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COMMISSION DELEGATED REGULATION (EU) 2016/161

of 2 October 2015

supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use

(Text with EEA relevance)

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CHAPTER I

SUBJECT MATTER AND DEFINITIONS

Article 1

Subject matter

This Regulation lays down:

(a) the characteristics and technical specifications of the unique identifier that enables the authenticity of medicinal products to be verified and individual packs to be identified;

(b) the modalities for the verification of the safety features;

(c) the provisions on the establishment, management and accessibility of the repositories system where the information on the safety features shall be contained;

(d) the list of medicinal products and product categories subject to prescription which shall not bear the safety features;

(e) the list of medicinal products and product categories not subject to prescription which shall bear the safety features;

(f) the procedures for the notification to the Commission by national competent authorities of non-prescription medicinal products judged at risk of falsification and prescription medicinal products not deemed at risk of falsification in accordance with the criteria set out in Article 54a(2)(b) of Directive 2001/83/EC;

(g) the procedures for a rapid evaluation of and decision on the notifications referred to in point (f) of this Article.

Article 2

Scope

1. This Regulation applies to:

(a) medicinal products subject to prescription which shall bear safety features on their packaging pursuant to Article 54a(1) of Directive 2001/83/EC, unless included in the list set out in Annex I to this Regulation;

(b) medicinal products not subject to prescription included in the list set out in Annex II to this Regulation;

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(c) medicinal products to which Member States have extended the scope of application of the unique identifier or of the anti-tampering device in accordance with Article 54a(5) of Directive 2001/83/EC.

2. For the purposes of this Regulation, where reference is made to the packaging in a provision of this Regulation, the provision shall apply to outer packaging or to the immediate packaging if the medicinal product has no outer packaging.

Article 3

Definitions

1. For the purposes of this Regulation, the definitions in Article 1 of Directive 2001/83/EC shall apply.

2. The following definitions shall apply:

(a) ‘unique identifier’ means the safety feature enabling the verification of the authenticity and the identification of an individual pack of a medicinal product;

(b) ‘anti-tampering device’ means the safety feature allowing the verification of whether the packaging of a medicinal product has been tampered with;

(c) ‘decommissioning of a unique identifier’ means the operation changing the active status of a unique identifier stored in the repositories system referred to in Article 31 of this Regulation to a status impeding any further successful verification of the authenticity of that unique identifier;

(d) ‘active unique identifier’ means a unique identifier which has not been decommissioned or which is no longer decommissioned;

(e) ‘active status’ means the status of an active unique identifier stored in the repositories system referred to in Article 31;

(f) ‘healthcare institution’ means a hospital, in- or outpatient clinic or health centre.

CHAPTER II

TECHNICAL SPECIFICATIONS OF THE UNIQUE IDENTIFIER

Article 4

Composition of the unique identifier

The manufacturer shall place on the packaging of a medicinal product a unique identifier which complies with the following technical specifications:

(a) The unique identifier shall be a sequence of numeric or alphanumeric characters that is unique to a given pack of a medicinal product.

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(b) The unique identifier shall consist of the following data elements:

(i) a code allowing the identification of at least the name, the common name, the pharmaceutical form, the strength, the pack size and the pack type of the medicinal product bearing the unique identifier (‘product code’);

(ii) a numeric or alphanumeric sequence of maximum 20 characters, generated by a deterministic or a non-deterministic randomisation algorithm (‘serial number’);

(iii) a national reimbursement number or other national number identifying the medicinal product, if required by the Member State where the product is intended to be placed on the market;

(iv) the batch number;

(v) the expiry date.

(c) The probability that the serial number can be guessed shall be negligible and in any case lower than one in ten thousand.

(d) The character sequence resulting from the combination of the product code and the serial number shall be unique to a given pack of a medicinal product until at least one year after the expiry date of the pack or five years after the pack has been released for sale or distribution in accordance with Article 51(3) of Directive 2001/83/EC, whichever is the longer period.

(e) Where the national reimbursement number or other national number identifying the medicinal product is contained in the product code, it is not required to be repeated within the unique identifier.

Article 5

Carrier of the unique identifier

1. Manufacturers shall encode the unique identifier in a two-dimensional barcode.

2. The barcode shall be a machine-readable Data Matrix and have error detection and correction equivalent to or higher than those of the Data Matrix ECC200. Barcodes conforming to the International Organization for Standardisation/International Electrotechnical Commission standard (‘ISO/IEC’) 16022:2006 shall be presumed to fulfil the requirements set out in this paragraph.

3. Manufacturers shall print the barcode on the packaging on a smooth, uniform, low-reflecting surface.

4. When encoded in a Data Matrix, the structure of the unique identifier shall follow an internationally-recognised, standardised data syntax and semantics (‘coding scheme’) which allows the identification and accurate decoding of each data element of which the unique identifier is composed, using common scanning equipment. The coding scheme shall include data identifiers or application identifiers or other character sequences identifying the beginning and the end of the sequence of each individual data element of the unique identifier and defining the information contained in those data elements. Unique identifiers having a coding scheme conforming to ISO/IEC 15418:2009 shall be presumed to fulfil the requirements set out in this paragraph.

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5. When encoded in a Data Matrix as data element of a unique identifier, the product code shall follow a coding scheme and begin with characters specific to the coding scheme used. It shall also contain characters or character sequences identifying the product as a medicinal product. The resulting code shall be less than 50 characters and be globally unique. Product codes which conform to the ISO/IEC 15459-3:2014 and ISO/IEC 15459-4:2014 shall be presumed to fulfil the requirements set out in this paragraph.

