Medicines Authority

Our Ref: 09/2012

CONSULTATION DOCUMENT ON IMPLEMENTATION OF DIRECTIVE 2011/62/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL OF 8 JUNE 2011 AMENDING DIRECTIVE 2001/83/EC ON THE COMMUNITY CODE RELATING TO MEDICINAL PRODUCTS FOR HUMAN USE, AS REGARDS THE PREVENTION OF THE ENTRY INTO THE LEGAL SUPPLY CHAIN OF FALSIFIED MEDICINAL PRODUCTS.

Objectives and Scope

There is an alarming increase in the European Union (EU) of medicinal products which are illegal and false representations relating to identity, history or source. These products (which are commonly referred to as "counterfeit medicinal products") usually contain sub-standard or false ingredients, or no ingredients or ingredients in the wrong dosage, including active pharmaceutical ingredients (APIs). They are substandard; their quality is unknown as often is their origin and they are a major threat to European patients and European industry.

To this adds that the risk profile has changed. The number of false representations of innovative and life-saving medicines is increasing and in order to increase volume, these falsified products are frequently channelled through the lawful supply chain towards the patient.

Moreover, this phenomenon can have disastrous consequences for the trust of the public in the industry and in the policy maker. The underlying causes for false representations of medicinal products remaining undetected in the lawful supply chain are manifold, but can be reduced to four aspects:
• False representations of medicinal products cannot always be easily distinguished from originals;
• The distribution chain has become very complex and is only as "strong as its weakest link";
• There are legal uncertainties as to the regime applicable to products introduced into the EU while not being placed on the market; and
• Already the active pharmaceutical ingredients ("API") entering the manufacturing process may be a false representation of the original API.

These aspects relate in particular to the pharmaceutical legislation in the EU which ensures the functioning of the internal market for medicinal products while safeguarding a high level of protection of public health in the EU. To the extent that this legislation establishes exhaustive rules, Member States are not allowed to "add to" these rules. Moreover, the aim to combat counterfeit medicines in the legal supply chain (without hampering the functioning of the internal market for medicinal products) cannot be sufficiently achieved by the Member States and can be better achieved by the Community.

Therefore Directive 2011/62/EU addresses these problems as defined. The national regulations implement the provisions of Directive 2011/62/EU of the European Parliament and of the Council of 8th June 2011 amending, Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products.

Main Changes

The Directive is directly applicable to all Member States as from the 2 January 2013.

Major changes to Directive 2001/83/EC:

• A legal basis for the Commission to render obligatory specific safety-features on the packaging for prescription medicines and for over-the-counter medicines which are deemed to be at high risk of falsification.

- Giving harmonised definitions amongst member states including that for falsified medicines;

• An extension of certain rules for wholesalers to other economic actors in the distribution chain who are involved in the transactions without actually handling the products, namely brokers.

• Harmonised rules for official inspections and particularly certificates and authorisations for wholesalers. Moreover, compliant wholesalers would be listed in a European database to enhance transparency of reliable traders.

• Strengthened requirements for importations of API if it is established that the regulatory framework in the respective third country does not ensure a comparable level of protection of human health for products exported to the EU.

• Audits and notification of economic actors handling API in the EU – both importers and wholesale dealers of APIs.

- Introduce a set of minimum requirements, including a common EU Logo, for internet pharmacies where their establishment is allowed in the EU.

DIRECTIVE 2011/62/EU:

Comments

Your comments on the proposed Legal Notices are invited.

Due to a tight deadline, comments are to reach the Medicines Authority in writing or via email on **consultations.medicinesauthority@gov.mt** by the **30th July 2012.**

Should any further information be required kindly contact the *Inspectorate and Enforcement Directorate,* Medicines Authority using the following contact details:

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Minister of Health,
the Elderly and Community Care

L.N. of 2012

MEDICINES ACT, 2003
(CAP. 458)

Good Manufacturing Practice in Respect of Medicinal Products, Active Substances and Investigational Medicinal Products for Human Use Regulations, 2012

IN exercise of the powers conferred by article 106 of the Medicines Act, 2003, the Minister of Health, the Elderly and Community Care has made the following regulations:

Title.

1. The title of these regulations is the Good Manufacturing Practice in Respect of Medicinal Products, Active Substances and Investigational Medicinal Products for Human Use Regulations, 2012.

Scope.

