PUBLISHED REPLACEMENT EU ACT
INITIAL ASSESSMENT OF IMPACT

DSC REF: DSC/13/2024

Published Replacement EU Act

Regulation (EU) 2024/1938 of the European Parliament and of the Council of 13 June 2024 on standards of quality and safety for substances of human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC Text with EEA relevance. OJ L, 2024/1938, 17.7.2024.

This regulation replaces Directives 2002/98/EC (the Blood Directive) and 2004/23/EC (the Tissues and Cells Directive) which are listed in Northern Ireland (NI) Protocol Annex 2, Heading 22 on Substances of Human Origin.

Summary of the Act

This regulation establishes measures that set high standards of quality and safety for all substances of human origin (SoHO) intended for human application and for activities related to those substances. It ensures a high level of human health protection, for SoHO donors, SoHO recipients and offspring from medically assisted reproduction, including by strengthening the continuity of supply of critical SoHO.

Under Article 13(3) of the Ireland/Northern Ireland Protocol ("the Protocol") this regulation will apply in NI.

The regulation applies to:

(i) SoHO intended for human application;
(ii) SoHO donors, SoHO recipients and offspring from medically assisted reproduction;
(iii) SoHO activities that have a direct impact on the quality, safety or effectiveness of SoHO.

It does **not** apply to:

(i) organs intended for transplantation;
(ii) breast milk when for feeding own child; without processing by a SoHO entity.

<u>Competent authorities</u>
The regulation stipulates Member States should designate the SoHO competent authorities to which they entrust responsibility for SoHO monitoring activities. The

designated SoHO competent authorities should be independent from any SoHO entity.

SoHO donor and recipient protection

The regulation requires SoHO entities to:

(i) ensure respect for the dignity and integrity of SoHO donors;
(ii) ensure high levels of safety and protect the health of living SoHO donors from risks related to the SoHO donation, by identifying and minimising such risks before, during and after the SoHO collection.

Where SoHO is collected from a SoHO donor, SoHO entities should:

(i) provide SoHO donors or, where applicable, any person giving consent on their behalf;
    - information in a manner appropriate to their ability to understand;
    - the contact details of the SoHO entity responsible for the collection, from which they may, where appropriate, request further information;
(ii) safeguard the living SoHO donor's rights to physical and mental integrity, non-discrimination, privacy and the protection of personal data;
(iii) verify the eligibility of the living SoHO donor based on an assessment of his or her state of health aimed at identifying, with a view to minimising, the risk that SoHO donation could represent for his or her health;
(iv) check that living donors do not donate more frequently than is safe;
(v) draw up a plan for monitoring the donor's health after SoHO donation in cases where the donation of a substance of human origin involves a significant risk for a living donor.

The regulation also requires SoHO entities to protect the health of SoHO recipients and offspring from medically assisted reproduction from risks posed by SoHO and their human application, within the scope of their competences.

Critical SoHO supply sufficiency

The regulation requires Member States to collaborate with SoHO national authorities, SoHO competent authorities and SoHO entities, to consider all reasonable efforts for achieving a sufficient, adequate and resilient supply of critical SoHO with a view to appropriately meet recipient’s needs, contributing to European self-sufficiency.

EU SoHO Platform

The Commission should establish, manage and maintain a digital platform to facilitate efficient and effective exchange of information concerning SoHO activities in the Union.

The new regulation has been proposed to address shortcomings identified in the Blood Directive and the Tissues and Cells Directive. These shortcomings are because of scientific, technical, and medical advances since the publication of the Directives. Breast milk and intestinal microbiota are two additional SoHO products covered by this regulation which were not previously covered by the Blood or Tissues and Cells Directives.

It should be noted that **solid organs are outside of the scope** of this legislation and therefore the organ donation and transplantation system will be unaffected. Although most issues noted in the legislation are devolved, fertility issues are reserved.