6. Where necessary, different coding schemes may be used within the same unique identifier provided that the decoding of the unique identifier is not hindered. In that case, the unique identifier shall contain standardised characters permitting the identification of the beginning and the end of the unique identifier as well as the beginning and the end of each coding scheme. Where containing multiple coding schemes, unique identifiers which conform to ISO/IEC 15434:2006 shall be presumed to fulfil the requirements set out in this paragraph.

Article 6

Quality of the printing of the two-dimensional barcode

1. Manufacturers shall evaluate the quality of the printing of the Data Matrix by assessing at least the following Data Matrix parameters:

(a) the contrast between the light and dark parts;

(b) the uniformity of the reflectance of the light and dark parts;

(c) the axial non-uniformity;

(d) the grid non-uniformity;

(e) the unused error correction;

(f) the fixed pattern damage;

(g) the capacity of the reference decode algorithm to decode the Data Matrix.

2. Manufacturers shall identify the minimum quality of the printing which ensures the accurate readability of the Data Matrix throughout the supply chain until at least one year after the expiry date of the pack or five years after the pack has been released for sale or distribution in accordance with Article 51(3) of Directive 2001/83/EC, whichever is the longer period.

3. When printing the Data Matrix, manufacturers shall not use a quality of the printing lower than the minimum quality referred to in paragraph 2.

4. A quality of printing rated at least 1,5 in accordance with ISO/IEC 15415:2011 shall be presumed to fulfil the requirements set out in this Article.

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Article 7

Human-readable format

1. Manufacturers shall print the following data elements of the unique identifier on the packaging in human-readable format:

(a) the product code;

(b) the serial number;

(c) the national reimbursement number or other national number identifying the medicinal product, if required by the Member State where the product is intended to be placed on the market and not printed elsewhere on the packaging.

2. Paragraph 1 shall not apply where the sum of the two longest dimensions of the packaging equals or is less than 10 centimetres.

3. Where the dimensions of the packaging allow it, the human-readable data elements shall be adjacent to the two-dimensional barcode carrying the unique identifier.

Article 8

Additional information in the two-dimensional barcode

Manufacturers may include information other than the unique identifier in the two-dimensional barcode carrying the unique identifier, where permitted by the competent authority in accordance with Title V of Directive 2001/83/EC.

Article 9

Barcodes on the packaging

Medicinal products having to bear the safety features pursuant to Article 54a of Directive 2001/83/EC shall not bear on their packaging, for the purpose of their identification and verification of their authenticity, any other visible two-dimensional barcode than the two-dimensional barcode carrying the unique identifier.

CHAPTER III

GENERAL PROVISIONS ON THE VERIFICATION OF THE SAFETY FEATURES

Article 10

Verification of the safety features

When verifying the safety features, manufacturers, wholesalers and persons authorised or entitled to supply medicinal products to the public shall verify the following:

(a) the authenticity of the unique identifier;

(b) the integrity of the anti-tampering device.

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Article 11

Verification of the authenticity of the unique identifier

When verifying the authenticity of a unique identifier, manufacturers, wholesalers and persons authorised or entitled to supply medicinal products to the public shall check the unique identifier against the unique identifiers stored in the repositories system referred to in Article 31. A unique identifier shall be considered authentic when the repositories system contains an active unique identifier with the product code and serial number that are identical to those of the unique identifier being verified.

Article 12

Unique identifiers which have been decommissioned

A medicinal product bearing a unique identifier which has been decommissioned shall not be further distributed or supplied to the public except in any of the following situations:

(a) the unique identifier was decommissioned in accordance with Article 22(a) and the medicinal product is distributed for the purpose of exporting it outside the Union;

(b) the unique identifier was decommissioned earlier than the time of supplying the medicinal product to the public, pursuant to Articles 23, 26, 28 or 41;

(c) the unique identifier was decommissioned in accordance with Article 22(b) or (c) or Article 40, and the medicinal product is provided to the person responsible for its disposal;

(d) the unique identifier was decommissioned in accordance with Article 22(d) and the medicinal product is provided to the national competent authorities.

Article 13

Reversing the status of a decommissioned unique identifier

1. Manufacturers, wholesalers and persons authorised or entitled to supply medicinal products to the public may only revert the status of a decommissioned unique identifier to an active status if the following conditions are fulfilled:

(a) the person performing the reverting operation is covered by the same authorisation or entitlement and operates in the same premises as the person that decommissioned the unique identifier;

(b) the reverting of the status takes place not more than 10 days after the unique identifier was decommissioned;

(c) the pack of medicinal product has not expired;

(d) the pack of medicinal product has not been registered in the repositories system as recalled, withdrawn, intended for destruction or stolen and the person performing the reverting operation does not have knowledge that the pack is stolen;

(e) the medicinal product has not been supplied to the public.

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2. Medicinal products bearing a unique identifier which cannot be reverted to an active status because the conditions set out in paragraph 1 are not fulfilled shall not be returned to saleable stock.

CHAPTER IV

MODALITIES OF VERIFICATION OF THE SAFETY FEATURES AND DECOMMISSIONING OF THE UNIQUE IDENTIFIER BY MANUFACTURERS

Article 14

Verification of the two-dimensional barcode

The manufacturer placing the safety features shall verify that the two-dimensional barcode carrying the unique identifier complies with Articles 5 and 6, is readable and contains the correct information.