2. These regulations, which transpose Directive 2003/94/EC as amended by Directive 2011/62/EU, lay down the principles and guidelines of good manufacturing practice in respect of the manufacture of medicinal products, active substances and investigational medicinal products for human use.

Definitions.

3. For the purposes of these regulations and unless the context otherwise requires:

"the Authority" means the Medicines Authority;

"blinding" means the deliberate disguising of the identity of an investigational medicinal product in accordance with the instructions of the sponsor;

"good manufacturing practice" means the part of quality assurance which ensures that products are consistently produced and controlled in accordance with the quality standards appropriate to their intended use and in line with the current detailed good manufacturing practice guidelines published by the European Union Commission ;

"investigational medicinal product" means a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already having a marketing authorization but which are used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form;

"manufacturer" means any person engaged in the activities for which the licence referred to in the subsidiary legislation 458.36 is required:

"medicinal product" means any product as defined in Article 1(2) of Directive 2001/83/EC;

"pharmaceutical quality assurance" means the total sum of the organised arrangements made with the object of ensuring that medicinal products or investigational medicinal products are of the quality required for their intended use;

"qualified person" means any person who is a qualified person as provided by regulation 9 of subsidiary legislation 458.36.

"unblinding" means the disclosure of the identity of a blinded product.

Inspections.

4. (1) The Authority shall, by means of repeated inspections in the case of medicinals for human use and by means of inspections in the case of investigational medicinal products, ensure that manufacturers respect the principles and guidelines of good manufacturing practice laid down by these regulations.

(2) The Authority shall, by means of repeated inspections ensure that manufactures and importers of active substances, including active substances that are intended for export, comply with European Union good manufacturing practice for active substances.

(3) The Authority shall also take into account the compilation, published by the Commission, of Community procedures on inspections and exchange of information.

(4) For the interpretation of the principles and guidelines of good manufacturing practice, the Authority and the manufacturers shall take into account the detailed guidelines referred to in the second paragraph of Article 47 of Directive 2001/83/EC, published by the Commission in the "Guide to good manufacturing practice for medicinal products and for investigational medicinal products".

Conformity with good manufacturing practice.

5. (1) It shall be the duty of the manufacturer to ensure that manufacturing operations, including those of medicinal products intended only for export, and of intermediate products, active substances and excipients are carried out in accordance with EU good manufacturing practice and with the manufacturing authorisation.

(2) The holder of the manufacturing authorisation shall:

- comply with the principles and guidelines of good manufacturing practice for medicinal products and to use only active substances, which have been manufactured in accordance with 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 this Directive, through an entity acting on his behalf under a contract.

- 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. 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;

- 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;

- 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;

- verify the authenticity and quality of the active substances and the excipients.

(3) 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.

(4) It shall be the duty of the manufacturers and importers of active substances, including active substances that are intended for export, to comply with the current European Union good manufacturing practice for active substances.

Compliance with marketing authorisation.

6. (1) It shall be the duty of the manufacturer to ensure that all manufacturing operations for medicinal products subject to a marketing authorisation are carried out in accordance with the information provided in the application for marketing authorisation as accepted by the Licensing Authority.

(2) In the case of investigational medicinal products, the manufacturer shall ensure that all manufacturing operations are carried out in accordance with the information provided by the sponsor as provided in the Clinical Trials Regulations, and as accepted by the Licensing Authority.

(3) It shall be the duty of the manufacturer to review regularly his manufacturing methods in the light of scientific and technical progress and the development of the investigational medicinal product.

(4) If a variation to the marketing authorisation dossier or an amendment to the request provided for in the Clinical Trials Regulations is necessary, the application for modification shall be submitted to the Authority.

Quality Assurance system.

7. It shall be the duty of the manufacturer to establish and implement an effective pharmaceutical quality assurance system involving the active participation of the management and personnel of the different departments.

Personnel.

8. It shall be the duty of the manufacturer to ensure that: (a)

(a) there is at each manufacturing site, a sufficient number of competent and appropriately qualified personnel at his disposal to achieve the pharmaceutical quality assurance objective;

(b) the duties of the managerial and supervisory staff, including the qualified persons, responsible for implementing and

operating good manufacturing practice, are defined in the job descriptions;

(c) the hierarchical relationships of the manufacturer's staff are defined in an organisation chart;

(d) the organisation charts and job descriptions are approved in accordance with the manufacturer's internal procedures;

(e) the staff have sufficient authority to discharge their responsibility correctly;

(f) the personnel receives initial and ongoing training, the effectiveness of which shall be verified, covering in particular the theory and application of the concept of quality assurance and good manufacturing practice, and, where appropriate, the particular requirements for the manufacture of investigational medicinal products;

(g) the hygiene programmes adapted to the activities to be carried out shall be established and observed and such programmes shall, in particular include procedures relating to health, hygiene practice and clothing of personnel.

