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**WORKING DOCUMENT**

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|---|---|
| From: | Presidency |
| To: | Delegations |
| No. prev. doc.: | 6442/25 |
| Subject: | Proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC<br>Proposal for a Regulation of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006<br>*- Exchange of views* |

Delegations will find in Annex the revised Articles on manufacturing and import to be discussed at the meeting of the Working Party on 8 April 2025.

Changes compared to the Commission proposals are indicated in ~~strikethrough~~ for deletions and **bold/underline** for new text made in document . In addition, changes compared to document 6442/25 are highlighted in grey.

# DIRECTIVE

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(109) There may be cases where manufacturing or testing steps of medicinal products need to take place in sites close to patients, for example advanced therapy medicinal products with short shelf-life. In such cases, these manufacturing or testing steps may need to be decentralised to multiple sites to reach patients across the Union. When the manufacturing or testing steps are decentralised, they should be carried out under the responsibility of the qualified person of an authorised central site. The decentralised sites should not require a separate manufacturing authorisation from the one granted to the relevant central site but should be registered by the competent authority of the Member State in which the decentralised site is established. In the case of medicinal products containing, consisting or derived from ~~autologous~~ SoHO, the decentralised sites have to be registered as a SoHO entity as defined in and pursuant to [SoHO Regulation] for the activities of donor review and eligibility assessment, donor testing and collection, **where applicable** ~~or just for collection in the case of products manufactured for autologous use~~.

**Article 4**

***Definitions***

**(67a) 'manufacture of medicinal products' means any total or partial operation as part of the process of bringing the active substance(s) and excipient(s) to a medicinal product, including processing, filling, sterilisation, assembly, immediate and outer packaging, storage, quality control testing, and release of the medicinal product;**

**(67b) 'decentralised manufacturing' means the manufacturing and testing activities for medicinal products that rely on the existence of a central site that ensures supervision and control of one or several decentralised sites located in proximity to patients, where parts of the manufacturing and testing operations take place;**

**(67c) 'manufacture of active substances' used in the manufacturing process of a medicinal product' means any total or partial operation of receipt of materials, production, packaging, repackaging, labelling, relabelling, quality control or release of active substances, and the related controls;**

# Chapter II

# Application requirements for national and centralised marketing authorisations

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## Section 4

## Specific dossier requirements

***Article 26a***

***Medicinal products concerned with decentralised manufacturing***

**1. When justified by the specific properties of the manufactured medicinal product and consideration related to the quality, safety and efficacy of a medicinal product, such as short shelf life, or where proximity to the treated patient or customisation for an individual patient ~~is required~~ to their benefit, the marketing authorisation applicant may request the competent authority ~~for agreement~~ to approve the use of a decentralised manufacturing ~~site~~ as referred to in Chapter XI as part of the manufacturing of the medicinal product concerned.**

**~~2. 'Decentralised manufacturing' means an approach to the manufacturing and testing activities for medicinal products that relies on the existence of a central site that ensures supervision and control of one or several decentralised sites located in proximity to patients, where parts of the manufacturing and testing operations take place.~~**

**3. The request referred to in paragraph 1 shall be submitted as part of the marketing authorisation application in accordance with Annex II.**

**4. The competent authority shall assess the request referred to in paragraph 1 as part of the assessment of the marketing authorisation application.**

**4a. The competent authority referred to in paragraph 4, shall cooperate with all relevant regulatory authorities, including with the supervisory authority in charge of the authorisation of the central site identified in the application. The manufacturing authorisation of the central site referred to in Article 142 shall be provided as part of the application procedure for a marketing authorisation.**

**5. The ~~agreement~~ approval to use decentralised manufacturing shall be included in the terms of the marketing authorisation.**

**6. The ~~agreement~~ approval to use decentralised manufacturing may be withdrawn by the competent authority, where it concludes that the justification referred to in paragraph 1 is no longer fulfilled or that the conditions for decentralised manufacturing as referred to in chapter XI are not complied with. The competent authority shall inform the the supervisory authority in charge of the authorisation of the central site of such a circumstance without delay.**

**7. The ~~M~~marketing authorisation holders making use of decentralised manufacturing shall provide the competent authority with any new information that might entail an amendment to the terms of the marketing authorisation as referred to in paragraph 5, ~~introduce any required changes~~ in accordance with Article 90.**

**8. ~~The Agency, in consultation with the competent authorities of the Member States, shall publish scientific guidelines on the justification referred to in paragraph 1.~~ The Commission may adopt implementing acts to set out the format and content of the request and on the application of principles as referred to in paragraph 1.**

# Chapter XI

# Manufacturing and import

## Section 1

## Manufacturing and import of medicinal products

*Article 142*

*Manufacturing authorisation*

1. Member States shall take all appropriate measures to ensure that the manufacture of the medicinal products within their territory is subject to authorisation (the "manufacturing authorisation"). The manufacturing authorisation shall be required also if the medicinal products manufactured are intended for export.

2. The manufacturing authorisation referred to in paragraph 1 shall be required for both total and partial manufacture, and for the various processes of dividing up, packaging or presentation. **The manufacturing authorisation shall apply only to the categories of medicinal products, pharmaceutical forms, the manufacturing operations and the premises specified in the application ~~and to the premises specified in the application~~.**

3. By derogation from paragraph 2, the manufacturing authorisation shall not be required for the following:

(a) preparation, dividing up, changes in packaging or presentation where these processes are carried out, solely for retail supply, by pharmacists in dispensing pharmacies or by persons legally authorised in the Member States to carry out such processes; or

(b) decentralised sites carrying out manufacturing or testing steps**, in accordance with Article 26a and Article 148,** under the responsibility of the qualified person of a central site referred to in Article 151(3).

4. A manufacturing authorisation shall also be required for imports of medicinal products coming from third countries into a Member State.

This Chapter and Articles 195(5) and 198 shall apply to imports of medicinal products from third countries.

5. Member States shall enter the information relating to the manufacturing authorisation referred to in paragraph 1 in the Union database referred to in Article 188(15).

*Article 143*

*Requirements for a manufacturing authorisation*

1. In order to obtain the manufacturing authorisation, the applicant shall submit an application by electronic means to the competent authority of the Member State concerned. **Member States may provide for the possiblity of submission in paper format.**

That application shall include **at least** the following particulars:

(a) **name or corpoarate name and permanent address~~,~~;**

**(aa)** the medicinal products, the pharmaceutical forms and the manufacturing operations that are to be manufactured, imported or carried out and the place where the activity will take place;

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(b) proof that the applicants have at their disposal, for the manufacture or import of the above, suitable and sufficient premises, technical equipment and control facilities complying with the legal requirements that the Member State concerned lays down as regards both manufacture and control and the storage of medicinal products, in accordance with Article 8;

(c) proof that the applicants have at their disposal the services of at least one qualified person within the meaning of Article 151;

~~(d) explanation on whether the site is the central site responsible for the oversight of decentralised sites.~~

**1a. In the case of an application for a central site responsible for decentralised manufacturing, the particulars referred to in paragraph 1 shall also include:**

**(a) proof that that the use of decentralised ~~sites~~ manufacturing has been referenced in the marketing authorisation application ~~authorised~~ in accordance with Article 26a for the medicinal product(s) concerned;**

**(b) ~~details~~ description of the medicinal product(s) that are subject to manufacturing or testing steps in the decentralised sites, including the manufacturing or testing activities to be performed for those medicinal products at the decentralised sites;**

**(c) proof that the applicants have at their disposal appropriate procedures and resources for the oversight of decentralised sites in accordance with Article 147(1), first subparagraph, point (f);**

**(d) for each decentralised site at the time of the application, a written confirmation that the applicant has verified its compliance with principles and guidelines of good manufacturing practice referred to in Article 160 by conducting an audit.**

2. The applicant shall provide, by electronic means, particulars in support of the above in their application. **Member States may provide for the possiblity of a submission in paper format.**

*Article 144*

*Granting of a manufacturing authorisation*

1. The ~~official representatives of the~~ competent authority of the Member State concerned shall carry out an inspection to ensure the accuracy of the particulars included in the application submitted in accordance with Article 143.

   Where the accuracy of the particulars is confirmed in accordance with the first subparagraph**, or in any event,** ~~and~~ no later than 90 days after the receipt of the application submitted in accordance with Article 143, the competent authority of the Member State shall grant or refuse a manufacturing authorisation.

   **By way of derogation from the second subparagraph, in justified cases, the inspection may be carried out after the manufacturing authorisation has been granted.**

2. To ensure that the particulars referred to in Article 143 are duly submitted, the competent authority of the Member State may grant a manufacturing authorisat~~i~~on subject to conditions.

   ~~For central sites, a manufacturing authorisation shall include for each decentralised site a written confirmation that the manufacturer of the medicinal product has verified compliance of the decentralised site with principles of good manufacturing practice referred to in Article 160 by conducting regular audits in accordance with Article 147(1), first subparagraph, point (f).~~

~~3. The manufacturing authorisation shall apply only to the medicinal products, pharmaceutical forms, the manufacturing operations and the premises specified in the application and to the premises of the corresponding central site where decentralised manufacturing or testing activities are carried out in decentralised sites, which are registered in accordance with Article 148.~~

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*Article 145*

*Changes in a manufacturing authorisation*

If the manufacturing authorisation holder requests a change in any of the particulars referred to in Article 143(1) **and (1a) points (a), (b) and (c)**, second subparagraph, the competent authority of the Member State shall **take a decision on the requested** amend**ment of** the manufacturing authorisation no later than 30 days from such request. In exceptional cases this period of time may be extended to 90 days.

*Article 146*

*Request for additional information*

The competent authority of the Member State may request the applicant to submit additional information on the particulars supplied pursuant to Article 143~~(1)~~ and on the qualified person referred to in Article 151; where the competent authority of the Member State makes such request, the time limits referred to in Articles 144(1), second subparagraph, and 145 shall be suspended until the additional information has been supplied.