Article 15

Record keeping

The manufacturer placing the safety features shall keep records of every operation he performs with or on the unique identifier on a pack of medicinal product for at least one year after the expiry date of the pack or five years after the pack has been released for sale or distribution in accordance with Article 51(3) of Directive 2001/83/EC, whichever is the longer period, and shall provide those records to competent authorities on request.

Article 16

Verifications to be performed before removing or replacing the safety features

1. Before removing or covering, either fully or partially, the safety features in accordance with Article 47a of Directive 2001/83/EC, the manufacturer shall verify the following:

(a) the integrity of the anti-tampering device;

(b) the authenticity of the unique identifier and decommission it if replaced.

2. Manufacturers holding both a manufacturing authorisation according to Article 40 of Directive 2001/83/EC and an authorisation to manufacture or import investigational medicinal products to the Union as referred to in Article 61 of Regulation (EU) No 536/2014 of the European Parliament and of the Council [1] shall verify the safety features and decommission the unique identifier on a pack of medicinal product before repackaging or re-labelling it for the purpose of using it as authorised investigational medicinal product or authorised auxiliary medicinal product.

[1] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (OJ L 158, 27.5.2014, p. 1).

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Article 17

Equivalent unique identifier

When placing an equivalent unique identifier for the purposes of complying with Article 47a(1)(b) of Directive 2001/83/EC, the manufacturer shall verify that the structure and composition of the unique identifier placed on the packaging complies, with regard to the product code and the national reimbursement number or other national number identifying the medicinal product, with the requirements of the Member State where the medicinal product is intended to be placed on the market, so that that unique identifier can be verified for authenticity and decommissioned.

Article 18

Actions to be taken by manufacturers in case of tampering or suspected falsification

Where a manufacturer has reason to believe that the packaging of the medicinal product has been tampered with, or the verification of the safety features shows that the product may not be authentic, the manufacturer shall not release the product for sale or distribution and shall immediately inform the relevant competent authorities.

Article 19

Provisions applicable to a manufacturer distributing his products by wholesale

Where a manufacturer distributes his products by wholesale, Article 20(a), and Articles 22, 23 and 24 shall apply to him in addition to Articles 14 to 18.

CHAPTER V

MODALITIES OF VERIFICATION OF THE SAFETY FEATURES AND DECOMMISSIONING OF THE UNIQUE IDENTIFIER BY WHOLESALERS

Article 20

Verification of the authenticity of the unique identifier by wholesalers

A wholesaler shall verify the authenticity of the unique identifier of at least the following medicinal products in his physical possession:

(a) medicinal products returned to him by persons authorised or entitled to supply medicinal products to the public or by another wholesaler;

(b) medicinal products he receives from a wholesaler who is neither the manufacturer nor the wholesaler holding the marketing authorisation nor a wholesaler who is designated by the marketing authorisation holder, by means of a written contract, to store and distribute the products covered by his marketing authorisation on his behalf.

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Article 21

Derogations from Article 20(b)

Verification of the authenticity of the unique identifier of a medicinal product is not required under Article 20(b) in any of the following situations:

(a) that medicinal product changes ownership but remains in the physical possession of the same wholesaler;

(b) that medicinal product is distributed within the territory of a Member State between two warehouses belonging to the same wholesaler or the same legal entity, and no sale takes place.

Article 22

Decommissioning of unique identifiers by wholesalers

A wholesaler shall verify the authenticity of and decommission the unique identifier of the following medicinal products:

(a) products which he intends to distribute outside of the Union;

(b) products which have been returned to him by persons authorised or entitled to supply medicinal products to the public or another wholesaler and cannot be returned to saleable stock;

(c) products which are intended for destruction;

(d) products which, while in his physical possession, are requested as a sample by competent authorities;

(e) products which he intends to distribute to the persons or institutions referred to in Article 23, where required by national legislation in accordance with the same Article.

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By way of derogation from point (a), from 1 January 2021 to 31 December 2021 the obligation to decommission the unique identifier of medicinal products which the wholesaler intends to distribute outside of the Union shall not apply to products which he intends to distribute in the United Kingdom ([1]).

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Article 23

Provisions to accommodate specific characteristics of Member States' supply chains

Member States may require, where necessary to accommodate the particular characteristics of the supply chain on their territory, that a wholesaler verifies the safety features and decommissions the unique identifier of a medicinal product before he supplies that medicinal product to any of the following persons or institutions:

([1]) In accordance with the Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community, and in particular Article 5(4) of the Protocol on Ireland/Northern Ireland in conjunction with Annex 2 to that Protocol, for the purposes of this Article, references to the United Kingdom do not include Northern Ireland.

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(a) persons authorised or entitled to supply medicinal products to the public who do not operate within a healthcare institution or within a pharmacy;

(b) veterinarians and retailers of veterinary medicinal products;

(c) dental practitioners;

(d) optometrists and opticians;

(e) paramedics and emergency medical practitioners;

(f) armed forces, police and other governmental institutions maintaining stocks of medicinal products for the purposes of civil protection and disaster control;

(g) universities and other higher education establishments using medicinal products for the purposes of research and education, with the exceptions of healthcare institutions;

(h) prisons;

(i) schools;

(j) hospices;

(k) nursing homes.

Article 24

Actions to be taken by wholesalers in case of tampering or suspected falsification

A wholesaler shall not supply or export a medicinal product where he has reason to believe that its packaging has been tampered with, or where the verification of the safety features of the medicinal product indicates that the product may not be authentic. He shall immediately inform the relevant competent authorities.

