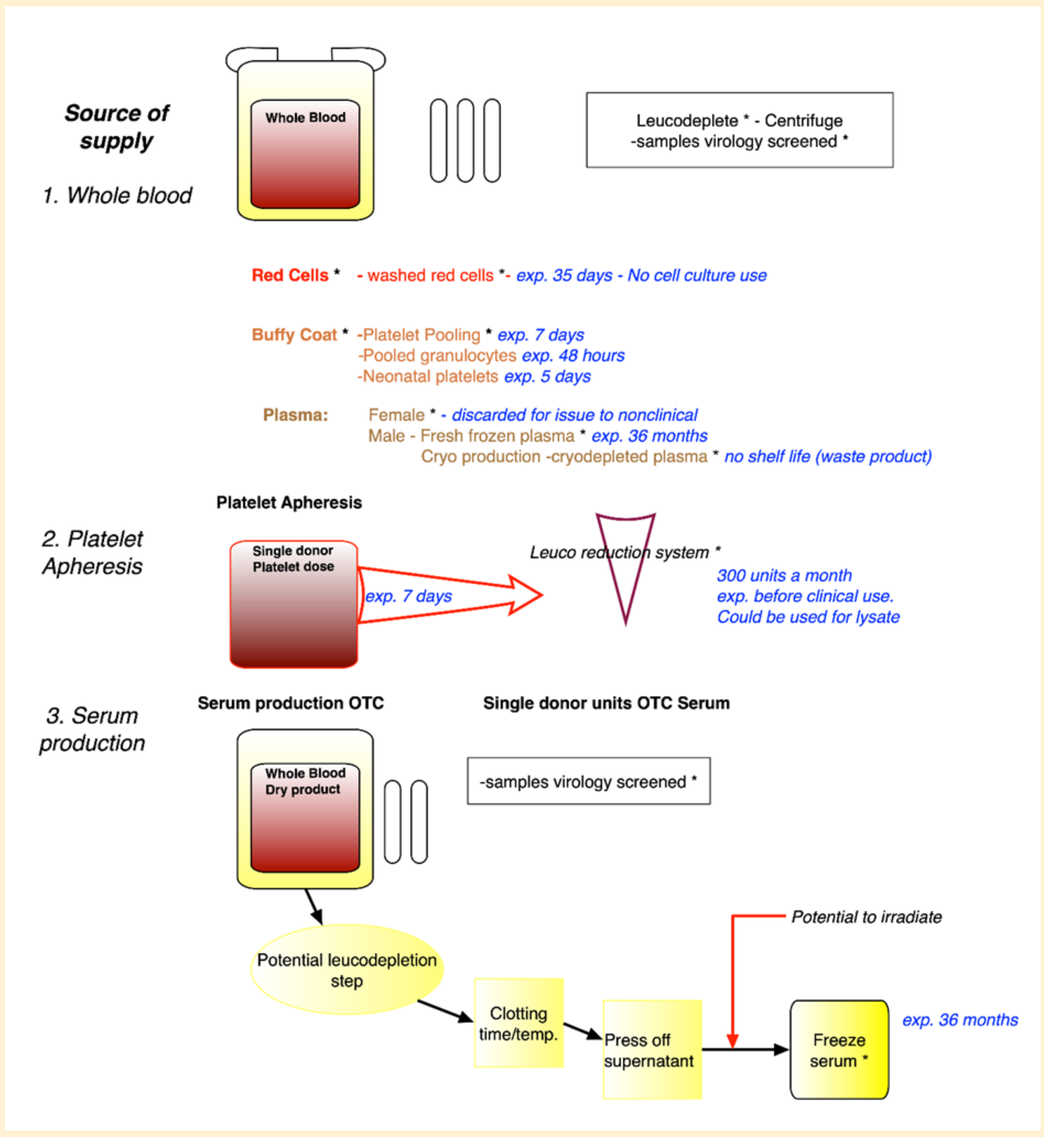

Figure 1. Identification of sources of expired blood no longer of use to the medical/clinical sciences.

