

Linea guida EDQM su tessuti e cellule e Regolamento Europeo

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Fondazione Banca degli Occhi del Veneto

XVIII Corso Nazionale SIBO - Milano, 5-6 giugno 2026



DICHIARO

di non avere alcun conflitto di interessi, diretto o indiretto, in relazione all'oggetto del mio intervento o alle tematiche trattate nel congresso.





2024/1938

17.7.2024

REGOLAMENTO (UE) 2024/1938 DEL PARLAMENTO EUROPEO E DEL CONSIGLIO

del 13 giugno 2024

sui parametri di qualità e sicurezza per le sostanze di origine umana destinate all'applicazione sugli esseri umani e che abroga le direttive 2002/98/CE e 2004/23/CE

- Abroga la «legislazione BTC» (sangue, tessuti e cellule) costituita dalle Direttive 2002/98/CE e 2004/23/CE
- Si applica dal 7 agosto 2027



Regolamento SoHO: aspetti generali

Il Regolamento SoHO riguarda tutte le sostanze di origine umana, anche prive di cellule, destinate all'applicazione umana o utilizzate per la fabbricazione di dispositivi medici e prodotti medicinali

Sono esclusi dal regolamento:

- gli organi per trapianto
- le SoHO utilizzate per ricerca *in vitro* o su animali



Regolamento SoHO: aspetti generali

Il regolamento SoHO non contiene i requisiti tecnici, per i quali si rimanda alle linee guida pubblicate da:

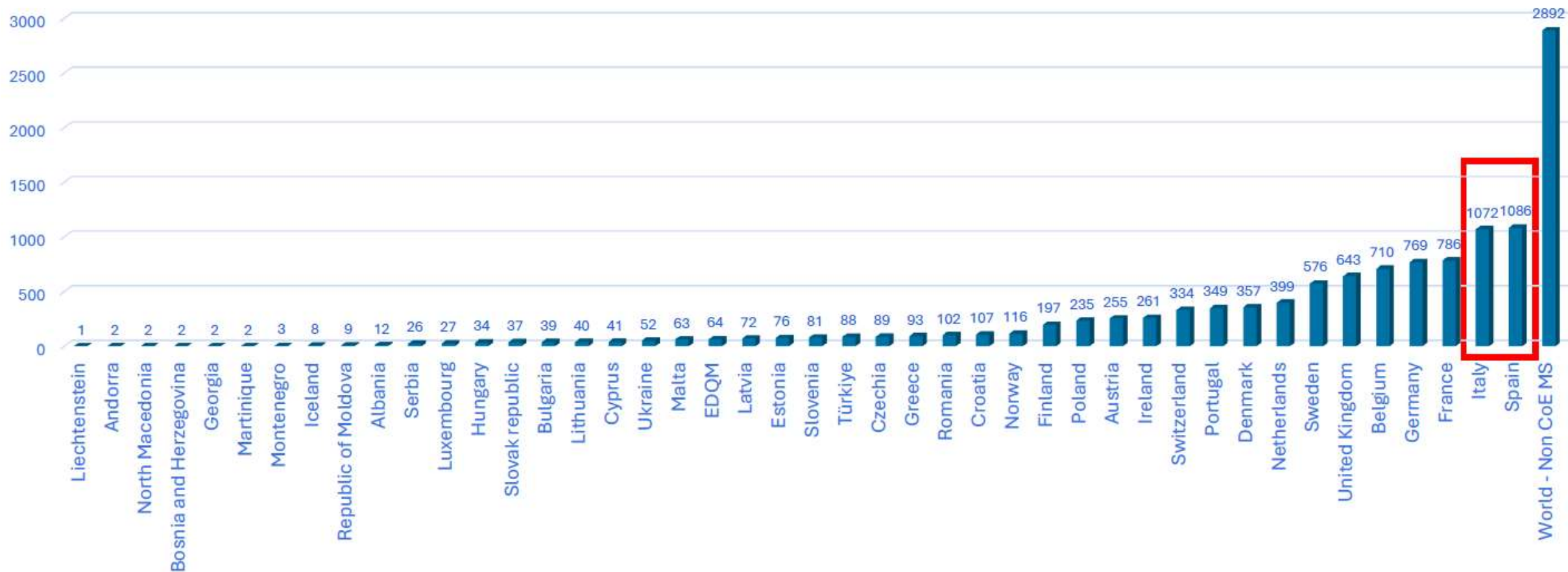
- **Direzione europea per la qualità della medicina e dell'assistenza sanitaria (EDQM)**
- Centro europeo per la prevenzione e il controllo delle malattie (ECDC)
- eventuali linee guida nazionali, purché siano almeno equivalenti alle indicazioni EDQM-ECDC



Downloads of the 5th edition of the TC Guide

N= 14,517
(4th edition N= 10,367)

Publication of the Guide: 15 December 2022
Date of analysis: 1 March 2025



Guide to the quality
and safety of
TISSUES AND CELLS
for human application



European Committee
(Partial Agreement)
on Organ Transplantation
(CD-P-TO)

EDQM
5th Edition
2022



Linea Guida Tessuti e Cellule

5° ed.