*Article 147*

*Obligations of the manufacturing authorisation holder*

1. Member States shall ensure that manufacturing authorisation holders shall:
   (a) have at their disposal the services of staff who comply with the legal requirements existing in the Member State both as regards manufacture and controls;
   (b) dispose of the medicinal products that have been granted a marketing authorisation only in accordance with the legislation of the Member States;
   (c) give prior notice to the competent authority of the Member State of any changes they may wish to make to any of the particulars provided in accordance to Article 143;
   (d) allow the official representatives of the competent authority of the Member State access to their premises ~~and, where sites carry out manufacturing or testing activities in connection with a central site in the decentralised site, to the premises of the central or the decentralised sites~~ at any time;

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(e) enable the qualified persons referred to in Article 151 to carry out their duties, where ~~appropriate~~ **applicable** also in decentralised sites, for example by placing at their disposal all the necessary resources **and ensuring their access to the premises of the decentralised site(s)**;

(f) comply, in any relevant site and at all times with the principles of good manufacturing practice for medicinal products;

(g) use only active substances that have been manufactured in accordance with good manufacturing practice for active substances and distributed in accordance with good distribution practices for active substances;

(h) inform the competent authority of the Member State and the marketing authorisation holder immediately if they obtain information that medicinal products that come under the scope of their manufacturing authorisation are, or are suspected of being, falsified irrespective of the way the medicinal products were distributed;

(i) verify that the manufacturers, importers or distributors from whom they obtain active substances are registered with the competent authority of the Member State in which they are established; and

(j) verify the authenticity and quality of the active substances and the excipients.

As regards the first subparagraph, point (c), the competent authority of the Member State shall, in any event, be immediately informed if the qualified person referred to in Articles 143(1), point (c), and 151 is replaced unexpectedly.

For the purposes of points (f) and (g), manufacturing authorisation holders shall verify compliance~~, respectively,~~ by the manufacturer or distributors of active substances with good manufacturing practice and good distribution practice~~s~~ **respectively,** by conducting **regular** audits at the manufacturing and distribution sites of the manufacturer and distributors of active substances. Manufacturing authorisation holders shall verify such compliance either by themselves or through an entity acting on their behalf under a contract.

2. The manufacturing authorisation holder shall ensure that the excipients are suitable for use in medicinal products by ascertaining the appropriate good manufacturing practice on the basis of a formalised risk assessment.

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3. The manufacturing authorisation holder shall ensure that the appropriate good manufacturing practice ascertained in accordance with paragraph 2, is applied. The manufacturing authorisation holder shall document the measures taken in accordance with paragraphs 1 and 2.

*Article 148*

*Registration and ~~listing process of~~ **supervision of** decentralised sites*

1. The manufacturing authorisation holder of the central site shall register all of its decentralised sites in accordance with the provisions of this Article.

2. The manufacturing authorisation holder of the central site shall request the competent authority of the Member State in which the decentralised site is established, to register the decentralised site.

**The competent authority of the Member State where the decentralised site is located shall not register the decentralised manufacturing site when ~~justified by the properties of the manufactured medicinal product, such as short shelf life, or where proximity to the treated patient or customisation for an individual patient is required, as~~ the conditions set out in Article 26a paragraph 3 or 5 are not met.**

3. ~~The marketing authorisation holder may commence the activity in the decentralised site in connection with the central site only when the decentralised site is registered in the Union database referred to in Article 188(15) and the link is made in the database with the authorisation of the corresponding central site by the competent authority of the Member state where the decentralised site is located.~~

**The marketing authorisation holder shall ensure that all the activities at the central and decentralised sites are carried out in compliance with the principles and guidelines referred to in Articles 160 and 161 and the marketing authorisation referred to in Article 26a.**

**The manufacturing authorisation holder may commence the activity in the decentralised site in connection with the central site only when the marketing authorisation holder has ensured that:**

**(a) the central site is authorised by the competent authority of the Member state where it is located;**

**(b) the decentralised site is registered by the competent authority of the Member state where it is located; and**

**(c) the registration of the decentralised site is referenced with the authorisation of the corresponding central site by the competent authority of the Member state where the central site is located~~;~~ in the Union database referred to in Article 188(15).**

4. The competent authority of the Member State in which the decentralised site is established, is responsible, in accordance with Article 188, for the supervision of the manufacturing and testing activities carried out in the decentralised site.

5. For the purpose of paragraph 2 the manufacturing authorisation holder of the central site shall submit a registration form that shall include~~,~~ at least~~,~~ the following information:

(a) name or corporate name and permanent address of the decentralised site**,** ~~and~~ a proof of **its** establishment in the Union **and the name and contact details of a person designated as the local contact for the decentralised site~~;~~ along with a written confirmation of the decentralised site that it supports the application for registration;**

(b) **the pharmaceutical forms and** the medicinal products that are subject to manufacturing or testing steps in the decentralised site, including the manufacturing or testing activities ~~-~~to be performed for those medicinal products**~~-~~and the reference to the relevant marketing authorisation or the marketing authorisation application referred to in Article 26a, paragraph 1**;

(c) particulars regarding the premises of the decentralised site and the technical equipment to carry out the relevant activities;

(d) the reference to the manufacturing authorisation of the central site;

(e) the written confirmation ~~referred to in Article 144(2), second subparagraph, -~~that the manufacturer of the medicinal product has verified compliance of the decentralised site with principles of good manufacturing practice referred to in Article 160 by conducting audits**~~;, as well as -~~the latest audit report shall be submitted if the competent authority of the Member State in which the decentralised site is established so requests**;

**(f) proof that the appropriate resources are available at the central site for the qualified person referred to in Article 151 to carry out the tasks referred to in Article 153(4) regarding the supervision of the decentralised site**.

6. The competent authority of the Member State supervising the decentralised site pursuant to paragraph 4 may decide to carry out an inspection as referred to in -Article 188(1), first subparagraph, point (a). In such cases, that competent authority shall cooperate with the competent authority of the Member State responsible for the supervision of the central site. ~~The manufacturing authorisation holder of the central site shall ensure access of t~~**The competent authority of the Member State shall have access to the premises of the decentralised site. If the outcome of the inspection shows that the applicant does not comply with the principles of good manufacturing practices as referred to in Article 160, the competent authority shall not register that entity in the Union database referred to in Article 188(15).**

~~7. Following the registration of the decentralised site pursuant to paragraph 2, the manufacturing authorisation holder of the central site shall list the registered decentralised site in the manufacturing authorisation of the central site.~~

8. The competent authority of the Member State supervising the decentralised site pursuant to paragraph 4 shall cooperate with the relevant authorities responsible for the supervision of the manufacturing or testing activities under other Union acts as regards the following:
   (a) the medicinal products that were manufactured in a decentralised site, the testing or manufacturing of which involves using raw material, medicinal products regulated under other relevant Union law, or medicinal products that are intended to be combined with medical devices;
   (b) where specific manufacturing or testing activities are applied to the medicinal products containing, consisting or derived from SoHO for which specific manufacturing or testing activities are applied within a decentralised site that is also authorised under ~~[SoHO Regulation]~~ **Regulation (EU) 2024/1938.**

**The respective competent authorities of the Member States supervising the central and decentralised sites shall cooperate and exchange information as regards the authorisation of the central site, the regisitration of the decentralised site(s) and their supervision.**

~~9. Where relevant, competent authorities of the Member State supervising the central and decentralised sites may liaise with the competent authority of the Member State responsible for the supervision of the marketing authorisation.~~

**Where appropriate, the competent authorities~~y~~ of the Member States supervising the central and decentralised sites and the Agency or the competent authority of the Member State responsible for the supervision of the marketing authorisation shall cooperate and exchange information. Where the supervisory authority detects any defi~~n~~ciency in the central site or the decentralised sites that may impact the quality or safety of the medicinal product concerned, it shall ~~immediately~~ inform the relevant national competent authorities~~y~~ or the Agency without delay.**

**10. In case of any situation having an impact on the quality or safety of the medicinal products that are manufactured or tested at the decentralised site, the marketing authorisation holder and the qualified person of the central site shall inform the competent authorities supervising the central and decentralised sites, and the competent authorities supervising the marketing authorisation respectively without delay, in order to take the appropriate actions.**

*Article 149*

*Conditions related to the safety feature**s***

1. The safety features referred to in Annex IV shall not be removed or covered, either fully or partially, unless the following conditions are fulfilled:
   (a) the manufacturing authorisation holder verifies, prior to partly or fully removing or covering those safety features, that the medicinal product concerned is authentic and that it has not been tampered with;

(b) the manufacturing authorisation holder complies with Annex IV by replacing those safety features with safety features that are equivalent as regards the possibility to verify the authenticity, identification and to provide evidence of tampering of the medicinal product. Such replacement shall be conducted without opening the immediate packaging.

Safety features shall be considered equivalent if they:

(i) comply with the requirements set out in the delegated acts adopted pursuant to Article 67(2); and

(ii) are equally effective in enabling the verification of authenticity and identification of medicinal products and in providing evidence of tampering with medicinal products;

(c) the replacement of the safety features is conducted in accordance with applicable good manufacturing practice for medicinal products; and

(d) the replacement of the safety features is subject to supervision by the competent authority of the Member State.

2. Manufacturing authorisation holders, including those performing the activities referred to in paragraph 1, shall be regarded as producers and therefore held liable for damages in the cases and under the conditions set forth in Directive 85/374/EEC.

*Article 150*

*Potentially falsified medicinal products*

1. By derogation from Article 1(2), and without prejudice to Chapter XII, Section 1, Member States shall take the necessary measures in order to prevent medicinal products that are introduced into the Union, but are not intended to be placed on the market in the Union, from entering into circulation if there are sufficient grounds to suspect that those products are falsified.

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2. ~~Member States shall organise meetings involving patients' and consumers' organisations and, as necessary, Member States' enforcement officers, in order to communicate public information about the actions undertaken in the area of prevention and enforcement to combat the falsification of medicinal products.~~

**Member States shall communicate public information about the actions undertaken in the area of prevention and enforcement to combat the falsification of medicinal products involving patients' and consumers' organisations and, as necessary, Member States' enforcement officers.**

3. In order to establish what the necessary measures referred to in paragraph 1 are the Commission is empowered to adopt delegated acts in accordance with Article 215, to supplement paragraph 1 by specifying the criteria to be considered and the verifications to be made when assessing the potential falsified character of medicinal products introduced into the Union but not intended to be placed on the market.

*Article 151*

*Availability of qualified person*

1. Member States shall take all appropriate measures to ensure that the manufacturing authorisation holder has permanently and continuously at their disposal the services of at least one qualified person residing and operating in the Union, in accordance with the conditions laid down in Article 152, responsible in particular for carrying out the duties specified in Article 153.