Premises and equipment.

9. (1) Premises and manufacturing equipment shall be located, designed, constructed, adapted and maintained to suit the intended operations.

(2) Premises and manufacturing equipment shall be laid out, designed and operated in such a way as to minimise the risk of error and to permit effective cleaning and maintenance in order to avoid contamination, cross contamination and, in general, any adverse effect on the quality of the product.

(3) Premises and equipment to be used for manufacturing operations, which are critical to the quality of the products, shall be subjected to appropriate qualification and validation.

Documentation.

10. (1) (a) It shall be the duty of the manufacturer to establish and maintain a documentation system based upon specifications, manufacturing formulae and processing and packaging instructions, procedures and records covering the various manufacturing operations performed.

(b) Documents shall be clear, free from error and kept up todate. Pre-established procedures for general manufacturing operations and conditions shall be kept available, together with specific documents for the manufacture of each batch. Such set of documents shall enable the history of the manufacture of each batch and the changes introduced during the development of an investigational medicinal product to be traced.

(2) (a) For a medicinal product, the batch documentation shall be retained for at least one year after the expiry date of the batches to which it relates or at least five years after the certification referred to in Manufacturing of Medicinal Products for Human Use Regulations.

(b) In the case of an investigational medicinal product, the batch documentation shall be retained for at least five years after the completion or formal discontinuation of the last clinical trial in which the batch was used. The sponsor or marketing authorisation holder, if different, shall be responsible for ensuring that records are retained as required for marketing authorisation in accordance with the Annex I to Directive 2001/83/EC, if required for a subsequent marketing authorisation.

(3). (a) When electronic, photographic or other data processing systems are used instead of written documents, the manufacturer shall first validate the systems by showing that the data will be appropriately stored during the anticipated period of storage.

(b) Data stored by those systems shall be made readily available in legible form and shall be provided to the competent authorities at their request.

(c) The electronically stored data shall be protected, by methods such as duplication or back-up and transfer on to another storage system, against loss or damage of data, and audit trails shall be maintained.

Production.

11. (1) (a) The different production operations shall be carried out in accordance with pre-established instructions and procedures and in accordance with good manufacturing practice.

(b) Adequate and sufficient resources shall be made available for the in-process controls.

(c) All process deviations and product defects shall be documented and thoroughly investigated.

(2) Appropriate technical or organisational measures shall be taken to avoid cross contamination and mix-ups. In the case of investigational medicinal products, particular attention shall be paid to the handling of products during and after any blinding operation.

(3) In the case of medicinal products, any new manufacture or important modification of a manufacturing process of a medicinal product shall be validated and the critical phases of manufacturing processes shall be regularly re-validated.

(4) In the case of investigational medicinal products, the manufacturing process shall be validated in its entirety in so far as is appropriate, taking into account the stage of product development. The critical process steps, such as sterilisation, shall be validated and all steps in the design and development of the manufacturing process shall be fully documented.

12. (1) (a) It shall be the duty of the manufacturer to establish and maintain a quality control system placed under the authority of a person who has the requisite qualifications and is independent of production. Quality control.

(b) Such person shall have at his disposal, or shall have access to, one or more quality control laboratories appropriately staffed and equipped to carry out the necessary examination and testing of the starting materials and packaging materials and the testing of intermediate and finished products.

(2) (a) In the case of medicinal products, including those imported from third countries, contract laboratories may be used if authorised in accordance with regulation 13 of these regulations.

(b) In the case of investigational medicinal products, the sponsor shall ensure that the contract laboratory complies with the content of the request referred to in the Clinical Trials Regulations, and accepted by the Authority:

Provided that when such products are imported from third countries, analytical control shall not be mandatory.

(3) During the final control of the finished product, before its release for sale or distribution or for use in clinical trials, the quality control system shall take into account, in addition to analytical results, any essential information such as the production conditions, the results of in-process controls, the examination of the manufacturing documents and the conformity of the product to its specifications, including the final finished pack.

