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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 *- Examination of the Presidency compromise text*

In document ST 13503/23 INIT, on page 20-24, Articles 22 and 22a should read as follows (changes in comparison to ST 13503/23 INIT are highlighted in yellow):

Article 22

Assessment of SoHO preparations

1. The assessment of a SoHO preparation~~,~~ shall include a review of all SoHO activities that are performed for that SoHO preparation and that might influence the safety, quality and **effectiveness** ~~efficacy~~ of the SoHO preparation.

2. The assessment of SoHO preparations shall be carried out by **SoHO preparation** assessors meeting the requirements set out in Article 24.

3. In cases where the SoHO preparation**,** subject to the application for authorisation pursuant to Article 21**,** has been duly authorised in another SoHO entity in the same or in another Member State **~~or by the transitional provisions referred to in Article 82~~**, **SoHO** competent authorities may authorise that SoHO preparation ~~in the applicant SoHO entity~~, provided that the **SoHO** competent authorities have verified that the SoHO activities performed **and the steps of the processing applied** for the SoHO preparation are carried out by the applicant ~~SoHO entity~~ in a manner such that the safety, quality and **effectiveness** ~~efficacy~~ results **of the SoHO preparation** will be equivalent to those demonstrated in the SoHO entity where the SoHO preparation was first authorised.

4. In cases where the SoHO preparation, subject to the application for authorisation pursuant to Article 21, has not been ~~duly~~ authorised in another SoHO entity, **or the SoHO competent authority chooses not to take SoHO preparation authorisation in another Member State into account, SoHO** competent authorities **shall**:

(a) ~~shall~~ assess **the adequacy of** ~~all~~ the information provided by the applicant pursuant to Article 41**(2) point (a);**

(b) ~~shall review the SoHO preparation dossier referred to in Article 41(2), point (a);~~

(c) ~~shall~~ initiate the consultation described in Article 14~~(1)~~, if during the review of the **information** ~~SoHO preparation dossier~~ referred to in point (~~a~~b), questions arise as to whether the SoHO preparation falls, in part or fully, within the scope of this Regulation or other Union legislation, taking into account the activities performed for the SoHO preparation and the intended human application;

(d) ~~shall review and~~ evaluate the **~~results of a benefit~~** risk assessment **carried out** ~~performed~~ by the applicant as pursuant to Article 41(2), point (b) **together with an evaluation of the scientific evidence and clinical data provided regarding expected benefit**;

(e) ~~shall~~ evaluate the plan for clinical outcome monitoring**,** and its proportionality to the level of risk **and expected benefit** of the SoHO preparation **according to Article 22a, where relevant;** ~~paraghap 4a as referred to in Article 41(3), points (a), (b) and (c), as applicable;~~

(f) ~~shall may~~ consult the SCB, pursuant to Article 68(1) on the evidence necessary and sufficient for the authorisation of a particular SoHO preparation **where the guidance referred to in paragraph 7 is not sufficient**;

(g) ~~shall~~ assess, in the case of **an approved clinical outcome monitoring plan** ~~a conditional authorisation~~ pursuant to Article 21(2), point (c), the results of ~~that plan that plan the clinical outcome monitoring~~ **the clinical outcome monitoring upon completion and submission by the applicant**.

~~**4a. When evaluating clinical outcome monitoring plans, as referred to in paragraph 4 point (e), SoHO competent authorities shall verify that the plan proposes clinical outcome monitoring as follows:**~~

~~**(a) in cases of low risk, pro-active clinical follow-up of a defined number of SoHO recipients;**~~

~~**(b) in cases of moderate risk, in addition to point (a), a clinical study of a pre-defined number of SoHO recipients assessing pre-defined clinical endpoints;**~~

~~**(c) in cases of high risk, in addition to point (a), a clinical study of a pre-defined number of SoHO recipients assessing pre-defined clinical endpoints with a comparison to standard therapy.**~~

5. When assessing the SoHO preparation pursuant to paragraph 4, points (e) and (g), **SoHO** competent authorities shall **verify** ~~consider~~, in the cases where the applicant has proposed to record, and recorded, the results of the clinical outcome monitoring in an existing clinical registry, that this ~~is an acceptable method, provided that those competent authorities have verified that the~~ registry has data quality management procedures in place that ensure **adequate** accuracy and completeness **of data**~~of data~~.

6. **SoHO c**~~C~~ompetent authorities shall conduct the assessment ~~steps~~ referred to in paragraphs 3 and 4 of this Article by means of a remote document review. **SoHO c**~~C~~ompetent authorities may also, as part of the SoHO preparation assessment, carry out inspections pursuant to Articles 29, 30 and 31. **Member States shall ensure communication and cooperation between SoHO preparation assessors and inspectors pursuant to Article 13.**

7. When conducting the assessment steps referred to in paragraph 4 **and 4a** of this Article, **SoHO** competent authorities shall **take into account** ~~consult~~ the best practices agreed and documented by the SCB as referred to in Article 68(1), point (c).

Article 22a

Clinical outcome monitoring plans

1. As a basis for the assessment of an authorisation for a new SoHO preparation a clinical outcome monitoring plan shall be approved by the SoHO compe~~n~~tent authority in cases where scientific and clinical evidence provided as part of the assessment carried out by the applicant, as referred to in Article 22(4)(d), is other than negligible. The approved clinical outcome monitoring plan shall be implemented, and the results of the monitoring assessed, before the SoHO preparation authorisation is granted pursuant to Article 21.

2. Clinical outcome monitoring plans shall not be approved in cases where scientific and clinical data provided as part of the benefit-risk analysis indicate a relevant level of risk without a significant expected benefit.

~~**The clinical outcome monitoring plan shall include:**~~

~~**(a) clinical outcome monitoring according to 22a (3) point c, where scientific data for clinical use are not available or sparse, where benefit and risk are not evaluable, or when a negative benefit-risk analysis based on current knowledge is confirmed.**~~

~~**(b) clinical outcome monitoring according to 22a (3) point a, in a case of a relevant risk despite a positive benefit-risk analysis.**~~

3. The design of clinical outcome monitoring plan referred to in paragraph 1, shall be proportionate to the level of risk assessed by the applicant, together with the expected benefit, and shall take into account the guidance and templates provided by their SoHO competent authority, in accordance with Article 21(1).

4. The clinical outcome monitoring plan shall include the clinical outcome monitoring as follows:

(a) in cases of low ~~benefit~~ risk, and a positive benefit-risk pro-active clinical follow-up of a defined number of SoHO recipients;

(b) in cases of moderate ~~benefit~~ risk, and a positive benefit-risk, in addition to point (a), a clinical study of a pre-specified number of SoHO recipients assessing pre-defined clinical endpoints;

(c) in cases of high ~~benefit~~ risk, and a positive benefit-risk, and cases where risk or benefit are not evaluable due to a lack of scientific and clinical data or knowledge, in addition to point (a), a clinical study of a pre-specified number of SoHO recipients assessing pre-defined clinical endpoints with a comparison to standard therapy.

5. To record the clinical data generated during the clinical outcome monitoring, the applicant shall record those data via their own registries or existing clinical registries. In cases where the applicant SoHO entity chooses to use existing clinical registries, those registries shall be verified by the SoHO competent authority, or shall be certified by an external institution, in terms of the reliability of their data quality management procedures.

6. In case where vigilance reports indicate a risk for SoHO donors, SoHO recipients or offspring from medically assisted reproduction, SoHO competent authorities may stop clinical outcome monitoring.