2. A manufacturing authorisation holder who is a natural person and personally fulfils the conditions laid down in Annex III may assume the responsibility referred to in paragraph 1.

3. Where the manufacturing authorisation is granted to a central site specified in the application pursuant to Article 144(3), the qualified person referred to in paragraph 1 shall also be responsible for carrying out the duties specified in Article 153(4) regarding the decentralised sites. **For this purpose, the available resources for the services referred to in paragraph 1 at a central site shall be commensurate with the number of decentralised sites and their activity.**

*Article 152*

*Qualification of qualified person*

1. Member States shall ensure that the qualified person referred to in Article 151 fulfils the conditions of qualification set out in Annex III.

2. The manufacturing authorisation holder and the qualified person shall ensure that the practical experience acquired is appropriate to the types of products to be certified.

3. The competent authority of the Member State may lay down appropriate administrative procedures to verify that a qualified person referred to in the paragraph 1 fulfils the conditions set out in Annex III.

*Article 153*

*Responsibilities of the qualified person*

1. Member States shall take all appropriate measures to ensure that the qualified person referred to in Article 151, without prejudice to their relationship with the manufacturing authorisation holder, are responsible, subject to the procedures referred to in Article 154, for securing:
   (a) in the case of medicinal products manufactured within the Member States concerned, that each production batch of medicinal products has been manufactured and checked in compliance with the laws in force in that Member State and in accordance with the requirements of the marketing authorisation;
   (b) in the case of medicinal products imported from third countries, irrespective of whether they have been manufactured in the Union**,** that each production batch has undergone in a Member State a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of the medicinal products in accordance with the requirements of the marketing authorisation.

   The qualified person referred to in Article 151 shall in the case of medicinal products intended to be placed on the Union market, ensure that the safety features referred to in Annex IV have been affixed on the packaging.

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The batches of medicinal products that have undergone the controls referred to in the first subparagraph, point (b), in a Member State shall be exempt from those controls if they are marketed in another Member State, accompanied by the control reports signed by the qualified person.

2. In the case of medicinal products imported from a third country, where appropriate arrangements have been made by the Union with the exporting country to ensure that the manufacturer applies standards of good manufacturing practice at least equivalent to those laid down by the Union, and to ensure that the controls referred to in paragraph 1, first subparagraph, point (b), have been carried out in the exporting country, the qualified person may be relieved of responsibility for carrying out those controls.

3. In all cases and particularly where the medicinal products are released for sale, the qualified person shall certify in a register or equivalent format provided for that purpose, that each production batch satisfies the provisions of this Article; that register or equivalent format shall be kept up to date during the time when operations are carried out and shall remain at the disposal of the official representatives of the competent authority of the Member State for the period specified in the provisions of the Member State concerned and in any event for at least five years.

4. For the purposes of Article 151(3), the qualified person shall, in addition:
   (a) supervise that the manufacturing or testing activities carried out at the decentralised sites comply with principles of ~~relevant~~ good manufacturing practices referred to in Article 160 and conform to the marketing authorisation;
   (b) **conduct regular audits, including periodic on site visits, ~~of~~ at the decentralised sites and** provide a written confirmation ~~as referred to in Article 144(2), second subparagraph~~ **that the holder of the manufacturing authorisation for the central site ~~manufacturer of the medicinal product~~ has verified compliance of the decentralised site with principles of good manufacturing practice referred to in Article 160**;

(c) notify **annually** to the competent authority of the Member State where the decentralised site is established, an inventory of the changes that have taken place as regards the information provided in the registration form submitted pursuant to Article 148(5). Any changes that may have an impact on the quality or safety of the medicinal products that are manufactured or tested at the decentralised site must be notified immediately.

The Commission is empowered to adopt a delegated act in accordance with Article 215 to supplement the first subparagraph, point (c), specifying the notification made by the qualified person.

*Article 154*

*Professional code of conduct*

1. Member States shall ensure that the duties of qualified persons referred to in Article 151 are fulfilled, either by means of appropriate administrative measures or by making such persons subject to a professional code of conduct.

2. Member States may provide for the temporary suspension of a qualified person referred to in Article 151 upon the commencement of administrative or disciplinary procedures against that qualified person for failure to fulfil its duties set out in Article 153. **Thei~~s~~ suspension of a qualified person applies to all manufacturing authorisations on which the qualified person is listed.**

**3. In the case of decentralised manufacturing, the supervisory authorities of the central site and of the decentralised sites, if different, shall cooperate to implement for the measures referred to paragraphs 1 and 2.**

**ANNEX III**

**CONDITIONS FOR QUALIFICATION OF A QUALIFIED PERSON**

1. The qualified person shall hold a university degree in one or more of the following scientific disciplines: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology. **The qualified person shall be in possession of evidence of formal qualifications awarded on completion of a university course of study, or a course recognised as equivalent by the Member State concerned, extending over a period of at least four years of theoretical and practical study.**

**However, the minimum duration of the university course may be three and a half years where the course is followed by a period of theoretical and practical training of a minimum duration of one year and including a training period of at least six months in a pharmacy open to the public, corroborated by an examination at university level.**

**Where two university courses or two courses recognised by the Member State as equivalent co-exist in a Member State and where one of these extends over four years and the other over three years, the three-year course leading to evidence of formal qualifications awarded on completion of a university course or its recognised equivalent shall be considered to fulfil the condition of duration referred to in the second subparagraph in so far as evidence of formal qualifications awarded on completion of both courses are recognised as equivalent by the Member State in question.**

**The course shall include theoretical and practical study bearing upon at least the following basic subjects:**

**(a) Physics**

**(b) General and inorganic Chemistry**

**(c) Organic chemistry**

**(d) Analytical chemistry**

**(e) Pharmaceutical -chemistry, including analysis of medicinal products**

**(f) Biochemistry**

**(g) Physiology**

**(h) Microbiology**

**(i) Pharmacology**

**(j) Pharmaceutical technology**

**(k) Toxicology.**

**Studies in these subjects ~~should~~ shall be so balanced as to enable the person concerned to fulfil the obligations specified in Article 153.**

**In so far as evidence of formal qualifications mentioned in the first subparagraph do not fulfil the criteria laid down in this paragraph, the competent authority of the Member State shall ensure that the person concerned provides evidence of adequate knowledge of the subjects involved.**

2. The qualified person shall have acquired practical full-time experience over at least two years, in one or more undertakings **or entities not engaged in an economic activity** that are authorised manufacturers, obtaining sufficient knowledge of manufacture, testing, supply chains, good manufacturing practice and pharmaceutical quality systems as well as regulatory processes and dossier content for ensuring the quality of medicinal products. **The duration of practical experience may be reduced by one year by the competent authority of the Member State where a university course lasts for at least five years.**

~~3. A qualified person shall be in possession of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course of study, or a course recognised as equivalent by the Member State concerned, extending over a period of at least four years of theoretical and practical study in one of the following scientific disciplines: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology.~~

~~However, the minimum duration of the university course may be three and a half years where the course is followed by a period of theoretical and practical training of a minimum duration of one year and including a training period of at least six months in a pharmacy open to the public, corroborated by an examination at university level.~~

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~~Where two university courses or two courses recognised by the State as equivalent co-exist in a Member State and where one of these extends over four years and the other over three years, the three-year course leading to a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course or its recognised equivalent shall be considered to fulfil the condition of duration referred to in the second subparagraph in so far as the diplomas, certificates or other evidence of formal qualifications awarded on completion of both courses are recognised as equivalent by the Member State in question.~~

~~The course shall include theoretical and practical study bearing upon at least the following basic subjects:~~

~~Experimental physics~~

~~General and inorganic chemistry~~

~~Organic chemistry~~

~~Analytical chemistry~~

~~Pharmaceutical chemistry, including analysis of medicinal products~~

~~General and applied biochemistry (medical)~~

~~Physiology~~

~~Micro biology~~

~~Pharmacology~~

~~Pharmaceutical technology~~

~~Toxicology~~

~~Pharmacognosy (study of the composition and effects of the natural active substances of plant and animal origin).~~

~~Studies in these subjects should be so balanced as to enable the person concerned to fulfil the obligations specified in Article 153.~~

~~In so far as certain diplomas, certificates or other evidence of formal qualifications mentioned in the first subparagraph do not fulfil the criteria laid down in this paragraph, the competent authority of the Member State shall ensure that the person concerned provides evidence of adequate knowledge of the subjects involved.~~

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~~4. The qualified person shall have acquired practical experience over at least two years, in one or more undertakings or not-for-profit entities that are authorised to manufacture medicinal products, in the activities of qualitative analysis of medicinal products, of quantitative analysis of active substances and of the testing and checking necessary to ensure the quality of medicinal products.~~

5. A person engaging in the activities of the person referred to in Article 152 from the time of the application of Second Council Directive 75/319/EEC[1], in a Member State without complying with the provisions of this Annex shall be eligible to continue to engage in those activities within the Union.

6. The holder of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course — or a course recognised as equivalent by the Member State concerned — in a scientific discipline allowing them to engage in the activities of the person referred to in Article 48 in accordance with the laws of that Member State may — if they began their course prior to 21 May 1975 — be considered as qualified to carry out in that Member State the duties of the person referred to in Article 152 provided that they have previously engaged in the following activities for at least two years before 21 May 1985 following notification of this directive in one or more undertakings or ~~not-for-profit~~ entities **not engaged in an economic activity** authorised to manufacture: production supervision or qualitative and quantitative analysis of active substances, and the necessary testing and checking under the direct authority of the person referred to in Article 152 to ensure the quality of the medicinal products.

[1] Second Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products (OJ L 147, 9.6.1975, p. 13). Directive is not in force anymore.

*Article 155*

*Certificate for export of a medicinal product*

1. At the request of the manufacturer, the exporter or the competent authorities of an importing third country, **the competent authority of the** Member State~~s~~ shall ~~certify~~ **issue a certificate** that a manufacturer of medicinal products is in possession of a manufacturing authorisation **or refer to the manufacturing authorisation available in the database referred to in Article 188(15)**.

**1a.** ~~When issuing such certificates~~ **For the purposes of paragraph 1, the competent authority of the** Member State~~s~~ shall:

(a) comply with the prevailing administrative arrangements of the World Health Organization;

(b) for medicinal products intended for export that are already authorised in their territory, supply the summary of product characteristics as approved by them in accordance with Article 43.