(4) (a) In the case of a finished medicinal product, samples of each batch shall be retained for at least one year after the expiry date.

(b) In the case of an investigational medicinal product, sufficient samples of each batch of bulk formulated product and of key packaging components used for each finished product batch shall be retained for at least two years after completion or formal discontinuation of the last clinical trial in which the batch was used, whichever period is the longer.

(c) In the case of samples of starting materials, other than solvents, gases or water, used in the manufacturing process, such samples shall be retained for at least two years after the release of the product;

Provided that such period may be shortened if the period of stability of the material, as indicated in the relevant specification, is shorter.

(d) All such samples shall be maintained at the disposal of the competent authorities.

Work given out.

13. (1) Any manufacturing operation or operation linked thereto which is given out shall be the subject of a written agreement.

(2) The agreement shall clearly define the responsibilities of each party and shall define, in particular, the observance of good manufacturing practice to be followed and the manner in which the qualified person responsible for certifying each batch is to discharge his responsibilities.

(3) A party to the agreement shall not subcontract any of the work entrusted to him under the agreement without written authorisation from the other party.

(4) Such party shall comply with the principles and guidelines of good manufacturing practice and shall submit to inspections carried out by the competent authorities as provided by the Medicines Act, and by the Clinical Trials Regulations.

Complaints, product recall and emergency unblinding.

14. (1) The manufacturer shall, in the case of medicinal products:

(a) implement a system for recording and reviewing complaints together with an effective system for recalling, promptly and at any time, medicinal products in the distribution network;

(b) record and investigate any complaint concerning a defect;

(c) inform the competent authority of any defect that could result in a recall or abnormal restriction on supply and, in so far as is possible, indicate the countries of destination. Any recall shall be made in accordance with the requirements referred to in the Medicines Act;

(2) In the case of investigational medicinal products, the manufacturer shall:

(a) in cooperation with the sponsor, implement a system for recording and reviewing complaints together with an effective system for recalling promptly and at any time investigational medicinal products which have already entered the distribution network;

(b) record and investigate any complaint concerning a defect and shall inform the competent authority of any defect that could result in a recall or abnormal restriction on supply;

(c) identify all trial sites and, in so far as is possible, indicate the countries of destination.

(3) In the case of an investigational medicinal product for which a marketing authorisation has been issued, the manufacturer of the investigational medicinal product shall, in cooperation with the sponsor, inform the marketing authorisation holder of any defect that could be related to the authorised medicinal product.

(4) It shall be the duty of the sponsor to implement a procedure for the rapid unblinding of blinded products, where this is necessary for a prompt recall referred to in sub-regulation (2), and to ensure that such procedure discloses the identity of the blinded product only in so far as is necessary.

15. The manufacturer shall: Self-inspection.

(a) conduct repeated self-inspections as part of the quality assurance system in order to monitor the implementation and respect of good manufacturing practice and to propose any necessary corrective measures; and

(b) maintain records of such self-inspections and any corrective action subsequently taken.

Labelling.

16. In the case of an investigational medicinal product, labelling shall be such as to ensure protection of the subject and traceability, to enable identification of the product and trial , and to facilitate proper use of the investigational medicinal product.

Importation of Active Substances

17. Active substances shall only be imported if the following conditions are fulfilled:

(a) the active substances have been manufactured in accordance with standards of good manufacturing practice at least equivalent to those laid down by the European Union pursuant to the third paragraph of Article 47; and

(b) the active substances are accompanied by a written confirmation from the competent authority of the exporting third country of the following:

(i) the standards of good manufacturing practice applicable to the plant manufacturing the exported active substance are at least equivalent to those laid down by the European Union;

(ii) the manufacturing plant 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 European 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 European Union without any delay.

(c) This written confirmation shall be without prejudice to any other obligations set out in this Act and its subsidiary legislation.

The requirement set out in point (b) of this regulation shall not apply if the exporting country is included in the list published by the European Union Commission as referred to in Article 111b of Directive 2001/83/EC as amended.

(d) Exceptionally and where necessary to ensure the availability of medicinal products, when a plant manufacturing an active substance for export has been inspected by a European Union Member State and was found to comply with the principles and guidelines of good manufacturing practice as defined in these regulations, the requirement set out in point (b) of this regulation may be waived for a period not exceeding the validity of the certificate of Good Manufacturing Practice. When such waiver is used, this shall be communicated to the European Union Commission.