CHAPTER VI

MODALITIES OF VERIFICATION OF THE SAFETY FEATURES AND DECOMMISSIONING OF THE UNIQUE IDENTIFIER BY PERSONS AUTHORISED OR ENTITLED TO SUPPLY MEDICINAL PRODUCTS TO THE PUBLIC

Article 25

Obligations of persons authorised or entitled to supply medicinal products to the public

1. Persons authorised or entitled to supply medicinal products to the public shall verify the safety features and decommission the unique identifier of any medicinal product bearing the safety features they supply to the public at the time of supplying it to the public.

2. Notwithstanding paragraph 1, persons authorised or entitled to supply medicinal products to the public operating within a healthcare institution may carry out that verification and decommissioning at any time the medicinal product is in the physical possession of the healthcare institution, provided that no sale of the medicinal product takes place between the delivery of the product to the healthcare institution and the supplying of it to the public.

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3. In order to verify the authenticity of the unique identifier of a medicinal product and decommission that unique identifier, persons authorised or entitled to supply medicinal products to the public shall connect to the repositories system referred to in Article 31 through the national or supranational repository serving the territory of the Member State in which they are authorised or entitled.

4. They shall also verify the safety features and decommission the unique identifier of the following medicinal products bearing the safety features:

(a) medicinal products in their physical possession that cannot be returned to wholesalers or manufacturers;

(b) medicinal products that, while in their physical possession, are requested as samples by competent authorities, in accordance with national legislation;

(c) medicinal products which they supply for subsequent use as authorised investigational medicinal products or authorised auxiliary medicinal products as defined in Articles 2(2)(9) and (10) of Regulation (EU) No 536/2014.

Article 26

Derogations from Article 25

1. Persons authorised or entitled to supply medicinal products to the public are exempted from the obligation to verify the safety features and decommission the unique identifier of medicinal products provided to them as free samples in accordance with Article 96 of Directive 2001/83/EC.

2. Persons authorised or entitled to supply medicinal products to the public who do not operate within a healthcare institution or within a pharmacy are exempted from the obligation to verify the safety features and decommission the unique identifier of medicinal products where that obligation has been placed on wholesalers by national legislation in accordance with Article 23.

3. Notwithstanding Article 25, Member States may decide, where necessary to accommodate the particular characteristics of the supply chain on their territory, to exempt a person authorised or entitled to supply medicinal products to the public operating within a healthcare institution from the obligations of verification and decommissioning of the unique identifier, provided that the following conditions are met:

(a) the person authorised or entitled to supply medicinal products to the public obtains the medicinal product bearing the unique identifier through a wholesaler belonging to the same legal entity as the healthcare institution;

(b) the verification and decommissioning of the unique identifier is performed by the wholesaler that supplies the product to the healthcare institution;

(c) no sale of the medicinal product takes place between the wholesaler supplying the product and that healthcare institution;

(d) the medicinal product is supplied to the public within that healthcare institution.

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Article 27

Obligations when applying the derogations

Where the verification of the authenticity and decommissioning of the unique identifier is carried out earlier than referred to in Article 25(1), pursuant to Articles 23 or 26, the integrity of the anti-tampering device shall be verified at the time the medicinal product is supplied to the public.

Article 28

Obligations when supplying only part of a pack

Notwithstanding Article 25(1), where persons authorised or entitled to supply medicinal products to the public supply only part of a pack of a medicinal product the unique identifier of which is not decommissioned, they shall verify the safety features and decommission that unique identifier when the pack is opened for the first time.

Article 29

Obligations in case of inability to verify the authenticity and decommission the unique identifier

Notwithstanding Article 25(1), where technical problems prevent persons authorised or entitled to supply medicinal products to the public from verifying the authenticity of and decommissioning a unique identifier at the time the medicinal product bearing that unique identifier is supplied to the public, those persons authorised or entitled to supply medicinal products to the public shall record the unique identifier and, as soon as the technical problems are solved, verify the authenticity of and decommission the unique identifier.

Article 30

Actions to be taken by persons authorised or entitled to supply medicinal products to the public in case of suspected falsification

Where persons authorised or entitled to supply medicinal products to the public have reason to believe that the packaging of the medicinal product has been tampered with, or the verification of the safety features of the medicinal product indicates that the product may not be authentic, those persons authorised or entitled to supply medicinal products to the public shall not supply the product and shall immediately inform the relevant competent authorities.

CHAPTER VII

ESTABLISHMENT, MANAGEMENT AND ACCESSIBILITY OF THE REPOSITORIES SYSTEM

Article 31

Establishment of the repositories system

1. The repositories system where the information on the safety features shall be contained, pursuant to Article 54a(2)(e) of Directive 2001/83/EC, shall be set up and managed by a non-profit legal entity or

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non-profit legal entities established in the Union by manufacturers and marketing authorisation holders of medicinal products bearing the safety features.

2. In setting up the repositories system, the legal entity or entities referred to in paragraph 1 shall consult at least wholesalers, persons authorised or entitled to supply medicinal products to the public and relevant national competent authorities.

3. Wholesalers and persons authorised or entitled to supply medicinal products to the public are entitled to participate in the legal entity or entities referred to in paragraph 1, on a voluntary basis, at no cost.

4. The legal entity or entities referred to on paragraph 1 shall not require manufacturers, marketing authorisation holders, wholesalers or persons authorised or entitled to supply medicinal products to the public to be members of a specific organisation or organisations in order to use the repository system.

5. The costs of the repositories system shall be borne by the manufacturers of medicinal products bearing the safety features, in accordance with Article 54a(2)(e) of Directive 2001/83/EC.