2. **For the purposes of paragraph 1,** ~~W~~**w**hen the manufacturer is not in possession of a marketing authorisation it shall provide the competent authorities responsible for issuing the certificate referred to in paragraph 1, with a declaration explaining why a marketing authorisation is not available.

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## Section 2

## Manufacturing, import and distribution of active substances

~~*Article 156*~~

~~*Manufacture of active substances*~~

~~For the purposes of this Directive,~~ **manufacture of active substances used in ~~the manufacturing process of a medicinal product means any total or partial operation of receipt of materials, production, packaging, repackaging, labelling, relabelling, quality control or release of active substances, and the related controls.~~** ~~manufacture of active substances used in the manufacturing process of a medicinal product shall include both total and partial manufacture or import of an active substance and the various processes of dividing up, packaging or presentation prior to its incorporation into a medicinal product, including repackaging or re-labelling, such as are carried out by a distributor of active substances~~.

*Article 157*

*Registration of importers, manufacturers and distributors of active substances*

1. Importers, manufacturers and distributors of active substances who are established in the Union shall register their activity with the competent authority of the Member State in which they are established.

2. The registration form, to be submitted by electronic means, shall include, at least, the following information:
   (a) name or corporate name and permanent address;
   (b) the active substances that are to be imported, manufactured or distributed;
   (c) particulars regarding the premises and the technical equipment for their activity.

**Member States ~~shall~~ may provide for the possiblity of a paper form submission.**

3. The persons referred to in paragraph 1 shall submit, by electronic means, the registration form to the competent authority of the Member State at least 60 days prior to the intended commencement of their activity. **Member States ~~shall~~ may provide for the possiblity of a paper form submission.**

4. The competent authority of the Member State may, based on a risk assessment, decide to carry out an inspection. If the competent authority of the Member State notifies the applicant within 60 days of the receipt of the registration form that an inspection will be carried out, the activity shall not begin before the competent authority of the Member State has notified the applicant that they may commence the activity. If within 60 days of the receipt of the registration form the competent authority of the Member State has not notified the applicant that an inspection will be carried out, the applicant may commence the activity.

**~~4~~a. If the outcome of the inspection carried out in accordance with paragraph 4 shows that the applicant does not comply with the principles of good manufacturing practice or good distribution practices for active substances as referred to in Article 160, the competent authority shall not register that entity in the Union database referred to in Article 188(15).**

5. Annually, the persons referred to in paragraph 1 shall communicate, by electronic means, to the competent authority of the Member State an inventory of the changes that have taken place as regards the information provided in the registration form. Any changes that may have an impact on the quality or safety of the active substances that are manufactured, imported or distributed must be notified immediately.

6. The comp~~t~~etent authority of the Member State shall enter the information provided in accordance with paragraph 2 in the Union database referred to in Article 188(15).

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*Article 158*

*Conditions for importing active substances*

1. Member States shall take appropriate measures to ensure that the manufacture, import and distribution on their territory of active substances, including active substances that are intended for export, comply with the principles of good manufacturing practice and good distribution practices for active substances specified in the delegated acts adopted in accordance with Article 160.

2. Active substances shall only be imported if the following conditions are fulfilled:
   (a) the active substances have been manufactured in accordance with the principles of good manufacturing practices at least equivalent to those laid down by the Union pursuant to Article160; and
   (b) the active substances are accompanied by a written confirmation issued by the competent authority of the exporting third country stating that:
      (i) the principles of good manufacturing practices applicable to the manufacturing site manufacturing the exported active substance are at least equivalent to those laid down by the Union pursuant Article 160;
      (ii) the manufacturing site concerned is subject to regular, strict and transparent controls and to the effective enforcement of good manufacturing practice, including repeated and unannounced inspections, so as to ensure a protection of public health at least equivalent to that in the Union; and
      (iii) in the event of findings relating to non-compliance, information on such findings is supplied by the exporting third country to the Union without undue delay.

3. The conditions set out in paragraph 2, point (b), shall not apply if the exporting country is included in the list referred to in Article 159(2).

4. The conditions set out in paragraph 2, point (b), may be waived by any competent authority of a Member State for a period not exceeding the validity of the certificate of good manufacturing practice issued in accordance with Article 188(13) where a site manufacturing an active substance for export has been inspected by the competent authority of a Member State and was found to comply with the principles of good manufacturing practice laid down pursuant to Article160.

*Article 159*

*Active substances imported from third countries*

1. At the request of a third country, the Commission shall assess whether that country's regulatory framework applicable to active substances exported to the Union and the respective control and enforcement activities ensure a level of protection of public health equivalent to that of the Union.

   The assessment shall take the form of a review of relevant documentation submitted by electronic means and, unless arrangements as referred to in Article 153(2) are in place that cover this area of activity, that assessment shall include an on-site review of the third country's regulatory system and, if necessary, an observed inspection of one or more of the third country's manufacturing sites for active substances.

2. Based on the assessment referred to in paragraph 1, the Commission may adopt implementing acts to include the third country in a list and to apply the requirements set out in the second subparagraph. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 214(2).

   When assessing the third country pursuant to paragraph 1, the Commission shall take account of the following:

   (a) the country's rules for good manufacturing practice;
   (b) the regularity of inspections to verify compliance with good manufacturing practice;
   (c) the effectiveness of enforcement of good manufacturing practice;
   (d) the regularity and rapidity of information provided by the third country relating to non-compliant manufacturers of active substances.

3. The Commission shall verify regularly whether the conditions laid down in paragraph 1 are fulfilled. The first verification shall take place no later than 3 years after the third country has been included in the list referred to in paragraph 2.

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4. The Commission shall perform the assessment referred to in par**a**g**r**a~~r~~ph 1 and verification referred to in paragraph 3 in cooperation with the Agency and the competent authorities of the Member States.

## Section 3

## Principles of good manufacturing and good distribution practices

*Article 160*

*Rules applicable to medicinal products and active substances*

The Commission ~~may~~ **shall** adopt ~~implementing~~ **delegated** acts in accordance with Article 21**5**~~4(2)~~ to supplement this Directive by specifying:

(a) the principles of good manufacturing and good distribution practices for medicinal products complemented, where relevant, by specific measures applicable notably to pharmaceutical forms, medicinal products or manufacturing activities in line with good manufacturing principles;

(b) the principles of good manufacturing and good distribution practices for active substances

**The Agency, in particular through its inspection working group referred to in Article 142(k) of [the revised Regulation (EU) 726/2004], in agreement with the Commission, shall draw up guidelines on good manufacturing and distribution practices for both competent authorities and marketing authorisation holders.**

Where relevant, these principles shall be specified in coherence with any principles of good practices established under any other Union legal framework.

*Article 161*

*Rules applicable to excipients*

The Commission is empowered to adopt delegated acts in accordance with Article 215 to supplement this Directive on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients referred to in Article 147(2). Such risk assessment shall take into account requirements under other appropriate quality systems as well as the source and intended use of the excipients and previous instances of quality defects.

# Chapter XII

# Wholesale distribution and sale at a distance

## Section 1

## Wholesale distribution and brokering of medicinal products

*Article 162*

*Wholesale distribution of medicinal products*

1. Without prejudice to Article 5, Member States shall take all appropriate action to ensure that only medicinal products in respect of which a marketing authorisation has been granted in accordance with Union law are distributed on their territory.

2. In the case of wholesale distribution including storage, medicinal products shall be covered by either a centralised marketing authorisation or by a national marketing authorisation.

**2a. For the purposes of parallel trade in medicinal products, the wholesale distributor shall ensure that the medicinal product it intends to obtain from a Member State ('source Member State') and distribute in another Member State ('destination Member State') ~~share a common origin~~ is essentially similar with the medicinal product already authorised in the destination Member State. Medicinal products are considered to be ~~sharing a common origin~~ essentially similar if they fulfil all the following conditions:**

~~(a) they have the same qualitative and quantitative composition in terms of active substances and excipients;~~

~~(b) they have the same pharmaceutical form;~~

~~(c) they have the same clinical information; and~~

~~(d) they have been manufactured by the same manufacturer or by a manufacturer working under licence according to the same formulation.~~

**(a) they consist of the same active substance or the same combination of active substances;**

**(b) they have the same strength;**

**(c) they have the same administration route;**

**(d) they have the same pharmaceutical form or a similar pharmaceutical form where the difference in the form does not result in differences with regard to the therapeutic effect of the medicinal product covered by the marketing authorisation in the destination Member State.**

3. **Wholesale** ~~D~~**d**istributors who intend to ~~import~~ **obtain** a medicinal product from ~~another~~ **a source** Member State shall notify the marketing authorisation holder and the competent authority of ~~the~~ **destination** Member State ~~to which the medicinal product is to be imported~~ of their intention to ~~import~~ **distribute** that medicinal product **in the destination Member State**.

4. In the case of medicinal products covered by a national marketing authorisation, the notification referred to in paragraph 3 to the competent authority of the Member State shall be without prejudice to additional procedures provided for in the legislation of that Member State and to fees payable to the competent authority of the Member State for examining the notification.

5. In the case of medicinal products covered by a centralised marketing authorisation, the distributor shall submit the same notification referred to in paragraph 3 to the Agency which will be in charge of checking that the conditions laid down in Union law on medicinal products and in the marketing authorisations are observed. For this check, a fee shall be payable to the Agency.

*Article 163*

*Authorisation for wholesale distribution of medicinal products*

1. The competent authority of the Member State concerned shall take all appropriate measures to ensure that the wholesale distribution of medicinal products is subject to an authorisation to engage in activity as a wholesaler in medicinal products ("wholesale distribution authorisation"). The wholesale distribution authorisation shall indicate the premises, the **categories of** medicinal products and the wholesale distribution operations for which it is valid.

2. Where persons authorised or entitled to supply medicinal products to the public may also, under national law, engage in wholesale business, such persons shall be subject to the authorisation provided for in paragraph 1.

3. A manufacturing authorisation required under Article 142 shall include an authorisation to distribute by wholesale the medicinal products that it covers. A wholesale distribution authorisation shall not give dispensation from the obligation set out in Article 142 to hold a manufacturing authorisation and to comply with the conditions set out in that respect, even where the manufacturing or import business is secondary.

4. The competent authority of the Member State concerned shall enter the information relating to the wholesale distribution authorisations in the Union database referred to in Article 188(15).