Offences and Penalties

18. Any breach to these regulations shall be liable to penalties under article 99(1b) of the Act.

19. The ‘Good Manufacturing Practise in Respect of Medicinal and Investigational Medicinal Products for Human Use Regulations, 2004’ are hereby being repealed.

Ministry of Health, the Elderly and Community Care

L.N. XXX of 2012

MEDICINES ACT
(CAP. 458)

Manufacture and Importation of Medicinal Products for Human Use Regulations (Amendment) Regulations, 2012

IN exercise of the powers conferred by article 106 of the Medicines Act, the Minister of Health, the Elderly and Community Care, after consultation with the Licensing Authority, has made the following regulations:-

Title and Scope

1. The title of these regulations is the Manufacture and Importation of Medicinal Products for Human Use Regulations (Amendment) Regulations, 2012 and they shall be read and construed as one with the Manufacture and Importation of Medicinal Products for Human Use Regulations, 2005 hereinafter referred to as "the principal regulations".

Amends regulation 2 of the principal regulations

2. Regulation 2 of the principal regulations shall be amended as follows:

(a) The definition of active substances shall be replaced by the following:

" "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."

Introduce a new sub-regulation in regulation 3 of the principal regulations

3. A new sub-regulation (6) is introduced after sub-regulation (5) in regulation 3 of the principal regulations as follows:

"(6) The Authority shall enter the information relating to the license referred to in subregulation (1) in the European Union database."

Introduces a new regulation in the principal regulations

4. A new regulation 3A is introduced after regulation 3 in the principal regulations as follows:

"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:

(i) name or corporate name and permanent address;

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

(iii) particulars regarding the premises and the technical equipment for their activity.

The persons referred to in sub regulation (1) above shall submit the registration form to the Licensing Authority at least 60 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 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 Licensing Authority has notified the applicant that he may commence the activity. If within 60 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) above 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 must be notified immediately.

(5) Persons referred to in sub regulation (1) above 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) of this Regulation in the 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."

Amends regulation 11 of the principal regulations.

5. A new sub regulation (3) to regulation 11 shall be added as follows:

"(3) The qualified person shall in the case of medicinal products intended to be placed on the market in the Union, ensure that the safety features referred to in paragraph (o) of regulation 3 in Legal Notice 393 of 2005 - MEDICINAL PRODUCTS (LABELLING AND PACKAGING) REGULATIONS - as amended, have been affixed on the packaging."

Amends regulation 7 of the principal regulations.

6. Regulation 7 of the principal regulations shall be amended as follows:

(a) new sub-regulations (3) and (4) shall be included as follows:

"(3) the safety features on medicinal products shall not be removed or covered, either fully or partially, unless the following conditions are fulfilled:

(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 authorisation holder should replace 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:

(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.

(4) Manufacturing Licence holders, including those performing the activities referred to in sub regulation (3) above, 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."

7. A new regulation 13 shall be introduced after regulation 12 in the principal regulations as follows:

"13. Offences and penalties

Any breaches of regulation:

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

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

(iii) 11 and 12 shall be regarded as an offence and shall be liable to penalties under article 99(1c) of the Act."

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Ministry of Health, the Elderly and Community Care

L.N. XXX of 2012

MEDICINES ACT, 2003 (ACT NO. III OF 2003)

Wholesale Distribution and Brokering of Medicinal Products and Active Substances Regulations, 2012

IN exercise of the powers conferred by article 106 of the Medicines Act, 2003, the Minister of Health, the Elderly and Community Care has made the following regulations:

Title and commencement.

1. (1) The title of these regulations is the Wholesale Distribution and Brokering of Medicinal Products and Active Substances Regulations, 2012.

(2) The scope of these regulations is to transpose Directive 2001/83/EC as amended by Directive 2011/62/EU.

Interpretation.

2. For the purposes of these regulations-

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

"applicant" includes a holder or licensee;

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

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

"responsible person" means a person registered as a pharmacist with the Pharmacy Council and recognised as suitable by the Medicines Authority since such person possesses adequate knowledge of the conditions required for the storage and distribution of medicinal products in order to avoid their deterioration or damage, has adequate knowledge of the regulations concerning the distribution of medicinal products, and has knowledge and understanding of good distribution practice.

Distribution of medicinal products.

3. (1) (a) Only products in respect of which a marketing authorisation has been granted by the Licensing Authority, hereinafter referred to as "the Authority", or the Agency shall be distributed or brokered in Malta.