Department(s) Responsible

Lead: Department of Health, NI (DoH) – Minister Mike Nesbitt, MLA

Lead: Department of Health and Social Care (DHSC):

- The Parliamentary Under Secretary of State (Minister for Public Health and Prevention) has policy responsibility for human breast milk, the EU future relationship, Windsor Framework and international trade in regard to health - Andrew Gwynne, MP.
- The Parliamentary Under Secretary of State (Minister for Patient Safety, Women's Health and Mental Health) has policy responsibility for blood, blood components, reproductive and non-reproductive tissues and cells - Baroness Merron.
- The Minister of State for Health (Secondary Care) has policy responsibility for IM and blood preparations that are not used for transfusion - Karin Smyth, MP.

Initial Assessment of Impact

Q: Does it appear likely that the application of the replacement EU act would have a significant impact specific to everyday life of communities in Northern Ireland in a way that is liable to persist?

A: Not known

Q: Does it appear likely that <u>not</u> applying the replacement EU act would have a significant impact specific to everyday life of communities in Northern Ireland in a way that is liable to persist?

A: Not known

Q: Other matters regarding the replacement act that the Department wishes to draw to the DSC's attention

The extent of any impact of the replacement EU act in Northern Ireland will depend on the position adopted by the UK Government (UKG) in relation to SoHO, and whether this ultimately affects the movement of SoHO between GB and NI. The current UKG position is summarised below under **UK Government Explanatory Memorandum**, which notes that *the UK Government will take action as needed to ensure GB-originating SoHO can be supplied to NI*, however it should be noted that this will be subject to any implementation acts following the establishment of a SoHO Co-ordination Board by the EU, to which the UK will be a 3rd party.

In the meantime, as the replacement EU Act covers various policy areas for the Department of Health (DoH), the following sections provide a high level summary of the relevant clinical services currently provided to patients in NI:

<u>Blood</u>
In relation to the supply of blood, during 2023/24 (April to March), the Northern Ireland Blood Transfusion Service (NIBTS) imported from England a total of 404 units of blood on three separate occasions, of which one occasion was for four special units.

<u>Tissues and Cells</u>
The full scope of what tissues and cells are included in the legislation and the potential impact will be considered in detail by United Kingdom (UK) expert bodies such as National Health Service Blood and Transplant (NHSBT) and the Advisory Committee on the Safety of Blood, Tissues, and Organs (SaBTO).

<u>Fertility services</u>
Currently publicly funded fertility treatment is provided in the Regional Fertility Centre (RFC) in the Belfast Health and Social Care Trust. Where donor sperm is required, the RFC sources donor sperm in bulk four times per year from Denmark and the USA.

There are occasions when patients at the RFC would wish to transfer their frozen embryos or gametes both to and from NI. This happens approximately 6 times per year between GB / Republic of Ireland (RoI) and internationally approximately once or twice per year.

Eye services

Eye retrievals in NI are carried out in the Mortuary on Royal Victoria Hospital (RVH) site in the Belfast Health and Social Care Trust.

Corneal transplant surgery and any other ocular surgery involving tissue is conducted on the RVH site with the importing of necessary tissue into NI from GB, currently a licensed activity via the Human Tissue Authority (HTA). Corneal, scleral and amniotic membrane tissues are sourced from NHSBT as part of its UK-wide tissue allocation arrangements.

Importation requires a large amount of licensing paperwork and imported tissue from outside the UK is significantly more expensive than that supplied by NHSBT. As a result, NI does not import but is supportive of NHSBT's moves to import tissue to augment the UK supply, ensure fair allocation, and avoid duplication of licencing paperwork.

Skin

With regards to skin grafts, this is generally autologous (i.e. using patient's own skin) and is completed during a single procedure. In very exceptional circumstances (less than once per year) imported cadaver skin is required for skin grafting. The last import of the product was September 2021.

Bone and Bone Products

Donor femoral heads are sourced within NI. All donations are collected in Musgrave Park Hospital and are used on site or distributed for use by other hospitals within the NI Health and Social Care system or by private sector clinics within NI. There are supply agreements in place with each of these sites.

Between 2021 and 2023 approximately 95 femoral heads were used annually at all sites.