5. The competent authority of the Member State that granted the wholesale distribution authorisation for premises located in its territory shall ensure that controls of the persons authorised to engage in activity as a wholesaler in medicinal products, and inspections of their premises, are carried out at an appropriate frequency.

   The competent authority of the Member State that granted the wholesale distribution authorisation shall suspend or revoke it if the conditions for granting it set out in Article 16~~2~~**4** cease to be met **or if the obligations set out in Article 166 are not being fulfilled**. In such event the Member State shall without undue delay inform the other Member States and the Commission thereof.

6. Where a competent authority of a Member State considers that the conditions for granting a wholesale distribution authorisation set out in Article 16~~42~~ are not met with respect to a wholesale distribution authorisation granted by the competent authority of another Member State, it shall without undue delay inform the Commission and the competent authority of the other Member State thereof. The competent authority of the other Member State shall take the measures it considers necessary and shall inform the Commission and the competent authority of the first Member State of those measures and the reasons for them.

*Article 164*

*Requirements for a wholesale distribution authorisation*

1. In order to obtain a wholesale distribution authorisation, applicants shall submit an application by electronic means to the competent authority of the Member State ~~concerned~~. **Member States ~~shall~~ may provide for the possiblity of a paper form submission.**

2. The application referred to in paragraph 1 shall include **at least** the following particulars:
   (a) a confirmation and proof that the applicants have **a permanent address in the Member State ~~Union~~ and have** at their disposal suitable and adequate premises, installations and equipment, to ensure proper conservation and distribution of the medicinal products;
   (b) a confirmation and proof that the applicants have at their disposal appropriately trained staff, and in particular~~, a qualified person designated as responsible, meeting the conditions provided for by the legislation of the Member State concerned;~~ **a responsible person, meeting the qualifications and conditions provided for by the legislation of the Member State;**
   (c) an undertaking to fulfil the obligations incumbent on them under the terms of Article 166.

*Article 165*

*Granting of a wholesale distribution authorisation*

1. The ~~official representatives of the~~ competent authority of the Member State concerned ~~shall~~ **may** carry out an inspection to confirm the accuracy of the particulars provided in accordance with Article 164.

Where the accuracy of the particulars is confirmed in accordance with the first subparagraph and**, or in any event,** no later than 90 days after the receipt of the application submitted in accordance with Article 164, the competent authority of the Member State shall grant or refuse a wholesale distribution authorisation.

2. The competent authority of the Member State concerned may require the applicant to supply, by electronic means, all necessary information concerning the particulars for granting the wholesale distribution authorisation. In such case, the period laid down in paragraph 1 shall be suspended until the requisite additional information is supplied.

3. The competent authority of the Member State may grant a wholesale distribution authorisation subject to conditions.

4. The wholesale distribution authorisation shall apply only to **the wholesale distribution activites, categories of medicinal products and** the premises specified in the authorisation.

*Article 166*

*Obligations of the wholesale distribution authorisation holder*

1. Member States shall ensure that wholesale distribution authorisation holders shall:
   (a) have at their disposal the services of staff who comply with the legal requirements existing in the Member State as regards wholesale distribution;
   (b) allow the official representatives of the competent authority of the Member State access to their premises, installations and equipment referred to in Article 164(2), point (a), at all times;
   (c) ~~obtain~~ **procure**, including by financial transactions, their supplies of medicinal products only from persons who are themselves in possession of a wholesale distribution authorisation in the Union or a manufacturing authorisation referred to in Article 163(3);
   (d) supply, including by financial transaction, medicinal products only to persons who are themselves wholesale distribution authorisation holders or who are authorised or entitled to supply medicinal products to the public;

(e) verify that the medicinal products received are not falsified by checking the safety features on the outer packaging, in accordance with the requirements laid down in the delegated acts adopted pursuant to Article 67(2), second subparagraph;

(f) have an emergency plan that ensures effective implementation of any recall from the market ordered by the competent authorities or carried out in cooperation with the manufacturer or marketing authorisation holder for the medicinal product concerned;

(g) keep records giving, for any medicinal products received, dispatched or brokered, at least the following information:

(i) the date of receipt, dispatch or brokering of the medicinal product,

(ii) the name of the medicinal product,

(iii) the quantity of the medicinal product received, supplied or brokered,

(iv) the name and address of the supplier of the medicinal product or the consignee, as appropriate,

(v) the batch number of the medicinal products, ~~at least for medicinal products bearing the safety features referred to in Article 67~~;

(h) keep the records referred to in point (g) available to the competent authorities of the Member States, for ~~inspection~~ **supervision** purposes, for a period of five years;

(i) comply with the principles of good distribution practices for medicinal products laid down in Article 160;

(j) maintain a quality system setting out responsibilities, processes and risk management measures in relation to their activities;

(k) immediately inform the competent authority of the Member State and, where applicable, the marketing authorisation holder, of medicinal products they receive or are offered that they identify as falsified or suspect to be falsified;

(l) continuously guarantee**, within the limits of their responsibility,** the appropriate and continued supply of an adequate range of medicinal products to meet the requirements of a specific geographical area, and deliver the supplies requested over the whole of the area in question, within a reasonable timeframe~~, which shall be defined~~ in **accordance with the requirements of** the national legislation;

(m) cooperate with marketing authorisation holders and competent authorities of the Member States on the security of supply.

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2. Where the medicinal product is obtained from another wholesale distributor, the wholesale distribution authorisation holders obtaining the product shall verify compliance with the principles of good distribution practices by the supplying wholesale distributor. This includes verifying whether the supplying wholesale distributor holds a wholesale distribution authorisation, or a manufacturing authorisation referred to in Article 163(3).

3. Where the medicinal product is obtained from a manufacturer or importer, wholesale distribution authorisation holders shall verify that the manufacturer or importer holds a manufacturing authorisation.

4. Where the medicinal product is obtained through brokering of medicinal products, wholesale distribution authorisation holders shall verify that the person brokering the medicinal product fulfils the requirements set out in Article 171.

*Article 168*

*Documentation accompanying supplied medicinal products*

1. For all supplies of medicinal products to a person authorised or entitled to supply medicinal products to the public in the Member State concerned, the authorised wholesaler must enclose a document that makes it possible to ascertain the following:
   (a) the date of the supply;
   (b) the name and pharmaceutical form of the medicinal product;
   (c) the quantity of the medicinal product supplied;
   (d) the name and address of the supplier of the medicinal product and consignee;
   (e) the batch number of the medicinal products ~~at least for products bearing the safety features referred to in Article 67~~.

2. Member States shall take all appropriate measures to ensure that persons authorised or entitled to supply medicinal products to the public are able to provide information that makes it possible to trace the distribution path of every medicinal product.

*Article 169*

*National requirements on wholesale distribution*

The provisions of this Chapter shall not prevent the application of more stringent requirements laid down by Member States in respect of the wholesale distribution of:

(a) narcotic or psychotropic substances;

(b) medicinal products derived from blood;

(c) immunological medicinal products; and

(d) radiopharmaceuticals.

*Article 170*

*Wholesale distribution to third countries*

In the case of wholesale distribution of medicinal products to third countries, Articles 162 and 166(1), point (**d**~~e~~), shall not apply.

Where wholesale distributors supply medicinal products to persons in third countries, they shall ensure that such supplies are only made to persons who are authorised or entitled to receive medicinal products for wholesale distribution or supply to the public in accordance with the applicable legal and administrative provisions of the third country concerned.

Article 168 shall apply to the supply of medicinal products to persons in third countries authorised or entitled to supply medicinal products to the public.

*Article 171*

*Brokering medicinal products*

1. Persons brokering medicinal products shall ensure that the brokered medicinal products are covered by a valid marketing authorisation **granted in accordance with Union law**.

   Persons brokering medicinal products shall have a permanent address and contact details in the Union, so as to ensure accurate identification, location, communication and supervision of their activities by competent authorities of the Member States.

The requirements set out in Article 166(1), points (~~e~~**f**) to (**k**~~j~~), shall apply *mutatis mutandis* to the brokering of medicinal products.

2. Persons may only broker medicinal products if they are registered with the competent authority of the Member State where they have their permanent address referred to in paragraph 1, second subparagraph. Those persons shall submit, by electronic means, at least, their name, corporate name and permanent address to the competent authority in order to register. They shall notify, by electronic means, the competent authority of the Member State of any changes thereof without delay.

   The competent authority of the Member State shall enter the information referred to in the first subparagraph in a register that shall be publicly available.

3. The principles referred to in Article 160 shall include specific provisions for brokering.

4. Inspections referred to in Article 188 shall be carried out under the responsibility of the Member State where the person brokering medicinal products is registered.

   If a person brokering medicinal products does not comply with the requirements set out in this Article, the competent authority of the Member State may decide to remove that person from the register referred to in paragraph 2. In such event, the competent authority of the Member State shall notify that person thereof.

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## Section 2

## Sale at a distance to the public

*Article 172*

*General requirements for sale at distance*

1. Without prejudice to national legislation prohibiting the offer for sale at a distance of prescription medicinal products to the public by means of information society services, Member States shall ensure that medicinal products are offered for sale at a distance to the public by means of services as defined in Directive (EU) 2015/1535 of the European Parliament and of the Council[1] laying down a procedure for the provision of information in the field of technical regulations and of rules on Information Society services under the following conditions:

   (a) the natural or legal person offering the medicinal products is authorised or entitled to supply medicinal products to the public, also at a distance, in accordance with national legislation of the Member State in which that person is established;

   (b) the person referred to in point (a) has notified the Member State in which that person is established of at least the following information:

      (i) name or corporate name and permanent address of the place of activity from where those medicinal products are supplied;

      (ii) the starting date of the activity of offering medicinal products for sale at a distance to the public by means of information society services;

      (iii) the address of the website used for that purpose and all relevant information necessary to identify that website;

      (iv) if applicable, the prescription status in accordance with Chapter IV of the medicinal products offered for sale at a distance to the public by means of information society services.

      Where appropriate, that information shall be updated;

[1] Directive (EU) 2015/1535 of the European Parliament and of the Council of 9 September 2015 laying down a procedure for the provision of information in the field of technical regulations and of rules on Information Society services (OJ L 241, 17.9.2015, p. 1).

