SUBSIDIARY LEGISLATION 458.36

MANUFACTURE AND IMPORTATION OF MEDICINAL PRODUCTS FOR HUMAN USE REGULATIONS

30th October, 2005

LEGAL NOTICE 381 of 2005, as amended by Legal Notices 252 of 2009 476 of 2012 and 234 and 283 of 2022.

Citation.

1. The title of these regulations is the Manufacture and Importation of Medicinal Products for Human Use Regulations.

Interpretation. *Amended by: L.N. 476 of 2012.* Cap. 458.

2. For the purposes of these regulations -

"Act" means the Medicines Act;

"active substance (API)" means any substance or mixture of substances intended to be used in the manufacture of a medicinal product and that, when used in its production, becomes an active ingredient of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions or to make a medical diagnosis;

"the Agency" means the European Medicines Agency established by Regulation (EC) No. 726/2004;

"the Commission" means the Commission in accordance with Council Decision 1999/468/EC of 28th June, 1999;

"the Community" means the European Community and the European Economic Area;

"imported medicinal products" means medicinal products obtained from a source outside the European Union or the European Economic Area;

"Member State" means a State which is a member of the European Union and includes Iceland, Norway and Liechtenstein.

(2) The provisions of these regulations shall not apply to:

(*a*) any medicinal product prepared in a pharmacy in accordance with a medical prescription for an individual patient (commonly known as the magistral formula);

(*b*) any medicinal product which is prepared in a pharmacy in accordance with the prescriptions of a pharmacopoeia and is intended to be supplied directly to the patients served by the pharmacy in question, (commonly known as the officinal formula);

(*c*) medicinal products intended for research and development trials but without prejudice to the provisions of the Clinical Trials Regulations, or Directive 2001/20/EEC of the European Parliament and of the Council of the 4th April, 2001 on the approximation of the laws, regulations and administrative provisions of the Member States

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relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products on human use;

(*d*) intermediate products intended for further processing by an authorised manufacturer;

(*e*) any radionuclides in the form of sealed sources;

(*f*) whole blood, plasma or blood cells of human origin, except for plasma which is prepared by a method involving an industrial process;

(*g*) medicinal products supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised health-care professional and for use by an individual patient under his direct personal responsibility.

Manufacturing licence.
Amended by: L.N. 252 of 2009; L.N. 476 of 2012.

3. (1)(*a*) No medicinal product, biological active substance, or active substance to be used directly as an investigational medicinal product, may be manufactured in Malta unless there is, in respect of such product or substance, a manufacturing licence, hereinafter referred to as "licence", to that effect. This manufacturing licence shall also be required for the processes of sterilisation of active substances.

(*b*) This manufacturing licence shall be required notwithstanding that the medicinal products manufactured are intended for export.

(2) (*a*) A licence, which shall remain in force for a period to be determined by the Licensing Authority, hereinafter referred to as "the Authority", shall be required for both total and partial manufacture, and for the various processes of dividing up, packaging or presentation.

(*b*) A licence shall not be required for preparation, dividing up, changes in packaging or presentation where such processes are carried out solely for retail supply by pharmacists in pharmacies, or by persons legally authorised to carry out such processes.

(3) An importer's licence, hereinafter also referred to as "licence", shall be required for the importation of medicinal products.

(4) A licence shall include a licence to distribute by wholesale the medicinal products in respect of which the licence has been issued.

(5) The Authority shall forward to the Agency a copy of the licence referred to in subregulation (1).

(6) The Authority shall enter the information relating to the licence referred to in sub-regulation (1) in the European Union database referred to in Article 111(6) of Directive 2001/83/EC as amended.

Registering of activity with the Authority. *Added by: L.N. 476 of 2012.*

3A. (1) Importers and manufacturers of active substances who are established in Malta shall register their activity with the Licensing Authority.

(2) The registration form shall include, at least, the following information:

(*a*) name or corporate name and permanent address;

(*b*) the active substances which are to be imported or manufactured;

(*c*) particulars regarding the premises and the technical equipment for their activity:

Provided that the persons referred to in sub-regulation (1) shall submit the registration form to the Licensing Authority at least sixty days prior to the intended commencement of their activity.

(3) The Licensing Authority may, based on a risk assessment, decide to carry out an inspection. If the Licensing Authority notifies the applicant within sixty days of the receipt of the registration form that an inspection will be carried out, the activity shall not begin before the Licensing Authority has notified the applicant that he may commence the activity. If within sixty days of the receipt of the registration form the Licensing Authority has not notified the applicant that an inspection will be carried out, the applicant may commence the activity.