Article 32

Structure of the repositories system

1. The repositories system shall be composed of the following electronic repositories:

(a) a central information and data router (‘hub’);

(b) repositories which serve the territory of one Member State (‘national repositories’) or the territory of multiple Member States (‘supranational repositories’). Those repositories shall be connected to the hub.

2. The number of national and supranational repositories shall be sufficient to ensure that the territory of every Member State is served by one national or supranational repository.

3. The repositories system shall comprise the necessary information technology infrastructure, hardware and software to enable the execution of the following tasks:

(a) upload, collate, process, modify and store the information on the safety features that enables the verification of the authenticity and identification of medicinal products;

(b) identify an individual pack of a medicinal product bearing the safety features and verify the authenticity of the unique identifier on that pack and decommission it at any point of the legal supply chain.

4. The repositories system shall include the application programming interfaces allowing wholesalers or persons authorised or entitled to supply medicinal products to the public to query the repositories system by means of software, for the purposes of verifying the authenticity of the unique identifiers and of decommissioning them in the repositories system. The application programming interfaces shall also allow national competent authorities to access the repositories system by means of software, in accordance with Article 39.

The repositories system shall also include graphical user interfaces providing direct access to the repositories system in accordance with Article 35(1)(i).

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The repositories system shall not include the physical scanning equipment used for reading the unique identifier.

Article 33

Uploading of information in the repositories system

1. The marketing authorisation holder or, in case of parallel imported or parallel distributed medicinal products bearing an equivalent unique identifier for the purposes of complying with Article 47a of Directive 2001/83/EC, the person responsible for placing those medicinal products on the market, shall ensure that the information referred to in paragraph 2 is uploaded to the repositories system before the medicinal product is released for sale or distribution by the manufacturer, and that it is kept up to date thereafter.

The information shall be stored in all national or supranational repositories serving the territory of the Member State or Member States where the medicinal product bearing the unique identifier is intended to be placed on the market. The information referred to in paragraphs 2(a) to (d) of this Article, with the exception of the serial number, shall also be stored in the hub.

2. For a medicinal product bearing a unique identifier, at least the following information shall be uploaded to the repositories system:

(a) the data elements of the unique identifier in accordance with Article 4(b);

(b) the coding scheme of the product code;

(c) the name and the common name of the medicinal product, the pharmaceutical form, the strength, the pack type and the pack size of the medicinal product, in accordance with the terminology referred to in Article 25(1)(b) and (e) to (g) of the Commission Implementing Regulation (EU) No 520/2012 ([1]);

(d) the Member State or Member States where the medicinal product is intended to be placed on the market;

(e) where applicable, the code identifying the entry corresponding to the medicinal product bearing the unique identifier in the database referred to in Article 57(1)(l) of Regulation (EC) No 726/2004 of the European Parliament and the Council ([2]);

(f) the name and address of the manufacturer placing the safety features;

(g) the name and address of the marketing authorisation holder;

(h) a list of wholesalers who are designated by the marketing authorisation holder, by means of a written contract, to store and distribute the products covered by his marketing authorisation on his behalf.

3. The information referred to in paragraph 2 shall be uploaded to the repositories system either through the hub or through a national or supranational repository.

([1]) Commission Implementing Regulation (EU) No 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council (OJ L 159, 20.6.2012, p. 5).

([2]) Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1).

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Where the upload is performed through the hub, the hub shall store a copy of the information referred to in paragraph 2(a) to (d), with the exception of the serial number, and transfer the complete information to all national or supranational repositories serving the territory of the Member State or Member States where the medicinal product bearing the unique identifier is intended to be placed on the market.

Where the upload is performed through a national or supranational repository, that repository shall immediately transfer to the hub a copy of the information referred to in paragraph 2(a) to (d), with the exception of the serial number, using the data format and data exchange specifications defined by the hub.

4. The information referred to in paragraph 2 shall be stored in the repositories where it was originally uploaded for at least one year after the expiry date of the medicinal product or five years after the product has been released for sale or distribution in accordance with Article 51(3) of Directive 2001/83/EC, whichever is the longer period.

Article 34

Functioning of the hub

1. Each national or supranational repository composing the repositories system shall exchange data with the hub using the data format and data exchange modalities defined by the hub.

2. When the authenticity of the unique identifier cannot be verified because a national or supranational repository does not contain a unique identifier with the product code and serial number that are identical to those of the unique identifier being verified, the national or supranational repository shall transfer the query to the hub in order to verify whether that unique identifier is stored elsewhere in the repositories system.

When the hub receives the query, the hub shall identify, on the basis of the information contained therein, all national or supranational repositories serving the territory of the Member State or Member States where the medicinal product bearing the unique identifier was intended to be placed on the market, and shall transfer the query to those repositories.

The hub shall subsequently transfer the reply of those repositories to the repository which initiated the query.

3. Where notified by a national or supranational repository of the change of status of a unique identifier, the hub shall ensure the synchronisation of that status between those national or supranational repositories serving the territory of the Member State or Member States where the medicinal product bearing the unique identifier was intended to be placed on the market.

4. When it receives the information referred to in Article 35(4), the hub shall ensure the electronic linking of the batch numbers before and after the repackaging or re-labelling operations with the set of unique identifiers decommissioned and with the set of equivalent unique identifiers placed.