(c) the medicinal products comply with the national legislation of the Member State of destination in accordance with Article 5(1);

(d) without prejudice to the information requirements set out in Directive 2000/31/EC of the European Parliament and of the Council[1], the website offering the medicinal products contains at least:

(i) the contact details of the competent authority of the Member State or the authority notified pursuant to point (b);

(ii) a hyperlink to the website referred to in Article 174 of the Member State of establishment;

(iii) the common logo referred to in Article 173 clearly displayed on every page of the website that relates to the offer for sale at a distance to the public of medicinal products. The common logo shall contain a hyperlink to the entry of the person in the list referred to in Article 174(1), point (c).

2. Member States may impose conditions, justified on grounds of public health protection, for the retail supply on their territory of medicinal products for sale at a distance to the public by means of information society services.

3. Without prejudice to Directive 2000/31/EC and the requirements set out in this Section, Member States shall take the necessary measures to ensure that other persons than those referred to in paragraph 1 that offer medicinal products for sale at a distance to the public by means of information society services and that operate on their territory are subject to effective, proportionate and dissuasive penalties.

[1] Directive 2000/31/EC of the European Parliament and of the Council of 8 June 2000 on certain legal aspects of information society services, in particular electronic commerce, in the Internal Market (Directive on electronic commerce (OJ L 178, 17.7.2000, p. 1).

*Article 173*

*Requirements for common logo*

1. A common logo shall be established that is recognisable throughout the Union, while enabling the identification of the Member State where the person offering medicinal products for sale at a distance to the public is established. That logo shall be clearly displayed on websites ~~**digital platforms**~~ offering medicinal products for sale at a distance to the public in accordance with Article 172(1), point (d).

2. In order to harmonise the functioning of the common logo, the Commission shall adopt implementing acts regarding:
   (a) the technical, electronic and cryptographic requirements for verification of the authenticity of the common logo;
   (b) the design of the common logo.

   Those implementing acts shall, where necessary, be amended to take account of technical and scientific progress. Those implementing acts shall be adopted in accordance with the procedure referred to in Article 214(2).

*Article 174*

*Information about the supply at distance to the public*

1. Each Member State shall set up a website ~~**digital platform**~~ providing at least the following:
   (a) information on the national legislation applicable to the offering of medicinal products for sale at a distance to the public by means of information society services, including information on the fact that there may be differences between Member States regarding classification of medicinal products and the conditions for their supply;
   (b) information on the purpose of the common logo;
   (c) the list of persons offering the medicinal products for sale at a distance to the public by means of information society services in accordance with Article 172 as well as their website addresses;

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(d) background information on the risks related to medicinal products supplied illegally to the public by means of information society services.

This website **~~digital platform~~** shall contain a hyperlink to the website **~~digital platform~~** referred to in paragraph 2.

2. The Agency shall set up a website **~~digital platform~~** providing the information referred to in paragraph 1, first subparagraph, points (b) and (d), information on the Union law applicable to falsified medicinal products as well as hyperlinks to the websites of the Member States referred to in paragraph 1. The Agency's website **~~digital platform~~** shall explicitly mention that the Member States' websites contain information on persons authorised or entitled to supply medicinal products by sales at a distance in the Member State concerned.

3. The Commission shall, in cooperation with the competent authorities, conduct or promote information campaigns aimed at the general public on the dangers of falsified medicinal products. Those campaigns shall raise consumer awareness of the risks related to medicinal products supplied illegally by sales at a distance as well as of the functioning of the common logo and the websites referred to in paragraphs 1 and 2.

## Chapter XIV
## Supervision and controls

### Section 1
### Supervision

*Article 188*

*System of supervision and inspections*

1. The competent authority of the Member State concerned shall, in cooperation with the Agency and where relevant, other Member States, ensure compliance with the rules of this Directive, **~~namely~~** **including** the principles of good manufacturing practice and good distribution practices referred to in Articles 160 and 161.

For the purposes of the first subparagraph, the competent authority of the Member State shall have in place a system of supervision that shall include the following measures:

(a) announced and, where appropriate, unannounced on-site inspections;

(b) remote inspections, **conducted** where justified ~~**and the effectiveness is demonstrated**~~;

(c) compliance control measures;

(d) the effective follow-up of the measures referred to in points (a), (b) and (c).

2. The competent authorities of the Member State concerned, and the Agency shall exchange information on the inspections referred to in paragraph 1, second subparagraph, points (a) and (b), that are planned or that have been conducted and shall cooperate in the coordination of such inspections.

3. The competent authority of the Member State shall ensure that the measures referred to in paragraph 1, second subparagraph, are carried out by the official representatives of the competent authority of the Member State **concerned**:

(a) at an appropriate frequency based on risk, at the premises or on the activities of manufacturers of medicinal products, located in the Union or in third countries, including where appropriate at central or decentralised site(s), and at the premises or on the activities of wholesale distributors of medicinal products located in the Union;

(b) ~~at an appropriate frequency~~ based on **a** risk **assessment**, at the premises or on the activities of the manufacturers of active substances located in the Union or in third countries and at the premises or on the activities of importers, or distributors of active substances, located in the Union.

4. To **implement** ~~determine the appropriate frequency based on~~ **a** risk **assessment** referred to in paragraph 3, point (b), the competent authority of the Member State may:

(a) rely on inspection reports from trusted non-Union regulatory authorities;

(b) take into account whether the manufacturer of active substance is located in a third country included in the list referred to in Article 159(2).

5. Where the competent ~~authority~~ of the Member State ~~considers~~ it necessary, ~~in particular~~ **including** where there are grounds for suspecting non-compliance with the rules of this Directive, including with the principles of good manufacturing practice and good distribution practices, referred to in Articles 160 and 161, it may have its official representatives carry out the measures referred to in paragraph 1, second subparagraph at the premises or on the activities of:

(a) **applicants** ~~manufacturers or importers of medicinal products applying~~ for a manufacturing ~~import~~ authorisation or wholesale distributors applying for a wholesale distribution authorisation **of medicinal products**;

(b) **applicants** ~~manufacturers of active substance applying~~ for a registration **of manufacturing, import and distribution** ~~**authorisation**~~ **of active substances** ~~or manufacturing sites applying for a registration as decentralised sites~~;

**(ba) decentralised sites subject to request for a registration and registered decentralised sites;**

(c) marketing authorisation holders;

(d) **without prejudice to paragraph 3, manufacturers, wholesale distributors of medicinal products, manufacturers and** distributors of ~~medicinal products or~~ active substances located in **the Union or in** third countries **and importers of medicinal products or active substances located in the Union;**

(e) manufacturers of excipients, functional excipients, starting materials or intermediate products located in its territory or in a third country;

(f) importers of excipients, functional excipients, starting materials or intermediate products located in its territory;

(g) persons brokering medicinal products located in its territory ~~.~~**;**

**(h) ~~legal persons~~ third parties, contracted by the marketing authorisation holder or a marketing authorisation applicant for the performance of certain of its tasks or the preparation of evidence or data submitted in accordance with Annex II.**

6. The measures referred to in paragraph 1, second subparagraph, may also be carried out at the request of a competent authority of a Member State, the Commission or the Agency in the Union or in third countries or, where appropriate, by asking an Official Medicines Control Laboratory or a laboratory that Member State has designated for that purpose to carry out tests on samples.

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7. Each Member State shall ensure that official representatives of its competent authorities are empowered and required to carry out one or more of the following activities:

(a) inspect the manufacturing or commercial establishments of manufacturers of medicinal products, of active substances or of excipients, and any laboratories employed by the manufacturing authorisation holder to carry out verifications and controls pursuant to Article 8;

**(aa) examine any documents and records to verify compliance with the particulars of this Directive, and obtain evidence, such as copies of documents, photographs or videos.**

(b) take samples during an inspection or request samples as part of the measures referred to in paragraph 1, second subparagraph, including any required essential testing material or reagent with a view to independent tests being carried out by an Official Medicines Control Laboratory or a laboratory that a Member States has designated for that purpose;

(c) inspect the premises, records, documents and pharmacovigilance system master file of the marketing authorisation holder or any undertaking employed by the marketing authorisation holder to perform the activities described in Chapter IX.

8. Inspections referred to in paragraph 1, second subparagraph, points (a) and (b), shall be carried out in accordance with the principles referred to in Article 190.

9. After every inspection carried out in accordance with paragraphs 3 and 5, the competent authority of the Member State concerned shall issue a report on the compliance of the ~~manufacturing~~ activities inspected with the good manufacturing practice and good distribution practices referred to in Articles 160 and 161, as applicable.

10. The competent authority of the Member State that had its official representatives carry out inspections in accordance with paragraphs 3 and 5, shall share its ~~draft~~ **initial** report with the inspected entity.

11. Before adopting the report, the competent authority of the Member State shall give the inspected entity the opportunity to submit comments.

PUBLIC

12. Without prejudice to any arrangements that may have been concluded between the Union and third countries, a Member State, the Commission or the Agency may require a manufacturer of a medicinal product or of an active substance established in a third country to submit to an inspection as referred to in this Article.

13. Within 90 days of the conclusion of an inspection carried out in accordace with paragraphs 3 and 5 the competent authority of the Member State concerned shall issue to the inspected entity a certificate of compliance of good manufacturing practice **(GMP)** or good distribution practices **(GDP)** if the outcome of that inspection shows that the inspected entity complies with the principles of good manufacturing practice or good distribution practices referred to in Articles 160 and 161.

14. If the outcome of the inspection carried out in accordance with paragraph 3, 4 and 5 shows that the inspected entity does not comply with the principles of good manufacturing practice or good distribution practices as referred to in Articles 160 and 161, the competent authority of the Member State concerned shall issue a statement of non-compliance **and ~~may~~ shall revoke the certificate of compliance with good manufacturing practice or good distribution practice fully or partially, as appropriate**.

15. The competent authority of the Member State shall enter the certificates of good manufacturing practice or good distribution practices in the relevant Union database managed by the Agency on behalf of the Union. Pursuant to Article 157, the competent authority of the Member States shall also enter information in that database regarding the registration of importers, manufacturers and distributors of active substances and decentralised sites performing decentralised manufacturing activities, **referred to in Article 148, paragraph 3, letter b.** ~~including their respective database link to the manufacturing authorisation of the central site~~.

16. If the outcome of the inspection carried out in accordance with paragraph 5 is that the inspected entity does not comply with the legal requirements or the principles of good manufacturing practice or good distribution practices as referred to in Articles 160 and 161 the information shall be entered in the Union database as referred to in paragraph 15.