(b) In the case of brokering, wholesale distribution and storage, medicinal products shall be covered by a marketing authorisation granted by the Agency or by the competent authority of a Member State;

Provided that in the case where medicinal products are stored but not distributed in Malta and in the case of wholesale distribution of medicinal products to third countries, only the licence laid down in regulation 4 hereof, shall be required.

(2) Any distributor, not being the marketing authorisation holder, who brings into Malta a product from another Member State, shall notify the marketing authorisation holder and the Authority of each product he intends to bring into Malta. In the case of products which have not been granted an authorisation pursuant to Regulation (EC) No 726/2004, the notification to the Authority shall be without prejudice to additional procedures provided for in the law at the time and to fees payable to the Authority for examining the notification ;

Provided that where the distributor intends to place the product on the market in Malta, he shall notify the Authority of each batch he brings into Malta.

(3) In the case of medicinal products which have been granted an authorisation pursuant to Regulation (EC) No 726/2004, the distributor shall submit the notification in accordance with sub regulation 2 of this regulation to the marketing authorisation holder and the European Medicines Agency. A fee shall be payable to the European Medicines Agency for checking that the conditions laid down in Union legislation on medicinal products and in the marketing authorisations are observed.

(4) Persons brokering medicinal products established in Malta shall have a permanent address and contact details, so as to ensure accurate identification, location, communication and supervision of their activities by the Licensing Authority.

4. No person shall engage in the wholesale distribution of medicinal products unless he is in possession of a wholesale dealer's licence, hereinafter referred to as "licence", to that effect.

5. (1) Distributors 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:

(i) name or corporate name and permanent address;

(ii) the active substances which are to be distributed;

(iii) particulars regarding the premises and the technical equipment for their activity.

The persons referred to in sub-regulation 1 shall submit the registration form to the Licensing Authority at least 60 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 60 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 60 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 paragraph 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 distributed must be notified immediately.

(5) Persons referred to in paragraph 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 paragraph 2 of this Regulation in the 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.

6. (1) The Licensing Authority, hereinafter referred to as "the Authority", may inspect any premises and check any person authorised to engage in the activity of wholesaler in medicinal products and of active substances, including active substances that are intended for export .

(2) If the Authority deems that any of the conditions of the licence issued by it has not been met, it shall suspend or revoke such licence.

(3) If a licence has been granted in another Member State and the Authority deems that the licensee is not fulfilling the conditions set therein, it shall inform the Commission and the Member State concerned.

7. (1) The Authority shall process an application for a wholesale dealer's licence within ninety days of receipt of the application. This period shall be suspended in those cases where the applicant is requested to furnish additional data.

(2) The application shall, apart from the particulars listed under article 55(1) of the Act, also include the pharmaceutical forms of the products to be distributed, in particular any sterile products and products requiring storage below 8 degrees Centigrade, and details of narcotic or psychotropic substances, blood, immunological medicinal products, or radiopharmaceuticals.

8. (1) A wholesale distribution licence shall only be granted if the Authority is satisfied that the applicant has at least -

(a) suitable and adequate premises, installations and equipment, so as to ensure proper conservation and distribution of the medicinal products;

(b) adequate staff, and in particular, a responsible person.

(2) A licence shall not be granted or renewed unless the applicant:

(a) makes the premises, installations and equipment accessible at all times for inspection;

(b) obtains the supplies of medicinal products from persons who are themselves in possession of a distribution licence, or who are exempt from obtaining such authorisation under the terms of regulation 3(4) of Subsidiary Legislation 458.36 and;
verifies that the medicinal products received are not falsified by checking the safety features on the outer packaging, in accordance with the requirements as may be adopted by the Commission:
Provided that the requirements of this paragraph shall not apply where a medicinal product is directly received from a third country but not imported, that is to say, not to be placed on any Member State market. However in such a case the wholesale distributor should exercise all necessary caution and precautions in order to ensure that these medicinal products not intended to be imported, remain in quarantine and do not in any way end up on any Member State market

(c) supplies medicinal products to persons who are themselves in possession of a wholesale distribution licence or who are otherwise authorised or entitled to supply medicinal products to the public:
Provided that in the case of distribution of medicinal products to third countries this shall not apply;

(d) has an emergency plan which ensures effective implementation of any recall of medicinal products from the market as ordered by the Authority or carried out in co-operation with the manufacturer or marketing authorization holder for the medicinal product concerned;

(e) must keeps records, either in the form of purchase/sales invoices, or on computer, or in any other form, available for inspection by the Authority, for a period of five years of any transaction in medicinal products received, dispatched or brokered, containing at least the following information;
(i) date;
(ii) name and pharmaceutical form of the medicinal product;
(iii) quantity received, supplied or brokered;
(iv) name and address of the supplier or consignee, as appropriate;
(v) batch number of the medicinal product
(f)complies with the principles and guidelines of good distribution practice for medicinal products as published by the Commission.

