Council of the European Union

Brussels, 9 December 2022
(OR. en)

14066/1/22
REV 1

LIMITE

SAN 574
IA 163
CODEC 1606

Interinstitutional File: 2022/0216(COD)

WORKING DOCUMENT

From:	Presidency
To:	Delegations
No. Cion doc.:	11396/22
Subject:	Proposal for a Regulation 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 *- Presidency compromise text on Recital 6 and Article 3*

Delegations will find in Annex a draft text as prepared by the Presidency on the above-mentioned subject for information of delegations.

The text intends to reflect the compromise wording proposed by the Presidency following the discussions at the Working Party on Public Health held on the topic under the Czech Presidency including the written comments received by 18 November. It does not intend to pre-empt future discussions on this subject.

Following the approach outlined in the first Presidency compromise text (14066/22) and in line with the progress report drawn up under the responsibility of the Presidency (14769/22), the Czech Presidency proposes to distinguish between the following categories of definitions:

1) Definitions which might be amended in the future as a result of discussions of relevant articles; ("keep open")

2) Definitions which are proposed to be deleted in Article 3. These concern text sections which are not used in the operative provisions, represent generally known terms or where the content could be better presented or explained in the relevant articles. ("possibly delete")

3) Definitions which are proposed to be revised based on the discussion at the Working Party on Public Health. ("amend"). This category includes a few amendments which will require further discussion.

The proposed changes are implemented visually as follows:

Changes compared to the Commission proposal are marked in **bold/underline** for additions and in ~~strikethrough~~ for deletions, with the following exceptions:

- Definitions and paragraphs in definitions that are in their entirety considered for possible deletion but require further discussion together with relevant articles are formatted in *italics* and put in ***[****square brackets****]***.
- Text modifications within definitions that are proposed for further discussion together with relevant articles are put in **[*square brackets + bold/underline + italics*]** for additions and in [~~*square brackets + strikethrough + italics*~~] for deletions.

(6) This Regulation should apply to blood and blood components, as regulated by Directive 2002/98/EC, as well as to tissues and cells, including haematopoietic peripheral blood, umbilical-cord blood and bone-marrow stem cells, reproductive cells and tissues, foetal tissues and cells and adult and embryonic stem cells, as regulated by Directive 2004/23/EC. Since donation and human application of **various** SoHOs other than **those regulated by Directives 2002/98/EC and 2004/23/EC** ~~blood, tissues and cells~~ are increasingly common, it is necessary to extend the scope of this Regulation to any SoHO, ~~regardless of whether it meets the definition of 'blood', 'tissue' or 'cell',~~ **in order** to avoid that certain groups of donors or recipients are not protected by an appropriate Union level quality and safety framework. This will, for example, ensure the protection of donors-and recipients of human breast milk, intestinal microbiota, blood preparations that are not used for transfusion, and any other SoHO that may be applied to humans in the future.

Article 3

Definitions

For the purpose of this Regulation the following definitions shall apply:

[*(1) 'blood' means the liquid that circulates in arteries and veins carrying oxygen to and carbon dioxide from the tissues of the body;****]***

[*(2) 'blood component' means a constituent of blood such as red cells, white cells, platelets and plasma, that can be separated from it;****]***

[*(3) 'cell' means a mass of cytoplasm with or without a nucleus, that is bound externally by a cell membrane. Usually microscopic in size, cells are the smallest structural and functional unit of an organism;****]***

[*(4) 'tissue' means a group of cells that function together as a unit;****]***

(5) 'substance of human origin' (SoHO) means any substance collected from the human body in whatever manner, whether it contains cells or not and whether those cells are living or not. For the purposes of this Regulation, SoHO does not include organs in the sense of Article 3, point (h), of Directive 2010/53/EU;

(6) 'human application' means inserted, implanted, injected, infused, transfused, transplanted, ingested, transferred ~~(as in transfer to the uterus or fallopian tube of a woman)~~**,** inseminated or otherwise added to the human body in order to create a biological~~, mechanical~~ [~~*or physiological*~~] interaction with that body;

[*(7) 'SoHO activity' means an action, or series of actions, that has a direct impact on the safety, quality or efficacy of SoHOs, as listed in Article 2(1);**]***