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Article 35

Characteristics of the repositories system

1. Each repository in the repositories system shall satisfy all of the following conditions:

(a) it shall be physically located in the Union;

(b) it shall be set up and managed by a non-profit legal entity established in the Union by manufacturers and marketing authorisation holders of medicinal products bearing the safety features and, where they have chosen to participate, wholesalers and persons authorised or entitled to supply medicinal products to the public;

(c) it shall be fully interoperable with the other repositories composing the repositories system; for the purposes of this Chapter, interoperability means the full functional integration of, and electronic data exchange between repositories regardless of the service provider used;

(d) it shall allow the reliable electronic identification and authentication of individual packs of medicinal products by manufacturers, wholesalers and persons authorised or entitled to supply medicinal products to the public, in accordance with the requirements of this Regulation;

(e) it shall have application programming interfaces able to transfer and exchange data with the software used by wholesalers, persons authorised or entitled to supply medicinal products to the public and, where applicable, national competent authorities;

(f) when wholesalers and persons authorised or entitled to supply medicinal products to the public query the repository for the purposes of verification of authenticity and decommissioning of a unique identifier, the response time of the repository, not considering the speed of the internet connection, shall be lower than 300 milliseconds in at least 95 % of queries. The repository performance shall allow wholesalers and persons authorised or entitled to supply medicinal products to the public to operate without significant delay;

(g) it shall maintain a complete record (‘audit trail’) of all operations concerning a unique identifier, of the users performing those operations and the nature of the operations; the audit trail shall be created when the unique identifier is uploaded to the repository and be maintained until at least one year after the expiry date of the medicinal product bearing the unique identifier or five years after the product has been released for sale or distribution in accordance with Article 51(3) of Directive 2001/83/EC, whichever is the longer period;

(h) in accordance with Article 38, its structure shall be such as to guarantee the protection of personal data and information of a commercially confidential nature and the ownership and confidentiality of the data generated when manufacturers, marketing authorisation holders, wholesalers and persons authorised or entitled to supply medicinal products to the public interact with it;

(i) it shall include graphical user interfaces providing direct access to it to the following users verified in accordance with Article 37(b):

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(i) wholesalers and persons authorised or entitled to supply medicinal products to the public, for the purposes of verifying the authenticity of the unique identifier and decommissioning it in case of failure of their own software;

(ii) national competent authorities, for the purposes referred to in Article 39;

2. Where the status of a unique identifier on a medicinal product intended to be placed on the market in more than one Member State changes in a national or supranational repository, that repository shall immediately notify the change of status to the hub, except in case of decommissioning by marketing authorisation holders in accordance with Articles 40 or 41.

3. National or supranational repositories shall not allow the upload or storage of a unique identifier containing the same product code and serial number as another unique identifier already stored therein.

4. For each batch of repackaged or relabelled packs of a medicinal product on which equivalent unique identifiers were placed for the purposes of complying with Article 47a of Directive 2001/83/EC, the person responsible for placing the medicinal product on the market shall inform the hub of the batch number or numbers of the packs which are to be repackaged or relabelled and of the unique identifiers on those packs. He shall additionally inform the hub of the batch number of the batch resulting from the repackaging or re-labelling operations and the equivalent unique identifiers in that batch.

Article 36

Operations of the repositories system

The repositories system shall provide for at least the following operations:

(a) the repeated verification of the authenticity of an active unique identifier in accordance with Article 11;

(b) the triggering of an alert in the system and in the terminal where the verification of the authenticity of a unique identifier is taking place when such verification fails to confirm that the unique identifier is authentic in accordance with Article 11. Such an event shall be flagged in the system as a potential incident of falsification except where the product is indicated in the system as recalled, withdrawn or intended for destruction;

(c) the decommissioning of a unique identifier in accordance with the requirements of this Regulation;

(d) the combined operations of identification of a pack of a medicinal product bearing a unique identifier and verification of the authenticity and decommissioning of that unique identifier;

(e) the identification of a pack of a medicinal product bearing a unique identifier and the verification of the authenticity and the decommissioning of that unique identifier in a Member State which is not the Member State where the medicinal product bearing that unique identifier was placed on the market;

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(f) the reading of the information contained in the two-dimensional barcode encoding the unique identifier, the identification of the medicinal product carrying the barcode and the verification of the status of the unique identifier, without triggering the alert referred to in point (b) of this Article;

(g) without prejudice to Article 35(1)(h), the access by verified wholesalers to the list of wholesalers referred to in Article 33(2)(h) for the purposes of determining whether they have to verify the unique identifier of a given medicinal product.

(h) the verification of the authenticity of a unique identifier and its decommissioning by manually querying the system with the data elements of the unique identifier;

(i) the immediate provision of information concerning a given unique identifier to the national competent authorities and the European Medicines Agency, upon request;

(j) the creation of reports that allow competent authorities to verify compliance of individual marketing authorisation holders, manufacturers, wholesalers and persons authorised or entitled to supply medicinal products to the public with the requirements of this Regulation or to investigate potential incidents of falsification;

(k) the reverting of the status of a unique identifier from decommissioned to active, subject to the conditions referred to in Article 13;

(l) the indication that a unique identifier has been decommissioned;

(m) the indication that a medicinal product has been recalled, withdrawn, stolen, exported, requested as a sample by national competent authorities, indicated as a free sample by the marketing authorisation holder, or is intended for destruction;

(n) the linking, by batches of medicinal products, of the information on unique identifiers removed or covered to the information on the equivalent unique identifiers placed on those medicinal products for the purposes of complying with Article 47a of Directive 2001/83/EC.

(o) the synchronisation of the status of a unique identifier between the national or supranational repositories serving the territory of the Member States where that medicinal product is intended to be placed on the market.

