EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – Quality, safety and efficacy

PHARM 633

PHARMACEUTICAL COMMITTEE
23 October 2013

Subject: **Implementation of the 'Falsified Medicines Directive' 2011/62/EU**
Transposition
Notifications under Article 117a
Delegated act on GMP for API
Guidelines on GDP for API and risk assessment for GMP for excipients

Agenda item 3c

1. BACKGROUND

The 'Falsified Medicines Directive' 2011/62/EU has been adopted in June 2011 and published on 1 July 2011.

It had to be transposed by Member States by 2 January 2013 and applied as of this date. However, the application date is extended for the rules on
- importation of active substances (application date 2 July 2013);
- rules in relation to Article 85c of Directive 2001/83/EC (application date one year after publication of the implementing act); and
- rules in relation to the safety feature (unique identifier and anti-tampering device) (application date three years after publication of the delegated act).

2. TRANSPOSITION BY MEMBER STATES

Some Member States have still not notified the transposing national laws to the Commission, according to Article 2(1) of Directive 2011/62/EU.

Commission européenne/Europese Commissie, 1049 Bruxelles/Brussel, BELGIQUE/BELGIË - Tel. +32 22991111
Office: DM24 - Tel. direct line +32 229-67543 - Fax +32 229-98046
Sanco-pharmaceuticals-d6@ec.europa.eu

This is a violation of EU law. The Commission has launched infringement procedures against the Member States not complying with Article 2(1) of Directive 2011/62/EU, and will step up measures where necessary.

3. NOTIFICATION BY MEMBER STATES IN ACCORDANCE OF ARTICLE 117A OF DIRECTIVE 2001/83/EC

Article 117a of Directive 2001/83/EC obliged Member States to notify the Commission, by 22 July 2013, of the details of their respective national systems for the receipt and handling of notifications of suspected falsified medicinal products, suspected quality defects of medicinal products, recalls of medicinal products by marketing authorisation holders, and withdrawals of medicinal products from the market.

The Commission has received only 4 notifications.

Member States not having notified are requested to comply with the requirement of the Directive.

4. APPLICATION BY MEMBER STATES

In the context of the actual application, Member States have requested the Commission to clarify some aspects.

The documents "PHARM 602 and PHARM 623, submitted for the meeting of the Pharmaceutical committee on 28 March 2012 and 27 March 2013, respectively, list in their Annexes some "questions and answers" as regards the application of various aspects of Directive 2011/62/EU.

Annex 1 to this document gives additional answers put forward in response to questions raised by Member States.

Do Member States have other questions they would want to raise as regards the application of the Directive 2011/62/EU?

5. IMPLEMENTATION MEASURES BY THE COMMISSION

Directive 2011/62/EU contains no less than 14 implementation measures (delegated acts, implementing acts, guidelines, reports) to be taken by the Commission.

Update from the Commission on the preparatory work on the common logo for online pharmacies.

Annex 2 contains the overview of these implementation measures, together with a state of play.

6. IMPLEMENTATION MEASURES BY THE EUROPEAN MEDICINES AGENCY

Annex 3 contains the overview of the implementation measures to be taken by the European Medicines Agency (EMA), together with a state of play.

7. CORRECTION OF GDP GUIDELINES OF 7 MARCH 2013

A new version of the guidelines on good distribution practice (GDP) will be adopted to correct mistakes in chapters 5.5 and 6.3, as well as to incorporate in the body of the guidelines important information such as the rationale for the revision and the date of coming into operation. This information was present in the text submitted for consultation to the Pharmaceutical Committee on 10 October 2012, but was omitted from the published Guidelines.

Mistakes in several linguistic versions will also be corrected.

Annex 4 contains the text of the corrected GDP Guidelines, with changes tracked to highlight differences compared to the previous version.

Annex 1: Questions relating to application of Directive 2011/62/EU

1. Question: Should registration of manufacturers, importers and distributors of active substances take place with the competent national authority of the Member State in which the site carrying out the registered activities is established.

   Answer: Yes.

2. Question: Does the registrant have a permanent or legally registered address in the Member State in which the registered activities are carried out?

   Answer: Yes.