-La struttura-

Parte A: Requisiti Generali (18 capitoli)

Requisiti generali applicabili a tutte le SoHO, agli enti e ai centri che svolgono attività relative alle SoHO

Chapter	Argument	Main Objective	Key Technical Requirements
1	Introduction	Define framework, risks and ethical principles	Consent, anonymity, equity, regulatory framework
2	Quality Management	Implement a Quality Management System (QMS)	Validation, audits, deviation management, staff training
3	Risk Management	Systematic risk control	HACCP, FMECA, root cause analysis
4	Donor Recruitment	Identification and consent	Structured process, ethical/legal compliance
5	Donor Evaluation	Clinical suitability assessment	Medical history, absolute/relative contraindications
6	Donor Testing	Biological safety	HIV, HBV, HCV, syphilis; sample quality control
7	Procurement	Safe tissue/cell retrieval	SOPs, qualified personnel, controlled transport
8	Premises	Environmental control	Cleanrooms, particulate and microbiological monitoring
9	Processing	Tissue/cell processing	Decontamination, sterilisation, process validation
10	Storage	Preservation conditions	Temperature control, liquid nitrogen, shelf-life monitoring
11	Microbiology	Contamination control	Sterility testing, bioburden, method validation
12	Release & Distribution	Product release for use	Release criteria, transport, import/export compliance
13	Clinical Interaction	Clinical application interface	Traceability, follow-up, supplier selection
14	IT Systems	Data management	Software validation, data integrity
15	Coding & Labelling	Product identification	SEC, ISBT 128, full labelling requirements
16	Traceability	End-to-end tracking	Donor → product → recipient traceability
17	Biovigilance	Post-application safety	SAE/SAR reporting, monitoring, prevention
18	Innovation	New processes and applications	Risk assessment, regulatory approval



Parte B: Requisiti Specifici (16 capitoli)

Requisiti specifici in
aggiunta e/o in deroga
ai requisiti elencati
nella parte generale

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Guide to the quality
and safety of
TISSUES AND CELLS
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for the Quality
& Safety of
Medicines
& Health-care
Products

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

Linea Guida Tessuti e Cellule

6° ed.

- La Lettura -

Primo livello

Standards

Questo livello contiene le norme derivanti dal regolamento SoHO.

Per gli Stati membri dell'UE, queste norme sono **obbligatorie**.

Alla fine di ogni norma è citato l'articolo di riferimento del regolamento SoHO.

Viene utilizzato il verbo 'deve' (*must*) per indicare la necessità di conformarsi.



1 Chapter 12. Microbiology

2 12.1 Introduction

3 This chapter addresses a comprehensive strategy for the assessment of the microbiological quality and safety
4 of human tissues and/or cells (TC) for human application. This outline of the test methods of the *European*
5 *Pharmacopoeia (Ph. Eur.)* [1] considers the specific characteristics and limitations of human TC. The selection
6 of test methods relies on a risk assessment that considers factors such as the initial microbial load (bioburden)
7 of TC after collection, the nature of the test sample, the availability of the sample given the scarcity of TC,
8 the ability to decontaminate or sterilise the final TC preparation (TCP), the mode and route of application to
9 the recipient and other relevant factors.

10 Additional guidance on microbiological testing for specific TC processes is available in the TC specific
11 chapters in Part B of this Guide.

12 Standards

13 S12.1 Substances of Human Origin (SoHO) entities must mitigate risks arising from microbial contamination
14 of SoHO from the environment, the personnel, the equipment and the materials coming into contact
15 with SoHO during collection, processing, storage or distribution. SoHO entities must mitigate such
16 risks by performing quality control testing of SoHO to detect microbial contamination and using
17 methods of inactivation or elimination of micro-organisms, where feasible and appropriate (Art.
18 58.5).

19 Good Practice Guidelines

20 G12.1 All establishments that process TC should have access to the services of a microbiology laboratory,
21 licensed or accredited to relevant national or international standards, and should have access to the
22 advice of a suitably qualified expert microbiologist.