Ensuring auditable steps in manufacture of human serum

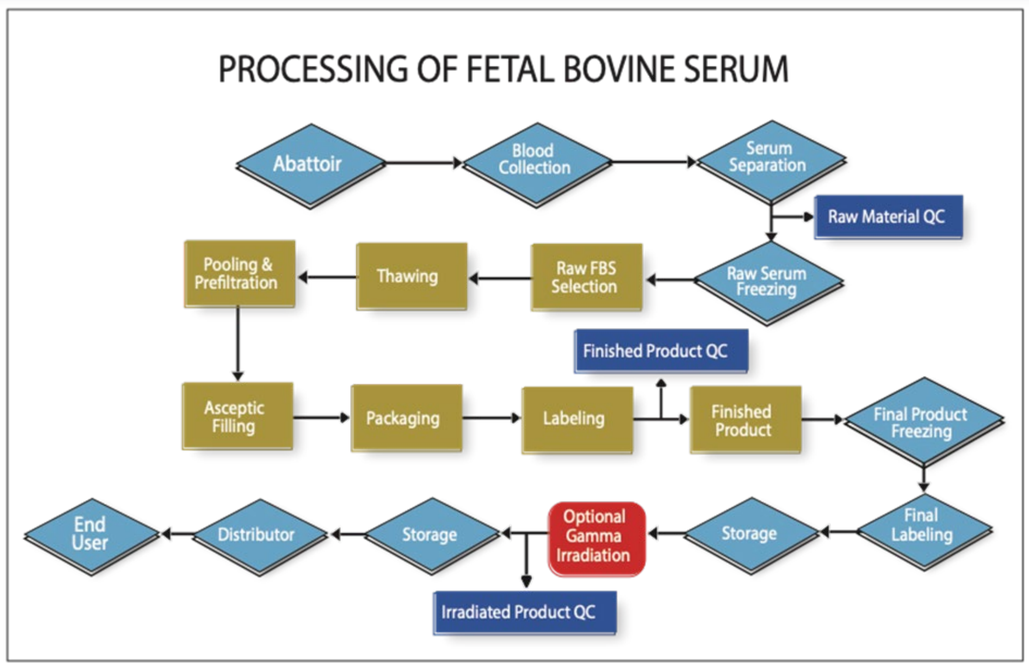

Figure 2. High level flow chart indicating the key processing and auditable steps in the manufacture of FBS

3. Checklist

Parties responsible for derivation and use of human blood derived products	Ethics and safety issues: Documentation needs	All materials of human origin
Nationally licensed/authorised blood collection centre or equivalent and geographical location	Source: surplus/expired	+
	Sex	+
	Payment or altruistic donation from nationally inspected blood collection centre's and equivalent, if authorised/licensed	+
	No. of donors	+
	Health status	+
	Quarantine results	+
	Specific pre-treatment	+
	Biosafety classification	+
	Organ/tissue of origin	+
	Isolation technique	+
	Date of isolation/extraction	+
	Operator	+
	Informed consent paperwork holding	+
	Material transfer agreement	+
	QC testing	+
	Shipping conditions	+
Supplier	Certificate of issue	+
	Import authorisation, if relevant (sometimes not possible)	+
	State of material on arrival	+
	Biosafety classification	+
	Certificate analysis	+
	Demonstrated membership of traceability audit scheme, when available	+
Test method/TG user	Evidence of and compliance with all of the above for completion of documentation required for submission of test results to Regulatory body	+
GLP monitoring regulatory authority	Compliance check that ethical checks have been carried out in accordance with recommendations and GLP principles	+
Data submitter	Similar to a GLP certificate, a statement that the study conducted complies with all of the above for completion of documentation required for submission of test results to Regulatory body	+
Study receiving regulatory authority	Similar to GLP certificate: a statement that the study conduct complies with all of requirements listed above	

Next steps

- **Working towards the development of a traceability scheme for human serum supply**
- Evident need still for ethical protections to be in place, with respect to human sourced *in vitro* method components for both regulatory and general research
- Important to ensure that there are processes in place for the use of human serum in cell culture, and that end-users look at how they can address this currently unmet need.
- The recommendations and solutions discussed herein on the use of human serum may be suitable for discussion with policymakers and legislators, particularly in light of a potential increase in the global demand for human serum for medical, scientific and regulatory sectors.

Reference: Jacobs MN, Bult JM, Cavanagh K, Chesne C, Delrue N, Fu J, Grange E, Langezaal I, Misztela D, Murray J, Paparella M, Stoddart G, Tonn T, Treasure C, Tsukano M, Versteegen R. OECD workshop consensus report: Ethical considerations with respect to human derived products, specifically human serum, in OECD test guidelines. Front Toxicol. 2023 Feb 27;5:1140698. doi: 10.3389/ftox.2023.1140698. PMID: 36923365; PMCID: PMC10010620.