Stem Cells

In 2023 the Belfast Health and Social Care Trust (BHSCT) adult haematological team completed 14 allogeneic transplants and 74 autologous transplants. These are typical annual numbers. All unrelated donor transplants are referred to centres in the UK or RoI for treatment, approximately 15 patients per year.

A stem cell or bone marrow transplant replaces damaged blood cells with healthy ones. In haematology, stem cell therapy can be used to treat conditions affecting the blood cells, such as leukaemia and lymphoma and also some haematological diseases. When a patient in NI requires a stem cell transplant, BHSCT clinicians will first test a sibling or related donor match. If a match is deemed compatible, BHSCT retrieve stem cells and perform a stem cell transplant. BHSCT select the most suitable match through the processes of tissue-typing / assessment of fitness; only then collecting cells for subsequent transplant to the patient.

If there is no suitable sibling or related donor, patients from NI are referred to an unrelated donor transplant centre. That centre will initiate an unrelated donor search using the network of national or international stem cell registries, including the British Bone Marrow Registry, Antony Nolan and Deutsche Knochenmarkspenderdatei (DKMS). These registries collaborate to match suitable donors with patients who require a transplant; if a match is found, they will arrange for the retrieval of stem cells from the matched donor and transplantation to the patient. This process is not carried out in the patient's home Trust but by one of these specialist centres.

Intestinal Microbiota (IM)

Intestinal Microbiota (IM) is material from a person's gastrointestinal system used in clinical trials in areas such as inflammatory bowel disease (IBD) therapy. This is a growing area in the field of medical research and it is anticipated that its importance will increase over time. Health and Social Care hospitals across NI use transplanted IM for the treatment of recurrent Clostridium Difficile (C-Diff) infection; a cause of recurrent hospital admission, severe morbidity and even mortality in some cases.

Whilst patient numbers are not significantly high, it should be noted that this is a growing area of treatment for acutely ill patients with C-Diff infection. For example, to date 6 patients in the Southern Health and Social Care Trust have received treatment using IM products and have not required readmission to hospital, with approximately 10 IM products being sourced annually from GB.

Supply of IM is reliant on access to GB suppliers such as the University of Birmingham Microbiome Treatment centre.

Human Breast Milk (HBM)

In NI there is one milk bank which provides and all-island service that supplies to HSC Trusts and babies across the island of Ireland. The milk bank was established and is managed by the Western Health and Social Care Trust (WHSCT), who rely on donations of HBM to provide special help for the most vulnerable babies.

In 2023 the Human Milk Bank provided 973 litres of donor breast milk to 31 units across 27 hospitals throughout Ireland. This lifesaving donor milk has helped 773 premature babies, of which 233 were either a twin or a triplet. Breast milk gives premature and sick babies the best possible start in life as it helps build their immune system, their eye and brain development and prevent Necrotising Enterocolitis (NEC), which is a devastating intestinal disease affecting premature or low birth weight babies.

UK Government Explanatory Memorandum

Input provided directly from DHSC colleagues – UK Government EM currently being cleared by UK Ministers.

The EU has adopted a new regulation making changes to in the Blood Directive 2002/98/EC and the Tissues and Cells Directive 2004/23/EC (BTC Directives). These changes reflect scientific, technical, and medical advances in transfusion and transplantation since the publication of the BTC Directives.

The EU's existing BTC Directives set a range of safety and quality standards, including:

- standards for all steps in the transfusion process for human blood and blood components from donation, collection, testing, processing, storage to distribution;
- standards for all the steps in the transplantation process for tissues and cells from donation, procurement, testing, processing, preservation, storage to distribution;
- traceability and technical requirements for blood, tissues and cells; and notification requirements in the event of a serious adverse event or reaction which may impact the safety and quality of blood, blood components, tissues and cells.

The proposed regulation on SoHO aims to ensure a high level of health protection and ensure access to safe and effective substances of human origin across EU Member States. The new regulation brings into scope all SoHO intended for human application and used to manufacture products regulated by other specific Union legislation, with the exception of solid organs intended for transplantation (as their donation and transplantation are significantly different, determined, inter alia, by the effect of ischemia in the organs, and so remain regulated separately under Directive 2010/53/EU) and human breast milk (HBM) used exclusively for feeding one's own child. The purpose of which is to provide harmonised preparation and consistent treatment for substances intended for human application, and improve the safety, effectiveness and accessibility of SoHO.