17. If the outcome of the activity carried out in accordance with paragraph 7, point (c), is that the marketing authorisation holder does not comply with the pharmacovigilance system as described in the pharmacovigilance system master file and with Chapter IX, the competent authority of the Member State concerned shall bring the deficiencies to the attention of the marketing authorisation holder and give the marketing authorisation holder the opportunity to submit comments.

In such case the Member State concerned shall inform the other Member States, the Agency and the Commission accordingly.

Where appropriate, the Member State concerned shall take the necessary measures to ensure that a marketing authorisation holder is subject to effective, proportionate and dissuasive penalties as laid down in Article 206.

*Article 189*

*Cooperation on inspections*

1. Upon request by one or more competent authorities **of the Member States**, inspections referred to in Article 188, paragraphs 3 and 5, may be carried out by official representatives from more than one Member State, together with the inspectors of the Agency **if specifically requested by the aforementioned competent authority** in accordance with Article 52(**1**~~2~~)~~,~~ ~~point (a)~~ of [revised Regulation (EC) 726/2004] ('the joint inspection').

The competent authority of the Member State receiving a request for a joint inspection, shall make all reasonable efforts**, taking into account their available resources,** to accept such a request, and coordinate and support that joint inspection, where:

(a) it is demonstrated, or there are reasonable ground for suspecting, that the activities carried out on the territory of the Member State receiving the request pose a risk to the safety and quality **of the medicinal product** in the Member State of the competent authority requesting the joint inspection **and the competent authorities of the concerned Member States agree that an inspection is needed**;

(b) competent authorities of the Member State requesting the joint inspection require specialist technical expertise available in the Member State receiving the joint inspection request;

(c) the competent authority of the Member State receiving the request agrees that there are other reasonable grounds such as training of inspectors, sharing of good practice, for ~~for~~ conducting a joint inspection.

2. The competent authorities participating in a joint inspection shall conclude an agreement prior to the inspection that defines at least the following:

(a) the scope and objective of the joint inspection;

(b) the roles of the participating inspectors during and following the inspection, including the designation of an authority leading the inspection.; ~~;~~ **Where the joint inspection is conducted on the territory of one of the Member States, the competent authority of that Member State shall act as the leading authority for the joint inspection, unless otherwise agreed between the Member States;**

(c) the powers and responsibilities of each of the competent authorities.

3. The competent authorities participating in the joint inspection shall commit themselves in that agreement to jointly accept the results of the inspection.

4. Where the joint inspection is conducted in one of the Member States, the competent authority ~~leading the joint inspection~~ **of that Member State** shall ensure that the joint inspection is carried out in accordance with the national legislation of the Member State in which the joint inspection takes place.

5. Member States may set up joint inspection programmes to facilitate routine joint inspections. Member States may operate such programmes under a agreement as referred to in paragraphs 2 and 3.

6. A competent authority of a Member State may request another competent authority to take over one of its inspections referred to in Article 188, paragraphs 3 and 5.

PUBLIC

7. The other competent authority of the Member State shall communicate to the requesting competent authority whether it accepts the request to conduct the inspection within 10 days. Where it accepts, it shall be responsible as the competent authority to carry out the inspections pursuant to this Section.

8. For the purposes of paragraph 6, and when the request is agreed, the requesting competent authority shall, in a timely manner, submit the relevant information necessary to conduct the inspection to the competent authority of the Member State that accepted the request.

*Article 190*

***Principles applicable to supervision and ~~I~~inspections ~~guidelines~~***

1. The Commission ~~may~~ **shall** adopt ~~implementing~~ **delegated** acts to lay down the principles applicable to:
   (a) the system of supervision referred to in Article 188(1);
   (b) the joint inspections referred to in Article 189(1);
   (c) the exchange of information and cooperation in the coordination of inspections in the system of supervision between the Member States and the Agency **referred to in Article 188(2)**; and
   (d) trusted non-Union regulatory authorities **referred to in Article 188(4)(a)** ~~.~~**;**
   **(e) the exchange of information and cooperation as regards decentralised manufacturing between the competent authorities in charge of the supervision of the central site and decentralised sites and of the marketing authorisation referred to in Article 148.**

   The ~~implementing~~ **delegated** acts referred to in the first subparagraph shall be adopted in accordance with the procedure referred to in Article **215** ~~214(2)~~.

2. Member States shall, in cooperation with the Agency, establish the form and content of the manufacturing authorisation referred to in Article 142(1) and of the wholesale distribution authorisation referred to in Article 163(1), of the report referred to in Article 188, of the certificates of good manufacturing practice and of the certificates of good distribution practices referred to in Article 188(13).

PUBLIC

## Section 2
## Controls

*Article 191*

*Controls on medicinal products*

Member States shall take all appropriate measures to ensure that the marketing authorisation holder for a medicinal product and, where appropriate, the manufacturing authorisation holder, furnish proof of the controls carried out on the medicinal product or the ingredients and of the controls carried out at an intermediate stage of the manufacturing process, in accordance with the methods laid down in Annex I.

*Article 192*

*Submission of control reports for immunological medicinal products* ***and of medicinal products derived from human blood or plasma***

For the purpose of implementing Article 191, Member States may require manufacturers of immunological products **and of medicinal products derived from human blood or plasma** to submit to a competent authority of the Member States copies of all the control reports signed by the qualified person in accordance with Article 153.

*Article 193*

*Batch control of specific medicinal product by Member States*

1. Where it considers it necessary in the interests of public health, a Member State may require the marketing authorisation holder of:
   (a) live vaccines,
   (b) immunological medicinal products used in the primary immunisation of infants or of other groups at risk,
   (c) immunological medicinal products used in public health immunisation programmes,
   (d) new immunological medicinal products or immunological medicinal products manufactured using new or altered kinds of technology or new for a particular manufacturer, during a transitional period normally specified in the marketing authorisation,

   to submit samples from each batch of ~~the bulk or~~ the medicinal product **and from ~~each batch of~~ the bulk if required** for examination by an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose before release on to the market unless the competent authority of another Member State has previously examined the batch in question and declared it to be in conformity with the approved specifications. In such a case the declaration of conformity issued by another Member States shall be ~~directly~~ recognised. **The marketing authorisation holder, in consultation with the Official Medicines Control Laboratory, shall make reasonable efforts to submit samples for examination at the beginning of their own controls.**

   Member States shall ensure that any such examination is completed within 30 days of the receipt **both** of the samples **and documentation of the controls carried out by the marketing authorisation holder in accordance with Article 191~~, unless otherwise justified by the nature of the testing methods employed or the need to repeat the testing, within 60 days of the receipt of the samples and documentation~~**. **This period of time shall be extended to 60 days if necessary to complete the examination.**

2. Where, in the interests of public health, the laws of a Member State so provide, the competent authorities of the Member State may require the marketing authorisation holder for medicinal products derived from human blood or human plasma to submit samples from each batch of ~~the bulk or~~ the medicinal product **and from ~~each batch of~~ the bulk if required,** for testing by an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose before being released ~~into~~ **on the market**~~free circulation~~, unless the competent authorities of another Member State have previously examined the batch in question and declared it to be in conformity with the approved specifications. **In such a case the declaration of conformity issued by another Member State shall be recognised. The marketing authorisation holder, in consultation with the Official Medicines Control Laboratory, shall make reasonable efforts to submit samples for examination at the beginning of their own controls.** Member States shall ensure that any such examination is completed within ~~60~~ **30** days of the receipt **both** of the samples **and documentation of the controls carried out by the marketing authorisation holder in accordance with Article 191, ~~unless otherwise justified by the nature of the testing methods employed or the need to repeat the testing, within 60 days of the receipt of the samples and documentation~~**. **This period of time shall be extended to 60 days if necessary to complete the examination.**

*Article 194*

*Processes for the preparation of medicinal products derived from human blood or human plasma*

1. Member States shall take all necessary measures to ensure that the manufacturing and purifying processes used in the preparation of medicinal products derived from human blood or human plasma are properly validated, attain batch-to-batch consistency and guarantee, insofar as the state of technology permits, the absence of specific viral contamination.

2. To this end manufacturers shall notify the competent authorities of the Member States of the method used to reduce or eliminate pathogenic viruses liable to be transmitted by medicinal products derived from human blood or human plasma. The competent authority of the Member State may submit samples of ~~the bulk or~~ the medicinal product **and from ~~each batch of~~ the bulk if required,** for testing by a State laboratory or a laboratory designated for that purpose, either during the examination of the application pursuant to Article 29, or after a marketing authorisation has been granted.

# REGULATION

**Recitals**

(23) Furthermore, without prejudice to the provisions laid down in Regulation (EU) 2019/6, which remain applicable for veterinary medicinal products, in order to create greater legal certainty, it is necessary to define the responsibilities regarding the transparency rules for the Agency's work, to set certain conditions for the marketing of medicinal products authorised by the Union, to confer on the Agency powers to monitor the distribution of medicinal products authorised by the Union~~, to carry out~~ **participate in** ~~inspections together with the Member States in third countries,~~ and to specify the sanctions and the procedures for implementing them in the event of failure to observe the provisions of this Regulation and the conditions contained in the marketing authorisations granted under the procedures it establishes.