23 12.2 Testing

38 G12.4 If an appropriately validated terminal sterilisation process is applied (SAL of $\geq 10^{-6}$ [2]), parametric
39 release allows SoHO establishments to replace post-processing microbiological testing as a release
40 criterion with acceptance criteria for the control of identified process parameters (*Ph. Eur.* 5.1.1).

41 G12.5 Despite the limited availability of TC, samples for testing should be representative of the whole TCP
42 and suitable to ensure that the chosen analytical method can be performed with acceptable
43 sensitivity and specificity to prevent false negative or false positive test results.

44 G12.6 In cases where the nature, scarcity or size of the collected TC prevents direct sampling, an alternative
45 sampling approach should be implemented which may include sampling adjacent TC, sampling liquids
46 in contact with the TC (e.g. storage media, transport media or rinsing solutions) or using swabs.

47 Recommendations

48 R12.1 It is recommended to perform a risk assessment to determine whether it is necessary to perform in-
49 process microbiological testing at relevant steps of the TCP process.

50 Supplementary information

51 Microbiological contaminants may be present within the TC, as well as on the surface of the TC (GPG 12.3).
52 Therefore, it is beneficial to process representative TC samples for microbiological testing [3, 4]. Most TC are
53 exposed to the direct environment at certain processing stages between collection and packaging. Avoiding
54 open processing unless it is absolutely necessary allows minimising the risk of contamination during open
55 processing. This will help to ensure that aseptic conditions are maintained throughout processing. The
56 standards for microbiological sampling and testing are expected to be most stringent in these situations.

57 By testing at relevant steps of the aseptic process, one can verify that the TC meet predefined standards
58 for microbiological quality throughout the whole preparation process. This helps in maintaining consistency
59 and ensures that the TCP will be safe for clinical application. In-process testing also enables the verification
60 that decontamination, sterilisation and other processing steps have been effective in reducing microbial
61 bioburden.

62 When a closed system is employed during processing, it may not be necessary to carry out in-process
63 testing because it does not provide any additional information regarding the microbiological status of TCP.
64 However, if the starting material is not sterile and the process involves prolonged incubations under
65 conditions conducive to microbial growth, a risk assessment may indicate the need for in-process testing.
66 Given the special nature of human body material and the desire to keep as much material as possible
67 available for transplantation, it is acceptable to base the release of terminally sterilised TC in their final
68 container only on process and validation data (parametric release) and not on microbiological testing of the
69 final TCP. This approach includes the validation of TC collection, transport, washing, antibiotic treatment and
70 other processing steps, packaging and storage. In some countries, such an approach may require permission

Secondo livello

Linee guida sulle buone pratiche (GPG)

Le GPG approfondiscono gli elementi che devono essere definiti, attuati e monitorati dagli enti/centri SoHO.

Le GPG sono **obbligatorie** per gli Stati membri UE, a meno che l'ente/centro SoHO non dimostri che discostarsene comporti una qualità e una sicurezza equivalenti o migliori.

In questo livello si utilizza il verbo 'dovrebbe' (*should*).



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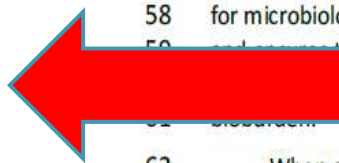
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Terzo livello

Raccomandazioni

Questo livello contiene le indicazioni che **non** sono ritenute sufficientemente rilevanti da essere classificate come obbligatorie.

I termini utilizzati sono ‘raccomandato’ o ‘consigliato’ (*recommended, advised*).



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Quarto livello

Informazioni supplementari

Questo livello comprende i testi che spiegano la motivazione alla base della norma, oppure le informazioni generali di contesto.



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Conclusioni

- Uniformità tra gli Stati dell'Unione relativamente ai criteri di qualità e sicurezza
- Flessibilità rispetto agli aggiornamenti dei requisiti tecnici (EDQM, ECDC)
- Migliore condivisione di dati e informazioni
- Ampliamento della disponibilità delle risorse per i pazienti



Grazie per l'attenzione!