Compared with the previous BTC Directives, this therefore brings in scope substances such as intestinal microbiota (IM), HBM (in non-exempt cases) and blood preparations that are not used for transfusion (e.g. serum eye drops, fibrin glue, platelet rich plasma). There is the potential for other SoHO to be brought into scope following scientific advances or other developments. For example, exosome or collagen products could come within scope but this is still to be determined by the SoHO Coordination Board (SCB).

The regulation provides measures to:

1) ensure high safety and quality for patients treated with substances of human origin (SoHO) therapies and fully protect them from avoidable risks. It also aims to facilitate the development of safe and effective, innovative SoHO therapies.
2) ensure safety and quality for SoHO donors and for offspring born from medically assisted reproduction.
3) strengthen and allow for harmonisation of practices among Member States to facilitate the movement of SoHO and access to SoHO therapies.
4) Improve the preparedness and resilience of the sector, to ensure continuity of supply.

The SoHO regulation also sets out the interaction between SoHO and medicinal products and medical devices as well as their regulatory status. Where SoHO is collected to manufacture a medical device that is regulated by EU 2017/745, medicinal product regulated by 2001/83/EC, advanced therapy medicinal products (AMTP) regulated by 1394/2007 or investigational medicinal product regulated by 536/2014 – the provisions of the regulation applicable to the SoHO activities referred to in Article 2 paragraph 1 (c)(i) to (iv) and (viii) apply. The aim is to provide clarity to industry and regulators on the complex interactions between the SoHO and pharmaceutical legal frameworks.

Blood, Tissues and Cells

Blood, blood components and non-reproductive tissues and cells policy is devolved. The Scottish Parliament, Welsh Assembly and Northern Ireland Executive therefore have an interest.

The Blood Safety and Quality Provisional Common Framework, and the Organs, Tissues and Cells (apart from embryos and gametes) Provisional Common Framework support the continuity of good working relations, open communication and the maintenance of a compatible minimum set of high standards of safety and quality for blood and non-reproductive tissues and cells.

Reproductive tissues and cells is a reserved policy, and therefore there is not a Common Framework for this area. However, close working continues between the UK Government and the Devolved Governments on reserved and excepted matters that impact significantly on devolved responsibilities including the donation, processing and use in treatment of human reproductive cells.

Both provisional Common Frameworks have been jointly developed by the UK Government and Devolved Governments and have been operational since March 2020. The Common Framework sets out a process by which a government can suggest future changes to the standards and how such a proposal will be collectively considered before one or more government(s) introduce a change.

Where rules in NI change, the Common Framework will form the basis of a mechanism to ensure consideration by the four governments of any changes, and will enable them to determine any impacts and subsequent actions arising from these changes.

These provisional Common Frameworks also reflect the specific circumstances that arise as a result of the Windsor Framework and reiterate the commitment to a UK-wide approach in terms of decision making, governance, and dispute resolution. The underlying principle is that administrations agree not to introduce changes to safety and quality standards legislation without first discussing proposals with each other and allowing sufficient scope for UK-wide discussion and decision making.

Human breast milk

HBM is devolved and currently considered to be a food under the definitions in assimilated Regulation 178/2002 Article 2 or Regulation (EC) No 178/2002 for NI. 'Food' is defined as '*any substance or product, whether processed, partially processed, or unprocessed, intended to be, or reasonably expected to be ingested by humans'* and currently falls under the Food and Feed safety and hygiene (FFSH) Common Framework.

In the UK, anyone selling or supplying HBM must comply with UK general food law (under EU Regulation 178/2002) and food hygiene legislation under EU Regulation 852/2004. The National Institute for Health and Care Excellence (NICE) also provides clear guidelines for HBM in a clinical context.

The new regulation will apply in NI and classify HBM as a SoHO product from 2027. As set out in the FFSH Framework, the UK Government will continue to work with the Department of Health (NI) on the implementation of this regulation.

