Executive Order on the production, import and distribution of active substances for the production of medicinal products[1)]

Pursuant to Section 39a(1)(4), Section 50c and Section 104(3) of the Danish Medicines Act, cf. Consolidated Act No 339 of 15 March 2023, as amended, the following is laid down:

Chapter 1

Scope of the executive order

Section 1. This executive order covers the production, import and distribution of active substances for the production of medicinal products for human use which are subject to a marketing authorisation.

Section 2. This executive order shall apply to companies and individuals registered with the Danish Medicines Agency as producers, importers or distributors of active substances intended for use in the production of medicinal products, in accordance with Section 50a (1) of the Danish Medicines Act, and to applicants for such registration where expressly provided for in the individual provisions.

Chapter 2

Definitions

Section 3. The following definitions apply for the purposes of this executive order:

1) Active substance: Any substance or mixture of substances intended for use in the production of a medicinal product and which, when used in its production, becomes an active ingredient of the medicinal product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions, or to making a medical diagnosis.
2) Good Manufacturing Practice (GMP): The part of quality assurance ensuring that active substances for the production of medicinal products are consistently produced and controlled in accordance with the quality requirements applicable to the intended use of the medicinal products.
3) Producer: Any party registered with the Danish Medicines Agency as a producer of active substances for medicinal products.
4) Production activities: The complete or partial production of an active substance used as a raw material, as well as the various processes related to division, packaging and presentation prior to its use in a medicinal product, including repackaging and relabelling.
5) Importer: Any party registered with the Danish Medicines Agency as an importer of active substances for medicinal products.
6) Import: The import of active substances for medicinal products from a country outside the EU/EEA (third country).

7) Good Distribution Practice (GDP): The part of quality assurance ensuring that the properties of active substances for medicinal products are not impaired during import and distribution, and that defective active substances can be traced and recalled.

8) Distributor: Any party registered with the Danish Medicines Agency as a distributor of active substances for medicinal products.

9) Distribution: Any activity consisting of the purchase, import, storage, supply, or export of active substances, except for brokering

10) Quality control: Procedures and documentation for sampling, self-inspection, auditing and qualitative and quantitative testing of active substances.

11) Quality assurance: All measures undertaken to ensure that active substances are of a quality appropriate to their intended use.

Chapter 3

Registration of the production, import and distribution of active substances for the production of medicinal products

Section 4. To obtain registration as a producer, importer or distributor of active substances for medicinal products, the applicant must:

1) use the electronic form provided by the Danish Medicines Agency, and

2) enter the following information in the form:

a) Name or company name and permanent address.

b) The active substances to be imported, produced or distributed.

c) Information on the premises and technical equipment to be used for their activity.

Section 5. The applicant must submit the registration form to the Danish Medicines Agency no later than 60 days before the planned commencement of the activity.

Section 6. On the basis of a risk assessment, the Danish Medicines Agency may decide to conduct an inspection at the applicant's premises.

(2) If, within 60 days of receipt of the registration form, the Danish Medicines Agency notifies the applicant that an inspection visit will be carried out, the activity may not commence until the Danish Medicines Agency has informed the applicant that the activity may begin. If, within 60 days of receipt of the registration form, the Danish Medicines Agency has not notified the applicant that an inspection visit will be carried out, the applicant may begin the activity.

Section 7. Each year, registered companies and persons shall submit to the Danish Medicines Agency a summary of any changes that have taken place in relation to the information provided in the registration form. Any change that may affect the quality or safety of the active substances produced, imported or distributed must be reported immediately to the Danish Medicines Agency.

Section 8. The Danish Medicines Agency shall enter the information received upon registration under section 4(1)(2) into the EU database (EudraGMDP) that the European Medicines Agency administers on behalf of the EU.

Chapter 4

Production

Section 9. It is the responsibility of producers of active substances to carry out production in accordance with good manufacturing practice for active substances, without prejudice to paragraph 2.

(2) Paragraph 1 shall not apply to the production of active substances that are biological or sterile, as such production is subject to the provisions on production in the Executive Order on the production and import of medicinal products and intermediate products.