2° edizione, 2004



3° edizione, 2009



5° edizione, 2022





Ente SoHO

Ente che svolge una delle seguenti attività: registrazione e selezione dei donatori, raccolta, processazione, controllo qualità, stoccaggio, rilascio, distribuzione, import/export, applicazione, registrazione esiti clinici (ad es. laboratorio di analisi)

Obblighi

- ▶ Registrazione nella Piattaforma UE per le SoHO o in un registro nazionale (ad eccezione degli enti accreditati prima del 7 agosto 2024 in base alla direttiva 2004/23/CE)
- ▶ Nomina della persona responsabile
- ▶ Attuazione di un sistema di gestione della qualità

Centro SoHO

Ente che svolge almeno una delle seguenti attività:

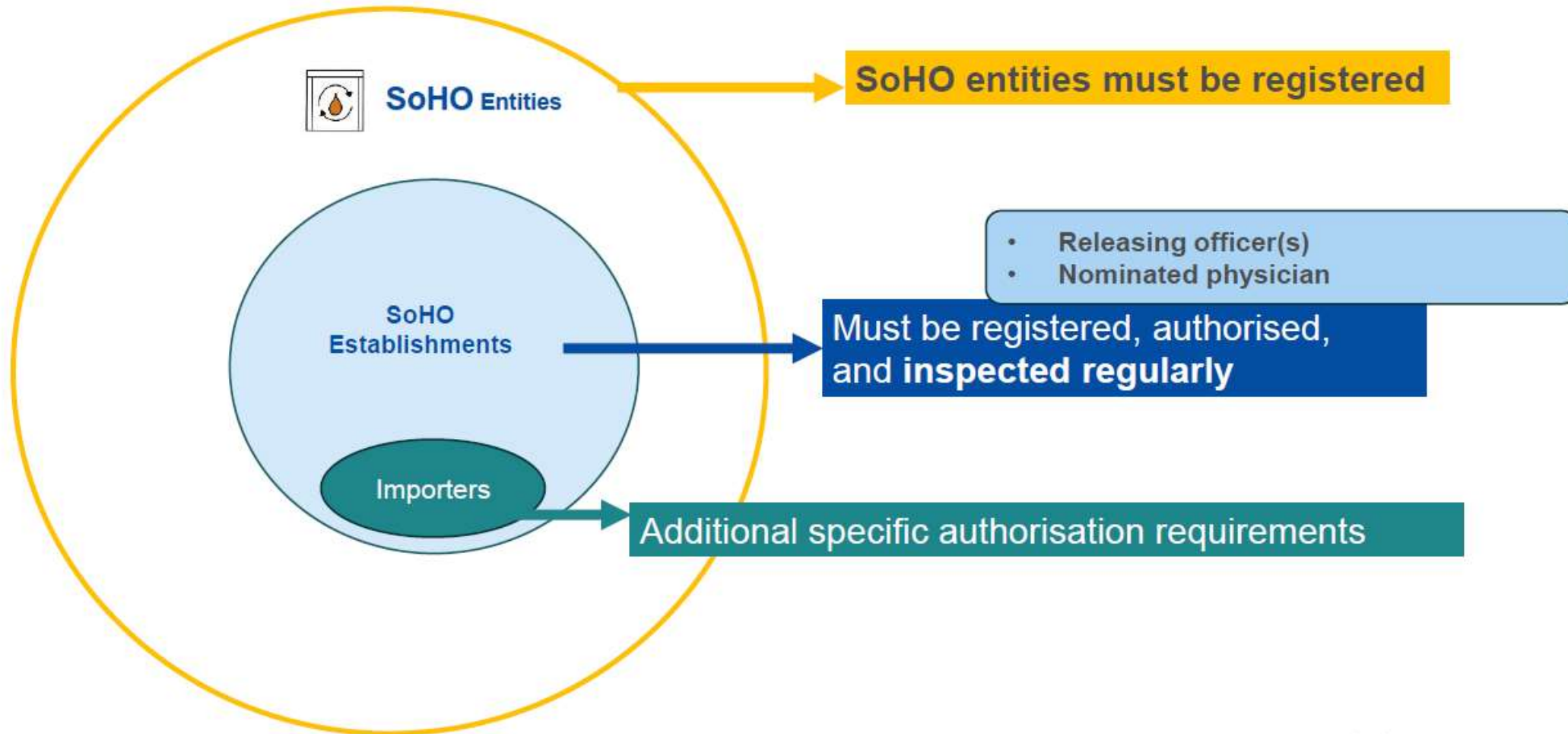
- processazione e stoccaggio
- rilascio
- importazione/esportazione

Deve essere **ispezionato e autorizzato** dall'autorità competente almeno ogni **4 anni** (in base al rischio associato all'attività)

Obblighi per i centri SoHO

- ▶ Registrazione nella Piattaforma UE per le SoHO o in un registro nazionale (eccetto gli istituti dei tessuti accreditati prima del 7 agosto 2024 in base alla direttiva 2004/23/CE)
- ▶ Nomina di:
 - ▶ persona responsabile
 - ▶ incaricato responsabile del rilascio
 - ▶ medico responsabile
- ▶ Attuazione di un sistema di gestione della qualità
- ▶ Domanda di autorizzazione di nuove preparazioni SoHO all'autorità competente
- ▶ Codifica e rintracciabilità delle SoHO (30 anni)
- ▶ Trasmissione annuale dei dati sulle attività alla Piattaforma UE