Intestinal microbiota and blood preparations that are not used for transfusion

IM (also referred to as faecal microbiota transplants) and blood preparations that are not used for transfusion are currently classed as a medicinal product by the Human Medicines Regulations 2012 (HMRs) (Directive 2001/83/EC). The regulation of human medicines is transferred to NI and reserved for Wales and Scotland, but MHRA regulates UK-wide. As with HBM, IM and blood preparations that are not used for transfusion will come under the SoHO regulation from 2027. Donor health and testing requirements would apply to IM and blood preparations that are not used for transfusion up to the point of processing even if they were then used for medicinal products.

The SoHO regulation sets out the interaction between SoHO and medicinal products and medical devices as well as their regulatory status. Where SoHO is

collected to manufacture a medical device that is regulated by Regulation 2017/745/EU, medicinal product regulated by Directive 2001/83/EC, advanced therapy medicinal products (AMTP) regulated by Regulation 1394/2007 or investigational medicinal products regulated by Regulation 536/2014 – the provisions of the regulation applicable to the SoHO activities referred to in Article 2 paragraph 1 (c)(i) to (iv) and (viii) apply.

Where SoHO activities referred to in Article 2 paragraph 1 (c)(vii), (ix), (x) and (xi) are carried out on SoHO up to and including distribution to a manufacturer regulated by other Union legislation (referred to in this paragraph) this regulation also applies.

Where SoHO (e.g. IM and blood preparations that are not used for transfusion) are used to manufacture products regulated by other Union legislation and those products are exclusively used for therapeutic use on the person from whom the SoHO was collected, the provision of this regulation relating to the SoHO activities referred to in Article 2 paragraph 1 (c)(iii) and (iv) apply.

As set out in the Joint Ministerial Committee (EU Negotiations) Communique 2017, although there is not a Common Framework for these areas the UK Government will continue to work closely with the Devolved Governments, including with the Department of Health in NI.

The UK is a leader in transfusion, transplantation, pharmaceuticals and food safety. The changes in the regulation that apply in NI will not come at the expense of public health, patient safety and access, as the regulation allows more stringent protective measures to be implemented. We also do not anticipate changes to the safety and quality standards set out in this regulation significantly impacting the movement of SoHO from GB to NI.

Movement of SoHO

In line with the Government's commitment to ensuring NI businesses have unfettered access to the rest of the UK internal market, the measures set out in the SoHO regulation will in no way impede the movement of qualifying Northern Ireland goods from Northern Ireland to Great Britain. Such goods will also continue to benefit from the market access principles set out in the United Kingdom Internal Market Act 2020. Accordingly, so long as those goods meet Northern Ireland standards, they can be supplied anywhere in the UK internal market.

The movement of SoHO from GB to NI facilitates its use in life-changing and life-saving treatments. Our assessment is that tissues and cells are the most commonly GB-NI moved substances, and we currently have equivalent standards in these areas. We will continue to engage with the European Commission on any updates to these standards/requirements and will keep this under close review.

Given the importance of SoHO, the UK Government will take action as needed to ensure GB-originating SoHO can be supplied to NI.

The scope of substances covered by the regulation has been increased compared to the BTC Directives and the UK Government will engage closely with the EU, regulators and affected stakeholders on changes to standards and requirements that apply. As noted, the UK maintains high standards in these areas and contributes to the pan-European body that the EU will continue to draw upon for technical and good practice guidelines. NI also will continue to have access to information through EU-UK structures/forums set up as a result of the Windsor Framework.

Analysis by the European Commission on its Impact Assessment

The evaluation of the Blood and Tissues and Cells Directives showed that patients, donors and children born from donated eggs, sperm or embryos are not fully protected from avoidable risks, as the legislation has not kept up to date with scientific and epidemiological developments; there are divergent approaches to oversight among Member States, leading to barriers for cross-border exchange of BTC; the full potential of innovative therapies is not reached for patients, who are also vulnerable to interruptions of BTC supply. There are also some undue burdens due to the absence of common IT systems.