(4) The persons referred to in sub-regulation (1) shall communicate annually to the Licensing Authority an inventory of the changes which 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 or imported shall be notified immediately.

(5) Persons referred to in sub-regulation (1) who had commenced their activity before 2 January 2013 shall submit the registration form to the competent authority by 2 March 2013.

(6) Member States shall enter the information provided in accordance with sub-regulation (2) in the European Union database referred to in Article 111(6) of Directive 2001/83/EC, as amended.

(7) This regulation shall be without prejudice to articles 101 and 102 of the Medicines Act.

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Grant or renewal of a licence.

4. The Authority, shall only grant or renew a licence, if the applicant:

(*a*) specifies the medicinal products and pharmaceutical forms which are to be manufactured or imported and the place where they are to be manufactured and, or controlled;

(*b*) has at his disposal, for the manufacture or import of medicinal products, suitable and sufficient premises, technical equipment and control facilities complying with requirements set by the Authority;

(*c*) has at his disposal the services of at least one qualified

person within the meaning of regulation 8; and

(*d*) provides all necessary documentation in support of his application.

Processing of licence.

5. (1)(*a*) The Authority shall issue the licence after verifying the contents of the application but in any case not later than ninety days from receipt of the application.

(*b*) This time period shall be suspended when the Authority requests additional information from the applicant.

(*c*) The Authority may grant a conditional licence subject to the carrying out of certain obligations imposed on the applicant.

(2) The licence shall apply only to the premises, medicinal products and pharmaceutical forms specified in the application.

Change in particulars.

6. When the holder of the licence requests a change in the particulars specified in regulation 4(*a*) and 4(*b*), the process of verification of such information shall not exceed thirty days. However, in exceptional cases, this period of time may be extended to ninety days.

Obligation of licence holder. *Amended by: L.N. 476 of 2012.*

7. (1) The holder of the licence, apart from his obligations in article 44 of the Act, shall:

(*a*) comply with the Community principles and guidelines of good manufacturing practice and any annexes thereof for medicinal products and use only active substances which have been manufactured in accordance with the Community guidelines on good manufacturing practice for active substances and distributed in accordance with good distribution practices for active substances. To this end, the holder of the manufacturing authorisation shall verify compliance by the manufacturer and distributors of active substances with good manufacturing practice and good distribution practices by conducting audits at the manufacturing and distribution sites of the manufacturer and distributors of active substances. The holder of the manufacturing authorisation shall verify such compliance either by himself or, without prejudice to his responsibility as provided for in these regulations and in the Act , through an entity acting on his behalf under a contract;

(*b*) ensure that the excipients are suitable for use in medicinal products by ascertaining what the appropriate good manufacturing practice is. This shall be ascertained on the basis of a formalised risk assessment in accordance with the applicable guidelines referred to in the fifth paragraph of Article 47 of Directive 2001/83/EC, as amended. 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. The holder of the manufacturing authorisation shall ensure that the appropriate good manufacturing practice, so ascertained, is applied. The holder of the manufacturing authorisation shall document the measures taken under this paragraph;

(*c*) inform the competent authority and the marketing authorisation holder immediately if he obtains information that medicinal products which come under the scope of his manufacturing authorisation are, or are suspected of being, falsified irrespective of whether those medicinal products were distributed within the legal supply chain or by illegal means, including illegal sale by means of information society services;

(*d*) verify that the manufacturers, importers or distributors from whom he obtains active substances are registered with the competent authority of the Member State in which they are established;

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

(2) For the purposes of this regulation, manufacture of active substances used as starting materials shall include both total and partial manufacture or import of an active substance used as a starting material as defined in Part I, point 3.2.1.1 (b) Annex I of Directive 2001/83, 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 starting materials.

(3) The safety features referred to in regulation 3(*o*) of the Medicinal Products (Labelling and Packaging) Regulations shall not be removed or covered, either fully or partially, unless the following conditions are fulfilled: S.L. 458.33

(*a*) the manufacturing licence 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 licence holder complies with regulation 3(*o*) of the Medicinal Products (Labelling and Packaging) Regulations, by replacing those safety features with safety features which 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: S.L. 458.33

(i) comply with the requirements as may be adopted by the European Union Commission pursuant to Article 54a(2) of Directive 2001/83/EC as amended; 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 Licensing Authority through inspections or any other means as may be determined by the same Authority.