Section 10. Detailed guidelines on Good Manufacturing Practice for active substances for the production of medicinal products have been published by the European Commission in Part II of the "Rules governing medicinal products in the European Union, Volume 4".

Section 11. Any manufacturer of active substances (contract giver) may entrust others (contract acceptors) to carry out production or analysis, provided that:

1) the contract acceptor holds a valid registration in accordance with section 50a(1) of the Danish Medicines Act or another relevant authorisation under the legislation of another EU/EEA country,

2) there is a written contract between the contract giver and the contract acceptor for each production process, including any analytical task or process related to production,

3) the responsibilities of the contract giver and the contract acceptor are clearly set out in the contract,

4) the contract states that the contract acceptor is obliged to comply with Good Manufacturing Practice for active substances,

5) the contract states that the contract acceptor cannot delegate the performance of tasks to a third party without the consent of the contract giver, and

6) the contract states that if the contract acceptor holds an authorisation under the legislation of another EU/EEA country, cf. point 1, the contract acceptor accepts that the Danish Medicines Agency may inspect the activity.

(2) Analytical laboratories in EU/EEA countries that are not subject to the registration requirement as referred to in paragraph 1(1) may, notwithstanding this provision, perform tasks for the contract giver, provided that the contract states that they accept that the performance of such analyses may be subject to inspection in accordance with the rules on Good Manufacturing Practice.

(3) The contract acceptor may only subcontract tasks to a third party in accordance with the provisions of this executive order.

(4) Prior to the commencement of activities by the contract acceptor and subsequently at regular intervals, the contract giver shall carry out documented audits and record audits at the contract acceptor's premises in order to verify the implementation of and compliance with the principles of Good Manufacturing Practice for active substances.

Chapter 5

Import and distribution

Section 12. Active substances may be imported only if the following conditions are met:

1) the active substances have been produced in accordance with guidelines on Good Manufacturing Practice which are at least equivalent to those established by the European Commission, and

2) the active substances are accompanied by a written confirmation from the competent authority of the exporting third country, stating the following:

a) that the Good Manufacturing Practice guidelines applicable to the establishment where the exported active substance was produced are at least equivalent to the guidelines laid down by the European Commission,

b) that the establishment where the active substance was produced is subject to regular, rigorous and transparent controls and effective enforcement of Good Manufacturing Practice, including repeated and unannounced inspections, in order to ensure a level of public health protection at least equivalent to that applicable in the Union, and

c) in the event of findings of non-compliance, the exporting third country will immediately provide information on such findings to the Union.

(2) The requirement in paragraph 1(b) shall not apply if the exporting country is included in the list referred to in Article 111b of Directive 2001/83/EC, as amended.

(3) The requirement referred to in point (b) of paragraph 1 may, by way of exception and where necessary to ensure the availability of medicinal products, be waived by the Danish Medicines Agency for a period not exceeding the validity of the Good Manufacturing Practice certificate, where a Member State has found, following an inspection, that an establishment producing an active substance for export complies with the Good Manufacturing Practice guidelines laid down in Article 47(3) of Directive 2001/83/EC, as amended. If this derogation is applied, the Danish Medicines Agency shall inform the European Commission.

(4) The requirements of paragraph 1 shall not apply to the import of active substances that are biological or sterile, as the provisions on importation laid down in the executive order on the production and importation of medicinal products and intermediate products shall apply to such imports.

Section 13. Holders of a registration under Section 50a of the Danish Medicines Act may distribute active substances to others with a similar registration or authorised producers of medicinal products.

(2) Holders of a registration under section 50a of the Danish Medicines Act may distribute active substances in the form of cannabis herbal drug and cannabis herbal preparation to companies holding an authorisation to produce cannabis bulk pursuant to section 9(1) of the Act on the Medicinal Cannabis Programme.

Section 14. It is the responsibility of distributors of active substances to carry out distribution in accordance with Good Distribution Practice for active substances. *(2)* Detailed guidelines on Good Distribution Practice for active substances have been published by the European Commission in the

“Guidelines on principles of Good Distribution Practice of active substances for medicinal products for human use”.