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

(h) immediately informs the Authority and, where applicable, the marketing authorisation holder, of medicinal products he receives or are offered which he identifies as falsified or suspect to be falsified.

(3) For the purposes of sub-regulation (2e) above, where the medicinal product is obtained from another wholesale distributor, the wholesale distribution authorisation holder must verify compliance with the principles and guidelines of good distribution practices by the supplying wholesale distributor. This includes verifying whether the supplying wholesale distributor holds a wholesale distribution authorisation.

Where the medicinal product is obtained from the manufacturer or importer, wholesale distribution authorisation holders must verify that the manufacturer or importer holds a manufacturing authorisation. Where the medicinal product is obtained through brokering, the wholesale distribution authorisation holder must verify that the broker involved fulfils the requirements set out in these regulations and in the Medicines Act.

(4) The requirements set out in paragraphs (a) and (d) to (h) of sub-regulation 2 shall apply *mutatis mutandis* to the brokering of medicinal products.

(5) The Authority shall enter the information relating to the licence referred to in sub-regulation (1) of this regulation, in the European Union database as may be established by the Commission. At the request of the Commission or any Member State, the Authority shall provide all appropriate information concerning the individual licences which were granted under sub-regulation (1) of this regulation.

9. (1) It shall be the duty of the wholesale dealer, when supplying medicinal products to a person authorised or entitled to supply them to the public, to enclose a document thereby making it possible to ascertain the date, name and pharmaceutical form of the medicinal product, quantity supplied, batch number of the medicinal products and the name and address of the supplier or consignee:
Provided that the requirements of the above shall also apply to the supply of medicinal products to persons in third countries authorised or entitled to supply medicinal products to the public.;

(2) In addition, the wholesale dealer shall, in respect of each product
he is distributing in Malta, furnish to the Authority an authenticated copy of the marketing authorization together with a letter of access issued by the marketing authorization holder granting the wholesale dealer the use of such marketing authorisation:

Provided that a wholesale dealer may only engage in the wholesale distribution of medicinal products in Malta in respect of which no such authenticated copy of a valid marketing authorization and letter of access has been forwarded to the Authority, if he is in possession of a parallel import licence issued in terms of the law.

(3) Every wholesale dealer shall, within the limits of his responsibilities, ensure that an appropriate and continuous supply of medicinal products is furnished to pharmacies and persons authorized to supply medicinal products in order to satisfy the needs of patients.

(4) It shall be the duty of wholesale distributors of active substances, including active substances that are intended for export, to comply with the current European Union good distribution practice for active substances.

10. It shall be the duty of the responsible person to:

(a) ensure that the licence conditions are adhered to;

(b) ensure that the conditions for storage of medicinal products are in accordance with the requirements of the marketing authorisation and labelling;

(c) monitor all areas used for storage and distribution;

(d) maintain records as required by these regulations;

(e) ensure that a quality system is maintained by the licensee in accordance with good distribution practice.

11. (1) The provisions of these regulations shall also apply to homeopathic medicinal products.

(2) Without prejudice to any of these regulations, the Licensing Authority 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 of the Union, from entering into circulation if there are sufficient grounds to suspect that those products are falsified. These measures shall include the application of these regulations to warehouses situated in free trade zones and customs bonded warehouses used to store medicinal products.

12. Offences and penalties

Any breaches of regulation:

(i) 3(1) and 4 shall be regarded as an offence and shall be liable to penalties under article 99(1a) of the Act;

(ii) 5 shall be regarded as an offence and shall be liable to penalties as prescribed under article 99(1b) of the Act;

(iii) 8, 9 and 10 shall be regarded as an offence and shall be liable to penalties as prescribed under article 99(1d) of the Act.

13. The Wholesale Distribution of Medicinal Products Regulations 2005 are hereby being repealed.