(8) 'SoHO donor' means **a living SoHO donor or deceased SoHO donor** ~~any person who has presented themselves to a SoHO entity with a view to making a donation of SoHOs, whether that donation is successful or not;~~

(8a) 'living SoHO donor' means a living person who has presented themselves to a SoHO entity, or been presented by a person granting consent on their behalf, in accordance with national legislation, with a view to making a donation of SoHOs, for the purpose of application to a person other than themselves, and other than situations of within couple use as defined in point (63);

(8b) 'deceased SoHO donor' means a person who has been referred to a SoHO entity and for whom consent or authorisation, or absence of expressed refusal to donation, in accordance with national legislation, is in place;

(9) 'SoHO recipient' means the person to whom SoHOs are applied **or such an application is envisaged;**

(10) 'medically assisted reproduction' means the facilitation of conception by intra-uterine insemination of sperm, in vitro fertilisation or any other laboratory or medical intervention that promotes conception;

(11) 'offspring from medically assisted reproduction' means fetuses and children that are born following medically assisted reproduction;

(12) 'SoHO preparation' means a particular type of SoHO that:

(a) has been subjected to one or more SoHO activities, including processing, in accordance with defined quality and safety parameters;

(b) meets a pre-defined specification; and

(c) is intended for application to a recipient for a specific clinical indication or is intended for distribution for manufacture of a product regulated by ~~other~~ Union legislation, **as referred to in Article 2(3),** or as the starting and raw material thereof;

[(13) 'donor recruitment' means any activity aimed at encouraging persons to become SoHO donors;]

(14) 'collection' means a process by which SoHOs are ~~removed, procured, excreted, secreted or~~ **obtained from a SoHO donor**~~by any other manner~~, including any ~~preparatory steps~~ **SoHO donor treatment**~~, such as hormone treatment,~~ needed to facilitate the process**, at or under the supervision of a SoHO entity**;

(15) 'processing' means any operation involved in the handling of SoHOs, including washing, shaping, separation, fertilisation, decontamination, sterilisation, preservation and packaging;

(16) 'quality control' means ~~several~~ **a pre-defined test, set of** tests or checks to confirm that ~~a SoHO activity or SoHO preparation meets~~ pre-defined quality criteria **are met**;

(17) 'storage' means the maintenance of SoHOs under appropriate controlled conditions [~~*until distribution*~~];

(18) 'release' means a process through which it is verified that a SoHO or a SoHO preparation meets defined safety and quality criteria and the conditions of any applicable authorisation before distribution;

(19) 'distribution' means ~~transportation and delivery~~ **the procedures for providing**~~, within the Union, of~~ released SoHOs ~~or SoHO preparations~~ intended for human application or for the manufacture of products regulated under ~~other~~ Union legislation, **as referred to in Article 2(3),** or as the starting and raw material thereof, **[*within the Union*]**~~including within the same organisation when SoHOs are delivered from a SoHO entity to a unit responsible for human application~~;

(20) 'import' means activities carried out to bring SoHOs ~~or SoHO preparations~~ into the Union from a third country~~, including the organisation of such activities and physical verification of coherence with associated documentation, the appropriateness of transport conditions, the integrity of packaging and the adequacy of labelling before release~~;

(21) 'export' means ~~distribution of~~ **activities carried out to send** SoHOs ~~or SoHO preparations~~ to **a** third countr**y**~~ies~~;

[*(22) 'clinical outcome monitoring' means evaluation of the health of a SoHO recipient for the purpose of monitoring the results of a SoHO preparation application, maintaining care and demonstrating safety and efficacy;****]***

(23) 'autologous use' means ~~collection~~ **application** of **a** SoHO **collected** from ~~one individual~~ **a person** ~~for subequent application~~ to the same ~~individual~~ **person,** ~~with or without further SoHO activities between collection and application~~;

(24) 'SoHO entity' means an organisation legally established in the Union that carries out one or more of the SoHO activities set out in Article 2(1);

[*(25) 'SoHO preparation authorisation' means the formal approval by a competent authority of a SoHO preparation, including the approval of the chain of activities carried out to obtain the SoHO preparation;****]***

(26) 'vigilance' means a set of organised surveillance and reporting procedures relating to adverse occurrences;