(4) Manufacturing licence holders, including those performing the activities referred to in sub-regulation (3), shall be regarded as producers and therefore held liable for damages in the cases and under the conditions set forth in the Consumers Affairs Act. Cap. 378.

(5) It shall be the duty of the importer to ensure that:

(*a*) in the case of medicinal products and investigational medicinal products imported from third countries, these have been manufactured in accordance with standards which are at least equivalent to the good manufacturing practice standards laid down by the Community;

(*b*) in the case of medicinal products, such products have been manufactured by manufacturers duly authorised for the purpose; and

(*c*) in the case of investigational medicinal products, such products have been manufactured by a manufacturer notified to the competent authorities and accepted by them for that purpose.

Requirement for qualified person and holder as qualified person.

8. (1) The holder of the licence shall have permanently and continuously at his disposal the services of at least one qualified person, in accordance with the conditions laid down in regulation 9, responsible in particular for carrying out the duties specified in regulation 11.

(2) If the manufacturing licence holder personally has the qualifications laid down in regulation 9, then he may himself assume the responsibility of a qualified person.

Qualified person.

9. For a person to be designated as qualified person, he must possess the following qualifications:

(*a*) (i) 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, extending over a period of at least four years of theoretical and practical study in any of the following scientific disciplines: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology;

(ii) 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, such period being corroborated by an examination at university level, then the minimum duration of the university course may be three and half years;

(iii) where two university courses or two courses recognised 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 above, in so far as the diplomas, certificates or other evidence of formal qualifications awarded on completion of both courses are recognised as equivalent;

(*b*) the course shall include theoretical and practical study on at least the following basic subjects:

(i) experimental physics;

(ii) general and inorganic chemistry;

(iii) organic chemistry;

(iv) analytical chemistry;

(v) pharmaceutical chemistry, including analysis of medicinal products;

(vi) general and applied biochemistry (medical);

(vii) physiology;

(viii) microbiology;

(ix) pharmacology;

(x) pharmaceutical technology;

(xi) toxicology;

(xii) pharmacognosy (study of the composition and effects of the natural active substances of plants and animal origin);

(*c*) studies in these subjects shall be so balanced as to enable the qualified person to fulfil the obligations specified in regulation 11;

(*d*) in those cases where diplomas, certificates or other evidence of formal qualifications do not fulfil the criteria above mentioned, the Authority shall ensure that the person concerned provides evidence of adequate knowledge of the subjects involved;

(*e*) (i) the qualified person shall have acquired practical experience over at least two years, in one or more undertakings which 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;

(ii) the duration of practical experience may be reduced by one year where a university course lasts for at least five years, and by a year and a half where the course lasts for at least six years.

Exemptions for existing qualified person.

10. (1) 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, in a scientific discipline allowing him to perform the duties of a qualified person, may, if he began his course prior to the 21st May, 1975, be considered as qualified to carry out the duties of a qualified person, provided that he was, for at least two years before the 21st May, 1985, engaged with one or more undertakings authorised to manufacture, and as having carried out the duties of production supervision and, or qualitative and quantitative analysis of active substances, and the necessary testing and checking under the direct authority of a qualified person in order to ensure the quality of the medicinal products.

(2) If the person concerned has acquired the practical experience referred to in subregulation (1) before the 21st May, 1965, a further one year's practical experience in accordance with the conditions referred to in subregulation (1) will be required to be completed immediately before he engages in such activities.

(3) A person engaging in the activities of a qualified person from the time of the application of Directive 75/319/EEC in a Member State without complying with the provisions of regulation 9 shall be eligible to continue to engage in those activities within the Community.

Responsibility of qualified person. *Amended by: L.N. 476 of 2012.*

11. (1) The qualified person, without prejudice to his relationship with the holder of the licence, shall be responsible to ensure that:

(*a*) each batch of medicinal products manufactured in Malta has been manufactured and checked in terms of the laws in force and is in accordance with the requirements of the marketing authorisation;

(*b*) in the case of medicinal products coming from third countries, irrespective of whether the product has been manufactured in the Community, 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 product in accordance with the requirements of the marketing authorisation:

Provided that when the batches of medicinal products have already undergone the controls above mentioned in a Member

State, they shall be exempt from further controls if they are accompanied by the control reports signed by the qualified person, and are marketed within the Community.

(2) The qualified person need not carry out the controls above mentioned in the case of imported medicinal products, where arrangements have been made by the Community with the exporting country to ensure that the manufacturer of the medicinal products applies standards of good manufacturing practice at least equivalent to those laid down by the Community, and to ensure that the controls referred to above have been carried out in the exporting country.