PUBLIC

(24) ~~In particular, the Agency should be empowered and given the capacity to carry out~~ **participate in** ~~inspections, where this is in the interest of the Union and where the competent authorities of the Member States request support in carrying out their tasks under revised Directive 2001/83/EC of the European Parliament and of the Council[1]. Without prejudice to the powers of the national competent authorities and without undermining their national inspection resources, the Agency should be provided with the targeted inspection capacity to contribute to the strenghtening of the supervision of the manufacturing of the medicinal products worldwide, in the interest of the Union.** The interest of the Union may concern situations where, to ensure faster access to medicinal products, challenges with inspections capacities at national level have to be addressed in a timely manner or where a response to a public health emergency or a major event requires immediate action. **Therefore, the Agency should be empowered and given the capacity to support Member States with regard to inspections in third countries. In particular, where the competent authorities of the Member States request support in carrying out their tasks under revised Directive 2001/83/EC of the European Parliament and of the Council,** ~~Providing~~ the Agency **should be able to participate in inspections. Where the competent authority of a Member State cannot carry out an inspection, the Agency should facilitate the delegation of the inspection to another competent authority of a Member State. As a last resort, where no other competent authority of a Member State is able to accept the delegation to carry out an inspection, the competent authority concerned should be able to request the Agency to carry out the inspection.** ~~with appropriate inspection capacity will also, in the interest of the Union, facilitate the dissemination of best practices, know-how, and improve the oversight of manufacturing of medicinal products worldwide. Following the request from a competent authority of the Member State, the Agency, at its own discretion, can accept to either provide support to the inspections of sites located in the Union or to carry out~~ **participate in** ~~inspections of sites located in third countries.~~

~~[1] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67).~~

*Article 52*

~~*Inspection capacity of the Agency*~~ ***Cooperation between national competent authorities and the Agency for inspections in third countries***

1. **Without prejudice to the responsabilities of the competent authorities as defined in Article 188 (1) of [revised Directive 2001/83/EC], w**~~W~~hen an inspection **is needed**~~, included in the system of supervision referred to in~~ **as per** Article 188(1), point (a) of [revised Directive 2001/83/EC] ~~is~~ **or** requested, as referred to in Article 11(2), for a site located in a third country, the ~~supervisory~~ **national competent** authority **concerned** ~~for this site~~ may**:** ~~request the Agency to participate in the inspection or to carry out the inspection~~ **or delegates the inspection to the Agency**~~.~~

~~2. The Agency, following a request in accordance with paragraph 1, may decide either of the following~~:

~~(a)~~ ~~to~~ **request the Agency to participate in the inspection. The Agency may** lend its assistance by participating in a joint inspection with the ~~supervisory~~ **requesting** authority of the site. In that case the ~~supervisory~~ **requesting** authority leads the inspection and the follow up thereof. ~~After completion of the inspection, the supervisory authority grants the relevant good manufacturing practice (GMP) certificate and enters the certificate in the Union database;~~ or

**(b) request the Agency to facilitate the cooperation among the competent authorities when a competent authority intends to delegate the inspection to another competent authority as reffered to in Article 189 (6) of [revised Directive 2001/83/EC]; and**

(**c**~~b~~) **if no national competent authority accepts the delegation to conduct the inspection as reffered to under point (b), request the Agency** to carry out the inspection and the follow up thereof ~~on behalf of~~ **by delegation** ~~the supervisory authority~~. **If the inspection is in the interest of the Union defined in Annex III, the Agency shall accept the delegation and conduct the inspection.** After completion of the inspection, the Agency grants the relevant GMP certificate and enters the certificate in the Union database referred to in Article 188(15) of [revised Directive 2001/83/EC].

Where the Agency ~~decides~~ **~~is delegated by the supervisory authority~~** ~~to~~ carr**ies**~~y~~ out the inspection, the Agency may request other Member States to participate in the inspection. To any such request, the provisions on joint inspections of Article 189 of [revised Directive 2001/83/EC] shall apply. ~~In case the Agency carries out the inspection in form of a joint inspection, the Agency leads the inspection.~~

The Agency may also request to be accompanied by a rapporteur or expert appointed by the Committee for Medicinal Products for Human Use.

Where a follow-up inspection is required in view of a ~~non-compliance~~ GMP **non-compliance** ~~certificate~~ **statement** issued by the Agency, the ~~supervisory authority of the site will be in charge of its performance; the procedure of paragraph 2 shall apply if the supervisory authority for this site requests the Agency to participate in the follow up inspection or to take over the performance of the inspection~~ **Agency shall accept a request of the competent authority to perform that follow up inspection**.

~~3. The Agency shall take into account the criteria set out in Annex III when taking its decision in accordance with paragraph 2.~~

4. Article 188, paragraph 6, and paragraphs 8 to 17 of [revised Directive 2001/83/EC] shall apply to the inspections referred to in paragraph ~~2~~**1(c) accordingly**.

~~The Agency's inspectors shall have the same powers conferred on official representatives of the competent authority pursuant to these provisions.~~

5. Following a request by a Member State, the inspectors of the Agency may provide support to such Member State when it performs inspections referred to in Article 78 of Regulation (EU) 536/2014. The Agency shall take a decision whether to carry out itself such inspection based on the criteria set out in Annex III.

6. The Agency shall ensure that
   (a) appropriate resources are made available for the performance of inspection tasks in accordance with the paragraphs ~~2~~**1** and ~~5~~**3**;

(b) the inspectors of the Agency possess expertise, technical knowledge, and formal qualifications equivalent to those of the national inspectors as detailed in the compilation, published by the Commission, on Union procedures on inspections and exchange of information.

(c) it **shall implement a quality system as provided for in Article 3 paragraph 3 of Directive 2017/1572 and** participates as an inspectorate in the Joint Audit Programme and be subjected to periodic audits.

**7. The cooperation between national competent authorities and the Agency for the inspections of the interest of the Union shall be facilitated by the inspection working groups referred to in Article 142, point (k).**

*Article 53*

*International Inspections*

1. The Agency shall in consultation with the Commission **and Member States**, coordinate a structured cooperation on inspections in third countries between Member States, and as relevant the European Directorate for the Quality of Medicines and Healthcare of the Council of Europe, the World Health Organisation and trusted international authorities, by means of international inspection programmes.

2. In cooperation with the Agency, the Commission may adopt detailed guidelines laying down the principles applicable to those international inspection programmes.

*Article 54*

*Joint Audit Programme*

1. The inspection working group referred to in Article 142, point (k), shall ensure the following:
   (a) establish and develop the joint audit programme ('JAP') and supervise it;
   (b) monitor any measure taken by the Member State **and the Agency** pursuant and limited to paragraph 4;

(c) ensure cooperation with relevant international and Union level bodies to facilitate the work of the joint audit programme **and to ~~allow~~ facilitate the recognition of the inspections carried out by the competent authorities at an international level**.

For the purposes of the first subparagraph, the inspection working group may establish an operational subgroup.

2. For the purposes of paragraph 1, point (a), each Member State shall:
   (a) provide trained auditors;
   (b) accept that the competent authority in charge of the implementation of good manufacturing and good distribution practice and related surveillance and enforcement activities applicable to medicinal products and active substances are audited, regularly and where appropriate, according to the joint audit programme.

3. The joint audit programme shall be considered an integral part of the quality system of the inspectorates referred to in Article 3(3) of Commission Directive (EU) 2017/1572[1] **and the inspectorate within the Agency** and ensure that adequate and equivalent quality standards are maintained within the Union network of national competent authorities.

4. Under the joint audit programme, the auditors shall issue an audit report after each audit. The audit report shall include, where relevant, appropriate recommendations on measures that the Member State concerned **or the Agency** shall consider to take to ensure that its relevant quality system and its enforcement activities are consistent with Union quality standards.
   At the request of the Member State, the Commission or the Agency may support that Member State in taking the appropriate measures pursuant to the first subparagraph.

5. For the purposes of paragraph 4, the Agency **in particular through its inspection working group referred to in Article 142(k),** shall:

[1] Commission Directive (EU) 2017/1572 of 15 September 2017 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of good manufacturing practice for medicinal products for human use (OJ L 238, 16.9.2017, p. 44).

(a) ensure **the harmonisation of the assessment during the joint audit programme's audits and the quality and consistency of audit reports;** ~~the quality and consistency of the joint audit programme's audit reports~~;

(b) establish the criteria for the provision of the joint audit programme's recommendations.

6. The compilation of Union procedures on inspections and exchange of information referred to in Article 3(1) of Directive 2017/1572 shall be updated by the Agency to cover rules applicable to the functioning, structure, and tasks of the joint audit programme.

7. The Union shall provide the financing for activities that support the work of the joint audit programme.

## ANNEX III

## INSPECTIONS IN THE INTEREST OF THE UNION ~~PROCEDURE AND CRITERIA GOVERNING INSPECTIONS CARRIED OUT BY THE AGENCY~~

~~**Reasoned request by the competent authority**~~

~~The supervisory authority may submit after consultation with the Agency, a reasoned request to the Agency to carry out an inspection or to participate with its inspectors to an inspection carried out of a site located in a third country. The reasoned request should specify:~~

- ~~The precise identification of the site, the scope of the inspections and if relevant the concerned products;~~
- ~~The timeline for this inspection to be completed;~~
- ~~The reasons for requesting the support of the Agency, by reference to the criteria set out in this Annex.~~

~~The Agency may refuse an inspection request after consideration of the request, the scope and availability of internal inspection capacity.~~

PUBLIC

~~Assessment by the Agency~~

~~The Agency~~**~~, taking into account the nature of the request from the supervisory authority~~** ~~decides whether it accepts to carry out such inspection or to participate with its inspectors in such inspection, based on the following criteria:~~

- ~~The site is located in a non-EU/EEA country;~~
- ~~The inspection is in the interest of the Union, when one or more of the following situations apply to ensure faster or continuous access to medicines of patients:~~
  - ~~to prevent, mitigate or address shortages of medicinal products or their active substances or other supply issues;~~
  - ~~to prevent, mitigate or address a possible threat to public health, a public health emergency or a major event which requires immediate action;~~
  - ~~to address a suspicion of non-compliance of the manufacturing site;~~
  - ~~to enable the process of granting of the marketing authorisation for centrally authorised products/emergency use authorisation and for their active substance master files;~~
  - ~~to improve the oversight of medicines production worldwide;~~
  - ~~to address serious challenges of an unexpected and temporary nature with inspections capacities at national level;~~
  - ~~other relevant situations.~~

~~The compilation of Union procedures on inspections and exchange of information referred to in Article 3(1) of Directive 2017/1572 might be updated to cover rules applicable to situations where the Agency may be requested to carry out an inspection or to participate in a joint inspection.~~

~~In the context of inspections referred under Article 78 of Regulation (EU) 536/2014, the above criteria apply mutatis mutandis.~~

**An inspection is in the interest of the Union when there is a need to ensure faster or continous access to medicines for patients and when the inspection is justified based on at least one of the following grounds:**

**(a) to prevent, mitigate or address shortages of medicinal products, or their active substances or other supply issues, or**

**(b) to prevent, mitigate or address a possible threat to public health, a public health emergency or a major event which requires immediate action, or**

**(c) to address a suspicion of non-compliance of the manufacturing site, or**

**(d) to enable the process of granting the marketing authorisation for centrally authorised products/emergency use authorisation and for their active substance master files.**

PUBLIC