Article 37

Obligations of legal entities establishing and managing a repository which is part of the repositories system

Any legal entity establishing and managing a repository which is part of the repositories system shall perform the following actions:

(a) inform the relevant national competent authorities of its intention to physically locate the repository or part of it in their territory and notify them once the repository becomes operational;

(b) put in place security procedures ensuring that only users whose identity, role and legitimacy has been verified can access the repository or upload the information referred to in Article 33(2);

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(c) continuously monitor the repository for events alerting to potential incidents of falsification in accordance to Article 36(b);

(d) provide for the immediate investigation of all potential incidents of falsification flagged in the system in accordance with Article 36(b) and for the alerting of national competent authorities, the European Medicines Agency and the Commission should the falsification be confirmed;

(e) carry out regular audits of the repository to verify compliance with the requirements of this Regulation. Audits shall take place at least annually for the first five years after this Regulation becomes applicable in the Member State where the repository is physically located, and at least every three years thereafter. The outcome of those audits shall be provided to competent authorities upon request;

(f) make the audit trail referred to in Article 35(1)(g) immediately available to competent authorities upon their request;

(g) make the reports referred to in Article 36(j) available to competent authorities upon their request.

Article 38

Data protection and data ownership

1. Manufacturers, marketing authorisation holders, wholesalers and persons authorised or entitled to supply medicinal products to the public shall be responsible for any data generated when they interact with the repositories system and stored in the audit trail. They shall only have ownership of and access to those data, with the exception of the information referred to in Article 33(2) and the information on the status of a unique identifier.

2. The legal entity managing the repository where the audit trail is stored shall not access the audit trail and the data contained therein without the written agreement of the legitimate data owners except for the purpose of investigating potential incidents of falsification flagged in the system in accordance with Article 36(b).

Article 39

Access by national competent authorities

A legal entity establishing and managing a repository used to verify the authenticity of or decommission the unique identifiers of medicinal products placed on the market in a Member State shall grant access to that repository and to the information contained therein, to competent authorities of that Member State for the following purposes:

(a) supervising the functioning of the repositories and investigating potential incidents of falsification;

(b) reimbursement;

(c) pharmacovigilance or pharmacoepidemiology.

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CHAPTER VIII

OBLIGATIONS OF MARKETING AUTHORISATION HOLDERS, PARALLEL IMPORTERS AND PARALLEL DISTRIBUTORS

Article 40

Products recalled, withdrawn or stolen

The marketing authorisation holder or, in case of parallel imported or parallel distributed medicinal products bearing an equivalent unique identifier for the purposes of complying with Article 47a of Directive 2001/83/EC, the person responsible for placing those medicinal products on the market shall promptly take all the following measures:

(a) ensure the decommissioning of the unique identifier of a medicinal product which is to be recalled or withdrawn, in every national or supranational repository serving the territory of the Member State or Member States in which the recall or the withdrawal is to take place;

(b) ensure the decommissioning of the unique identifier, where known, of a medicinal product which has been stolen, in every national or supranational repository in which information on that product is stored;

(c) indicate in the repositories referred to in points (a) and (b) that that product has been recalled or withdrawn or stolen, where applicable.

Article 41

Products to be supplied as free samples

The marketing authorisation holder intending to supply any of his medicinal products as a free sample in accordance with Article 96 of Directive 2001/83/EC shall, where that product bears the safety features, indicate it as a free sample in the repositories system and ensure the decommissioning of its unique identifier before providing it to the persons qualified to prescribe it.

Article 42

Removal of unique identifiers from the repositories system

The marketing authorisation holder or, in case of parallel imported or parallel distributed medicinal products bearing an equivalent unique identifier for the purposes of complying with Article 47a of Directive 2001/83/EC, the person responsible for placing those medicinal products on the market shall not upload unique identifiers in the repositories system before having removed from therein, where present, older unique identifiers containing the same product code and serial number as the unique identifiers being uploaded.

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CHAPTER IX

OBLIGATIONS OF THE NATIONAL COMPETENT AUTHORITIES

Article 43

Information to be provided by national competent authorities

National competent authorities shall make the following information available to the marketing authorisation holders, manufacturers, wholesalers and persons authorised or entitled to supply medicinal products to the public, upon their request:

(a) the medicinal products placed on the market on their territory which shall bear the safety features in accordance with Article 54(o) of Directive 2001/83/EC and this Regulation;

(b) the medicinal products subject to prescription or subject to reimbursement for which the scope of the unique identifier is extended for the purposes of reimbursement or pharmacovigilance, in accordance with Article 54a(5) of Directive 2001/83/EC;

(c) the medicinal products for which the scope of the anti-tampering device is extended for the purpose of patient safety, in accordance with Article 54a(5) of Directive 2001/83/EC.

Article 44

Supervision of the repositories system

1. National competent authorities shall supervise the functioning of any repository physically located in their territory, in order to verify, if necessary by means of inspections, that the repository and the legal entity responsible for the establishment and management of the repository comply with the requirements of this Regulation.

2. A national competent authority may delegate any of its obligations under this Article to the competent authority of another Member State or to a third party, by means of a written agreement.

3. Where a repository not physically located in the territory of a Member State is used for the purpose of verifying the authenticity of medicinal products placed on the market in that Member State, the competent authority of that Member State may observe an inspection of the repository or perform an independent inspection, subject to the agreement of the Member State in which the repository is physically located.

4. A national competent authority shall communicate reports of supervision activities to the European Medicines Agency, which shall make them available to the other national competent authorities and the Commission.