Enti e Centri SoHO



Note: CA may inspect any SoHO entity, as it considers necessary and may “upgrade” an entity to establishment status

Persona responsabile

Compiti: garantisce che le attività relative a SoHO rispettino i requisiti del regolamento

Requisiti: diploma universitario in scienze mediche, farmaceutiche o biologiche, con almeno due anni di esperienza nel settore

Incaricato responsabile del rilascio

Compiti: prima della distribuzione, verifica che le SoHO soddisfino i criteri di qualità e sicurezza

Requisiti: diploma universitario in scienze mediche, farmaceutiche o biologiche, con almeno due anni di esperienza nel settore

Medico

Compiti:

- ▶ elabora i criteri di idoneità dei donatori di SoHO, le procedure per la raccolta di SoHO e i criteri per l'assegnazione di SoHO
- ▶ gestisce gli aspetti clinici dell'indagine sulle sospette reazioni avverse
- ▶ progetta e gestisce i piani di monitoraggio degli esiti clinici negli studi finalizzati alle autorizzazioni di preparazioni di SoHO

Autorità Competente/i e Autorità Nazionale

- ▶ Gli Stati membri designano l'**Autorità o le Autorità competenti** per la sorveglianza sulle SoHO a livello nazionale, regionale o locale
- ▶ L'Autorità competente può nominare un **Organismo delegato** per svolgere attività di sorveglianza in uno specifico ambito
- ▶ L'**Autorità nazionale**, designata tra le autorità competenti, coordina le Autorità competenti all'interno del proprio Stato e si coordina con le Autorità nazionali degli altri Stati, con il Comitato di coordinamento per le SoHO (SCB) e con la Commissione

Comitato di coordinamento per le SoHO

-SoHO Coordination Board-

- ▶ Composto da due membri permanenti + due membri supplenti per ciascun Stato

Attività:

- ▶ Coordinamento e supporto per le Autorità nazionali
- ▶ Pareri sullo stato normativo delle SoHO, prodotti o attività
- ▶ Coordinamento con EDQM e ECDC per gli aggiornamenti
- ▶ Gestione del Compendio per le SoHO

Sottogruppi di lavoro di SCB per le SoHO

- ▶ 1. Registrazione degli enti e autorizzazione dei centri
- ▶ 2. Autorizzazione e valutazione delle preparazioni SoHO
- ▶ 3. Ispezioni
- ▶ 4. Vigilanza e tracciabilità
- ▶ 5. Approvvigionamento
- ▶ 6. Questioni normative

Compendio per le SoHO

- ▶ Elenco aggiornato dal Comitato di coordinamento per le SoHO contenente le decisioni e i pareri emessi dalle autorità competenti e dallo stesso Comitato
- ▶ Pubblicato sulla Piattaforma UE per le SoHO

La Commissione Europea

- ▶ Verifica che gli Stati membri rispettino il Regolamento
- ▶ Organizza la formazione e i programmi di scambio del personale tra le autorità competenti
- ▶ Fornisce il segretariato e il supporto per le attività del Comitato di Coordinamento per le SoHO
- ▶ Gestisce la Piattaforma UE per le SoHO

Piattaforma UE per le SoHO

Piattaforma digitale gestita dalla Commissione Europea

- ▶ Sezione ad accesso limitato:
 - ▶ Scambio di informazioni e dati a tutti i livelli: tra autorità di Stati diversi, ma anche tra enti all'interno dello stesso Stato
- ▶ Sezione pubblica:
 - ▶ Compendio sulle SoHO
 - ▶ Status autorizzativo dei centri
 - ▶ Elenco delle preparazioni SoHO autorizzate
 - ▶ Relazioni annuali
 - ▶ Orientamenti EDQM - ECDC

Disposizioni transitorie e finali

- ▶ Gli istituti dei tessuti accreditati prima del 7 agosto 2024 in base alla direttiva 2004/23/CE sono considerati centri SoHO
- ▶ Le preparazioni derivanti da processi di preparazione eseguiti in base alla direttiva 2004/23/CE prima del 7 agosto 2024 sono considerate autorizzate e vengono registrate nella Piattaforma UE per le SoHO
- ▶ Il regolamento SoHO è in vigore dal 6 agosto 2024 e si applica a decorrere dal 7 agosto 2027