(3) The qualified person shall, in the case of medicinal products intended to be placed on the market in the European Union, ensure that the safety features referred to in regulation 3(*o*) of the Medicinal Products (Labelling and Packaging) Regulations have been affixed on the packaging. S.L. 458.33

11A. With regard to quality control testing, carried out in parts of the United Kingdom other than Northern Ireland, regarding medicinal products included in the list referred to in regulation 5A of the Medicines (Marketing Authorisation) Regulations other than those authorised by the Commission, until the 31st December 2024, the Licensing Authority, may consider there is a justifiable case within the meaning of regulation 11(1)(b), without carrying out a case-by-case assessment provided that: Quality control testing in the United Kingdom. S.L. 458.34. *Added by: L.N. 234 of 2022. Amended by: L.N. 283 of 2022.*

(*a*) each batch of the medicinal products concerned is released by a qualified person on a site in the Union or in Northern Ireland or by a qualified person on a site in parts of the United Kingdom other than Northern Ireland applying quality standards that are equivalent to those laid down in regulation 11;

(*b*) the establishment designated by the third party conducting the quality control testing is supervised by the competent authority of the United Kingdom, including by performing on-the-spot checks;

(*c*) where the batch release is carried out by a qualified person who resides and operates in parts of the United Kingdom other than Northern Ireland, the manufacturing authorisation holder declares that it does not have at its disposal a qualified person who resides and operates in the Union on the 20th April 2022.

11B. By way of derogation from sub-regulations 1(a) and (b) of regulation 3, until the 31st December 2024, the Licensing Authority shall allow medicinal products to be imported from parts of the United Kingdom other than Northern Ireland by holders of a wholesale distribution authorisation as referred to in regulation 4 of the Wholesale Distribution and Brokering of Medicinal Products and Active Substances Regulations, that are not in possession of a relevant manufacturing authorisation provided that all of the following conditions are fulfilled: Derogation from the requirement of an importers' licence. S.L. 458.37.

(*a*) the medicinal products have undergone quality control testing, either in the Union, as provided for in regulation 12 or in parts of the United Kingdom other than Northern Ireland in compliance with regulation 11(1)(b);

(*b*) the medicinal products have been subject to batch release by a qualified person in the Union in accordance with regulation 11(1) or, for medicinal products authorised by the Licensing Authority and the United Kingdom in respect of Northern Ireland, in parts of the United Kingdom other than Northern Ireland applying quality standards that are equivalent to those laid down in regulation 11(1);

(*c*) the marketing authorisation for the medicinal product concerned has been granted in accordance with Union law, by the competent authority of a Member State or by the Commission or, as regards medicinal products placed on the market in Northern Ireland, by the competent authority of the United Kingdom in respect of Northern Ireland;

(*d*) medicinal products are only made available to patients or end-consumers in Malta;

(*e*) the medicinal products bear the safety features referred to in regulation 3(o) of the Medicinal Products (Labelling and Packaging) Regulations.

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Certain derogations from importation controls.

11C. For batches of medicinal products exported to parts of the United Kingdom other than Northern Ireland from a Member State and subsequently imported into Malta until the 31st December 2024 the controls upon importation referred to in the sub-regulations (1) and (2) of regulation 11, shall not be required, provided that those batches have undergone such controls in a Member State prior to being exported to parts of the United Kingdom other than Northern Ireland and that they are accompanied by the control reports referred to in the said regulation.

Derogation regarding the place of operation of the qualified person.

11D. Where the manufacturing authorisation is granted by the competent authority of the United Kingdom in respect of Northern Ireland, the qualified person referred to regulation 11(1) may reside and operate in parts of the United Kingdom other than Northern Ireland, unless the manufacturing authorisation holder already has at its disposal a qualified person who resides and operates in the Union on 20 April 2022.

Keeping of registers.

12. (1) It shall be the duty of the qualified person to keep a register to document and certify that each production batch satisfies the provisions of these regulations.

(2) The said register shall be kept up to date as operations are carried out and must be made available for inspection by the Authority for at least five years.

13. Any breaches of:

Offences and penalties. *Added by: L.N. 476 of 2012.*

(*a*) regulations 3 and 3A shall be an offence and shall be liable to penalties under article 99(1)(*a*) of the Act;

(*b*) regulations 7 and 8 shall be an offence and shall be liable to penalties under article 99(1)(*b*) of the Act;

(*c*) regulations 11 and 12 shall be an offence and shall be liable to penalties under article 99(1)(*c*) of the Act.