5. National competent authorities may contribute to the management of any repository used to identify medicinal products and verify the authenticity of or decommission the unique identifiers of medicinal products placed on the market in the territory of their Member State.

National competent authorities may participate to the management board of the legal entities managing those repositories to the extent of up to one third of the members of the board.

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CHAPTER X

LISTS OF DEROGATIONS AND NOTIFICATIONS TO THE COMMISSION

Article 45

Lists of derogations from bearing or not bearing the safety features

1. The list of medicinal products or product categories subject to prescription which shall not bear the safety features are set out in Annex I to this Regulation.

2. The list of medicinal products or product categories not subject to prescription which shall bear the safety features are set out in Annex II to this Regulation.

Article 46

Notifications to the Commission

1. National competent authorities shall notify the Commission of non-prescription medicinal products which they judge to be at risk of falsification as soon as they become aware of such risk. For that purpose, they shall use the form set out in Annex III to this Regulation.

2. National competent authorities may inform the Commission of medicinal products which they deem not to be at risk of falsification. For that purpose, they shall use the form set out in Annex IV to this Regulation.

3. For the purposes of the notifications referred to in paragraphs 1 and 2, national competent authorities shall conduct an assessment of the risks of and arising from falsification of such products taking into account the criteria listed in Article 54a(2)(b) of Directive 2001/83/EC.

4. When submitting to the Commission the notification referred to in paragraph 1, national competent authorities shall provide the Commission with evidence and documentation supporting the presence of incidents of falsification.

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Article 47

Evaluation of the notifications

Where, following a notification as referred to in Article 46, the Commission or a Member State considers, on the basis of casualties or hospitalisations of persons in the Union due to exposure to falsified medicinal products, that rapid action is required to protect public health, the Commission shall assess the notification without delay and at the latest within 45 days.

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CHAPTER XI

TRANSITIONAL MEASURES AND ENTRY INTO FORCE

Article 48

Transitional measures

Medicinal products that have been released for sale or distribution without the safety features in a Member State before the date in which this Regulation becomes applicable in that Member State, and are not repackaged or relabelled thereafter, may be placed on the market, distributed and supplied to the public in that Member State until their expiry date.

Article 49

Application in Member States with existing systems for the verification of the authenticity of medicinal products and for the identification of individual pack*s*

1. Each of the Member States referred to in Article 2, paragraph 2, second subparagraph, point (b), second sentence, of Directive 2011/62/EU shall notify the Commission of the date from which Articles 1 to 48 of this Regulation apply in its territory in accordance with the third subparagraph of Article 50. The notification shall take place at the latest 6 months before that application.

2. The Commission shall publish a notice of each of the dates notified to it in accordance with paragraph 1 in the *Official Journal of the European Union*.

Article 50

Entry into force

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 9 February 2019.

However, the Member States referred to in Article 2, paragraph 2, second subparagraph, point (b), second sentence, of Directive 2011/62/EU shall apply Articles 1 to 48 of this Regulation at the latest from 9 February 2025.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

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ANNEX I

List of medicinal products or product categories subject to prescription that shall not bear the safety features, referred to in Article 45(1)

Name of active substance or product category	Pharmaceutical form	Strength	Remarks
Homeopathic medicinal products	Any	Any	
Radionuclide generators	Any	Any	
Kits	Any	Any	
Radionuclide precursors	Any	Any	
Advanced therapy medicinal products which contain or consist of tissues or cells	Any	Any	
Medicinal gases	Medicinal gas	Any	
Solutions for parenteral nutrition having an anatomical therapeutical chemical (‘ATC’) code beginning with B05BA	Solution for infusion	Any	
Solutions affecting the electrolyte balance having an ATC code beginning with B05BB	Solution for infusion	Any	
Solutions producing osmotic diuresis having an ATC code beginning with B05BC	Solution for infusion	Any	
Intravenous solution additives having an ATC code beginning with B05X	Any	Any	
Solvents and diluting agents, including irrigating solutions, having an ATC code beginning with V07AB	Any	Any	
Contrast media having an ATC code beginning with V08	Any	Any	
Tests for allergic diseases having an ATC code beginning with V04CL	Any	Any	
Allergen extracts having an ATC code beginning with V01AA	Any	Any	
▼M2 Cicatrizants with ATC code D03AX	Fly larvae		

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ANNEX II

List of medicinal products or product categories not subject to prescription that shall bear the safety features, referred to in Article 45(2)

Name of active substance or product category	Pharmaceutical form	Strength	Remarks
omeprazole	gastro-resistant capsule, hard	20 mg	
omeprazole	gastro-resistant capsule, hard	40 mg	

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ANNEX III

Notification to the European Commission of medicinal products not subject to prescription judged to be at risk of falsification, pursuant to article 54a(4) of Directive 2001/83/EC

Member State:	Name of competent authority:

Entry No	Active substance (Common Name)	Pharmaceutical form	Strength	Anatomical Therapeutical Chemical (ATC) Code	Supporting Evidence (please provide evidence of one or more incidents of falsification in the legal supply chain and specify the source of the information).
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					

Note: The number of entries is not binding.

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ANNEX IV

Notification to the European Commission of medicinal products judged not to be at risk of falsification, pursuant to article 54a(4) of Directive 2001/83/EC

Member State:	Name of competent authority:

Entry No	Active substance (Common Name)	Pharmaceutical form	Strength	Anatomical Therapeutical Chemical (ATC) Code	Comments/Complementary information
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					

Note: The number of entries is not binding.