Section 15. Any distributor or importer of active substances (contract giver) may entrust to others (contract acceptors) to perform receipt (including incoming inspection), storage and distribution, provided that:

1) the contract acceptor holds a valid registration in accordance with section 50a(1) of the Danish Medicines Act or another relevant authorisation under the legislation of another EU/EEA country,
2) there is a written contract between the contract giver and the contract acceptor for each task,
3) the responsibilities of the contract giver and the contract acceptor are clearly set out in the contract,
4) the contract states that the contract acceptor is obliged to comply with Good Distribution Practice for active substances,
5) the contract states that the contract acceptor cannot delegate the performance of tasks to a third party without the consent of the contract giver, and
6) the contract states that if the contract acceptor holds an authorisation under the legislation of another EU/EEA country, cf. point 1, the contract acceptor accepts that the Danish Medicines Agency may inspect the activity.

(2) The final incoming inspection for deliveries from other EU/EEA countries may only be carried out in Denmark.

(3) The contract acceptor may only subcontract tasks to a third party in accordance with the provisions of this executive order.

(4) Prior to the commencement of activities by the contract acceptor and subsequently at regular intervals, the contract giver shall carry out documented audits of the contract acceptor in order to verify the implementation of and compliance with the principles of Good Distribution Practice for active substances.

Chapter 6

Inspection, disclosure of information, etc.

Section 16. Following any inspection under Section 44(1) of the Danish Medicines Act, the Danish Medicines Agency shall draw up a report on compliance with the guidelines on Good Manufacturing Practice and Good Distribution Practice. The contents of these inspection reports shall be communicated to the producer, importer, producer of active substances or the holder of the marketing authorisation subject to the inspection visit. Before the report is completed, the Danish Medicines Agency shall give the inspected entity concerned the opportunity to submit comments.

Section 17. No later than 90 days after an inspection as referred to in section 16, the Danish Medicines Agency shall issue a certificate of Good Manufacturing Practice to the manufacturer of active substances, provided that the inspection visit concludes that the entity concerned complies with the principles and guidelines of Good Manufacturing Practice.

(2) The Danish Medicines Agency shall enter the certificates referred to in paragraph 1 in the EU database (EudraGMDP) managed by the European Medicines Agency on behalf of the EU.

(3) If the conclusion of an inspection as referred to in paragraph 1 is that the producer or importer does not comply with the principles and guidelines of Good Manufacturing Practice, that information shall be entered in the Union database (EudraGMDP) referred to in paragraph 2.

Section 18. No later than 90 days after an inspection as referred to in section 14, the Danish Medicines Agency shall issue a certificate of Good Distribution Practice to the importer and the distributor of active substances, provided that the visit concludes that the entity concerned complies with the principles and guidelines of Good Distribution Practice.

(2) The Danish Medicines Agency shall enter the certificates referred to in paragraph 1 in the EU database (EudraGMDP) managed by the European Medicines Agency on behalf of the EU.

(3) If the conclusion of an inspection as referred to in paragraph 1 is that the distributor does not comply with the principles and guidelines of Good Distribution Practice, that information shall be entered in the Union database (EudraGMDP) referred to in paragraph 2.

Section 19. The Danish Medicines Agency may, upon a reasoned request from an authority in another EU/EEA country, from a third country with which appropriate mutual recognition agreements (MRAs) on regulatory inspections have been concluded, or from the European Medicines Agency, transmit electronically the inspection reports referred to in section 14.

Section 20. The Danish Medicines Agency may grant exemptions from one or more provisions of this executive order in exceptional circumstances.

Penalty provisions and entry into force

Section 21. Unless a higher penalty is imposed under other legislation, a fine shall be imposed on anyone who infringes section 5, section 6(2), section 7, section 9(1), section 11, section 12(1) and sections 13 to 15.

(2) Criminal liability may be imposed on enterprises etc. (legal entities) within the meaning of the rules in Chapter 5 of the Penal Code.

Section 22. The executive order enters into force on xx.

Section 23. Persons who commenced their activities under Section 1 before 1 January 2013 must have submitted the registration form to the Danish Health Authority no later than 1 March 2013.