By providing a framework for cross-border cooperation, based on a common set of rules, EU-level measures are best placed to address the above issues effectively, with EU expertise. Establishing high standards of quality and safety for BTC at an EU level brings equal levels of access to safe therapies.

Three options to set and update technical standards were assessed:

- **Option 1** - Decentralised regulation: blood and tissue establishments make reference to a variety of national and international guidance to set their internal technical standards for their own activities.
- **Option 2** - Joint regulation: blood and tissue establishments have to follow the technical standards defined in guidance developed and maintained by nominated EU expert bodies.
- **Option 3** - Central regulation: blood and tissue establishments have to follow the technical standards defined in EU law.

The preferred option is Option 2, which brings the highest effectiveness and efficiency as it builds on established BTC expertise to get timely standards that are applied across the EU.

In addition, a series of common measures was assessed, to fill some legal gaps in the BTC framework, strengthen oversight, facilitate innovation, with advice on

when the BTC legislation is applicable (the delineation with other frameworks will not change), a (risk-) proportionate authorisation for new processes, and (crisis) management of BTC supply. Regarding digital aspects, the preferred implementation is a new single IT system.

There is broad support among stakeholders for option 2, and for the common measures. However, national competent authorities flagged concerns on the resources needed for the implementation of measures to strengthen oversight. Also, while supported, stakeholders pointed out that crisis preparedness measures will bring significant efforts without direct impact in reducing the risks of shortages of critical BTC.

The preferred option would ensure that citizens are better protected when donating, or being treated with a substance of human origin, with more harmonised safety and quality rules across EU. It would also bring a positive impact for healthcare professionals, in blood and tissue establishments. Outdated, and sometimes costly, technical rules for safety and quality will be removed and replaced with standards based on the best scientific evidence and expertise available and updated in a timely manner. The common measures will also strengthen oversight by national competent authorities. Digitalisation will allow for further efficiencies in administrative processes, and the possibility for sharing information will limit duplication of work across Member States.

The main costs relate to monitoring measures (donors, offspring, supply), to registration of bedside preparations of BTC and to the risk-proportionate pathway to authorise BTC processed or used in new ways. Those costs mostly fall on professionals in blood and tissues establishments, hospitals and clinics and, to a lesser degree, on national competent authorities. For EU institutions, the set-up of a common EU IT platform brings an important cost but will allow to lighten (administrative) burden for national authorities and professionals. Further EU costs relate to coordination and co-funding of expert bodies. The overall costs for the measures under the preferred option are expected to be around EUR 38 million per year, above the baseline.

Only a small amount of for-profit ‘small and medium-sized enterprises’ (SMEs) will be directly impacted by the initiative; it concerns mostly establishments found in the sub-sector of medically assisted reproduction (private IVF clinics). The BTC sector is also dependent from developments in medical device technologies (e.g., test kits) and ICT (e.g., data-registries), two SME-rich sectors.

New measures such as authorisation of novel BTC preparations, oversight of bedside BTC preparations and of new SoHOs will require additional resources. The introduction of some risk-based measures will however enable a more efficient oversight with limited resources. Authorities will be further supported with measures like training, audits, common guidance and a dedicated EU IT platform.

There will be positive impacts on some fundamental rights of citizen (health protection, non-discrimination), although for most of the ethical aspects, in particular the rights of children born from medically assisted reproduction, the decisions are taken by Member States at national level. Digital impacts are expected: a single IT system can host flexible solutions, allowing Member States and blood and tissue establishments to maintain and connect with their own system or re-use existing components. It could become an important node in the European Health Data Space and more broadly the EU digital ecosystem.

The overall initiative is limited to aspects that Member States cannot achieve satisfactorily on their own, and where there is an EU added value. The added value of the EU approach is to ensure the full use of the high level of scientific and technical expertise already available in expert bodies such as the ECDC and the EDQM.

The EU Impact Assessment Report can be found at -
EUR-Lex - 52022SC0190 - EN - EUR-Lex (europa.eu)

The EU Impact Assessment is attached at **Annex A**.

Departmental Engagement

DoH officials have had some engagement with colleagues in the DHSC.