(27) 'adverse occurrence' means any incident **linked to any SoHO activity, as listed in Article 2(1),** that caused harm to a living SoHO donor, harm to a SoHO recipient or to offspring from medically assisted reproduction or that implied a risk of such harm;

(28) 'serious adverse occurrence' (SAO) means an adverse occurrence that resulted in, or implied a risk ~~of, any of the following~~**as described in Article [35]/[47].** ~~:~~

[*(a) death;****]***

[*(b) life-threatening, disabling or incapacitating condition, including transmission of a pathogen that might cause such condition;****]***

[*(c) transmission of a genetic condition to offspring from medically assisted reproduction with third party donation;****]***

[*(d) hospitalisation or prolongation of hospitalisation;****]***

[*(e) the need for a clinical intervention to prevent any of the above;****]***

[*(f) loss of a quantity of SoHOs that causes human applications to be postponed or cancelled;****]***

[*(g) loss of highly matched or autologous SoHOs;****]***

[*(h) a mix-up of reproductive cells in such a way that an oocyte is fertilised with sperm from an individual other than the intended individual or reproductive cells are inseminated or transferred to the uterus or fallopian tube of a woman other than the intended recipient;****]***

[*(i) prolonged sub-optimal health of a SoHO donor following single or multiple donations;****]***

[*(29) 'SoHO rapid alert' means a communication regarding a SAO, a communicable disease outbreak or other information that might be of relevance to the safety and quality of SoHOs in more than one Member State and is to be transmitted rapidly between competent authorities and the Commission to facilitate the implementation of mitigating measures;****]***

[(30) 'non-viable' means having no potential for metabolism or multiplication;]

[(31) 'EU SoHO Platform' means the digital platform established by the Commission to exchange information concerning SoHO activities;]

(32) 'SoHO supervisory activity' means any activity as provided for in ~~Chapter III~~ **the Regulation** performed by a competent authority or by a delegated body in order to verify and enforce compliance with this Regulation;

(33) 'the **SoHO** compendium' means a list kept up-to-date by the SoHO Coordination Board of decisions, taken at Member State level, and opinions, issued by competent authorities and by the SCB, on the regulatory status of specific substances, products or activities and published on the EU SoHO platform;

[(34) 'quality management system' means a formalised system that documents processes, procedures, and responsibilities to support achieving defined quality standards in a consistent manner;]

[(35) 'delegated body' means a legal body to which the competent authority has delegated certain SoHO supervisory activities in accordance with Article 6;]

[(36) 'audit' means a systematic and independent examination to determine whether activities and the related results of such activities comply with legislation and planned arrangements and whether these arrangements are applied effectively and are suitable to achieve the objectives;]

(37) 'inspection' means a formal and objective control by a competent authority or delegated body to assess compliance with **the requirements of** this Regulation and other relevant Union or national legislation and to identify**, if applicable,** the need for corrective or preventive action to achieve compliance;

[(38) 'Union training' means activities for the personnel of competent authorities and, where appropriate, for personnel of delegated bodies performing SoHO supervisory activities;]

[*(39) 'assessors' means personnel performing the assessment of SoHO preparations as referred to in Article 22;**]***

(40) 'SoHO establishment' means a SoHO entity that carries out both processing and storage of SoHOs;

(41) '~~critical~~ **essential** SoHO' means a SoHO for which an insufficient supply will result in serious harm or risk of harm to ~~patients~~ **recipients**;

(42) '~~critical~~ **essential** SoHO entity' means a SoHO entity that carries out activities contributing to the supply of critical SoHOs and the scale of those activities is such that a failure to carry them out cannot be compensated by activities of other entities or alternative substances or products for ~~patients~~ **recipients**;

[*(43) 'conditional authorisation' means the granting of permission by a competent authority to a SoHO entity to perform certain SoHO activities under specific conditions defined by that competent authority;**]***

[*(44) 'on-site inspection' means an inspection carried out at the premises of the SoHO establishment, or other SoHO entity, concerned;**]***

[*(45) 'technical guidelines' means a description of a series of methodological procedures and parameters that, if followed, achieve a level of quality and safety of a SoHO activity or a SoHO preparation that is considered to be acceptable as a means to comply with regulatory standards;**]***

[*(46) 'joint inspection' means an inspection carried out by inspectors from more than one Member State;**]***

(47) 'traceability' means the ability to locate and identify SoHOs during any step from collection through processing and storage to ~~distribution~~ **human application** or disposal, including the ability to:

(a) identify the SoHO donor and the SoHO entity processing or storing the SoHOs;

(b) identify the recipient at the SoHO entity applying the SoHOs to the recipient;

(c) locate and identify all relevant data relating to the safety and quality of the SoHOs and any materials **[*or devices*]** coming into contact with those SoHOs **that pose a risk to safety or quality**;

[*(48) 'Single European Code' (SEC) means the unique identifier applied to certain SoHOs distributed in the Union;****]***

[*(49) 'SAO notification' means the communication from a SoHO entity, a SoHO establishment or a SoHO donor or recipient to a competent authority, of a serious adverse occurrence or a suspected serious adverse occurrence associated with a SoHO donation or human application;****]***

[*(50) 'SAO investigation report' means the report from a SoHO entity or a SoHO establishment to a competent authority on a specific SAO, describing the outcome and including an assessment of the seriousness and the level of imputability, the likely cause and any corrective action taken;****]***

(51) 'imputability' means the likelihood that a**n** ~~serious~~ adverse occurrence, in a SoHO donor, is related to the ~~donation~~ **collection** process or**,** in a **SoHO** recipient~~,~~ **or an offspring from medically assisted reproduction,** to the application of the SoHOs;

(52) 'seriousness' means the degree of severity of an adverse occurrence, involving harm to a SoHO donor, recipient or offspring from medically assisted reproduction, at and above which the occurrence shall be notified to a competent authority;

[(53) 'self-reporting' means the notification of a SAO by a SoHO recipient or a SoHO donor directly to the competent authorities;]

[(54) 'Annual SoHO Vigilance Report' means the annual report published by the Commission aggregating the summaries from the SoHO National Authorities on SAO notifications and SAO investigation reports received;]

[(55) 'deferral' means temporary or permanent suspension of the eligibility of an individual to donate SoHO;]

[(56) 'responsible person' means the nominated individual in a SoHO entity that has responsibility for SoHO release;]

[(57) 'process validation' means establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce results meeting predetermined specifications and quality attributes;]

[(58) 'equipment qualification' means establishing documented evidence that provides a high degree of assurance that a specific piece of equipment will consistently perform to predetermined specifications;]

[(59) 'EDQM SoHO monograph' means a specification of the critical quality parameters of a particular SoHO preparation defined by the European Directorate for the Quality of Medicines and HealthCare of the Council of Europe;]

[(60) 'Annual SoHO Activity Report' means the annual report published by the Commission aggregating the data reports from SoHO entities carrying out the following activities: donor recruitment, collection, distribution, import, export and human application of SoHOs;]

(61) 'reproductive cells' means all cells intended to be used for the purpose of medically assisted reproduction;

(62) 'third party donation' means a donation of reproductive cells by a person to a person or a couple with whom the donor does not have an intimate physical relationship;

(63) 'within couple use' means use of reproductive cells for medically assisted reproduction from two persons with an intimate physical relationship, where one person supplies their own oocytes and the other person supplies their own sperm;

(64) 'compensation' means making good of any losses associated with donation;

(65) 'allogeneic use' means ~~collection~~ **application** of SoHO **collected** from **a SoHO donor who is a person other than the SoHO recipient** ~~one individual for subsequent application to another individual~~;

[*(66) 'SoHO supply alert' means a communication regarding a significant interruption to the supply of critical SoHOs that is to be transmitted to a competent authority, and when necessary, by a SoHO National Authority to the competent authorities of other Member States;****]***

[*(67) 'plasma master file' (PMF) means a compilation of the required scientific data, covering all aspects of the use of plasma, from collection to the creation of a plasma pool, on the quality and safety of human plasma relevant to the medicinal products, medical devices and investigational products that use human plasma in their manufacture;****]***

[*(68) 'plasma for transfusion' means plasma separated from whole blood or collected by apheresis for the purpose of transfusion to a recipient;****]***

[*(69) 'plasma for fractionation' means plasma separated from whole blood or collected by apheresis and used as the starting material for manufacturing of plasma-derived medicinal products;****]***

[*(70) 'apheresis' means a process by which a specific blood component or type of stem cell is separated from whole blood during the donation, allowing the remaining blood components to be returned immediately to the donor.****]***