Annex 2: Implementation measures of the Commission in the context of Directive 2011/62/EU – overview and state of play

	Article in Directive 2001/83/EC	Type of Commission measure	Topic	Target date for adoption/ publication	State of play Involvement of Member States/experts from Member States, Other comments
1.	47	**Delegated act**	**Good manufacturing practice for active substances**	2013	Public stakeholder consultation closed. Member States expert group consulted twice.[1] Act in preparation.
2.	52b	**Delegated act**	**Criteria to be considered and verifications to be made** when assessing the potential falsified character of **medicinal products introduced into the EU** but not intended to be placed on the market		Public stakeholder consultation closed. Member States expert group consulted once. Following consultation by Commission with stakeholders and Member States, adoption is not going to be pursued for the time being (NB: adoption is not mandatory - "may provision").
3.	111b	**Implementing act**	Implementing measure on the **requirements for the assessment of a third country in terms of API manufacturing**	2013	Adopted and published (OJ L 21, 24.1.2013, p. 36): http://ec.europa.eu/health/files/eudralex/vol-1/dec_2013_51/dec_2013_51_en.pdf
4.	111b	**Decisions ('Autonomous Decisions')** (at the request of a third country)	Inclusion of a **third country on a list**	Ongoing	Adopted and published (OJ L 325, 23.11.2012, p. 15): http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:325:0015:0016:EN:PDF Finalised and ongoing assessments: http://ec.europa.eu/health/human-use/quality/index_en.htm#ias
5.	47	**Guidelines**	Principles of **good distribution practices for active substances**	2013	Public consultation closed. Analysis of replies ongoing. Strong collaboration with Good Distribution and Manufacturing Practices

1 http://ec.europa.eu/transparency/regexpert/index.cfm?do=groupDetail.groupDetail&groupID=2752

2 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000161.jsp&mid=WC0b01ac05800296c9&jsenabled=true

Commission européenne/Europese Commissie, 1049 Bruxelles/Brussel, BELGIQUE/BELGIË - Tel. +32 22991111
Office: DM24 - Tel. direct line +32 229-67543 - Fax +32 229-98046
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	Article in Directive 2001/83/EC	Type of Commission measure	Topic	Target date for adoption/ publication	State of play Involvement of Member States/experts from Member States, Other comments
					Inspector's Working Group[2] (GMDP IWG).
6.	47	**Guideline**	Formalised risk assessment for verification of the appropriate **good manufacturing practice for excipients**	2013	Public consultation closed. Analysis of replies ongoing. Strong collaboration with GMDP IWG.
7.	85b	**Guideline**	Specific provisions for **brokering** in the **guidelines** on good distribution practices	2013	Adopted and published (OJ C68, 8.3.2013, p. 1): http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2013:068:0001:0014:EN:PDF A new version of the guidelines will be adopted to correct mistakes in chapters 5.5 and 6.3, as well as to incorporate in the body of the guidelines important information such as the rationale for the revision and the date of coming into operation . Mistakes in several linguistic versions will also be corrected.
8.	111a	**Guideline**	**Principles for inspections**	-	GMDP IWG.
9.	54a(4) of Directive 2001/83/EC and Article 2b of Directive 2011/62/EU	**Delegated act**	(a) the **characteristics and technical specifications** of the safety features (SF) (b) the **lists** of **prescription medicines that should not bear** the SF and the list of **non-prescription medicines that should bear the SF** (c) **procedures for the notification** of medicinal products at risk of falsification and **a rapid system for evaluation** and decision on these notifications (d) the **modalities of verifications** of the SF by the manufacturers, wholesalers, pharmacists (e) provisions on the **establishment, management**	2014	Public stakeholder consultation closed . Member States Expert group.[3] Impact assessment ongoing

[3] http://ec.europa.eu/transparency/regexpert/detailGroup.cfm?groupID=2719

	Article in Directive 2001/83/EC	Type of Commission measure	Topic	Target date for adoption/ publication	State of play Involvement of Member States/experts from Member States, Other comments
			and accessibility of the repositories system		
10	85c(2)	**Implementing act**	**Design of the common logo for legally-operating online-websites, including the technical, electronic, cryptographic requirements**	End 2013, beginning 2014	Public stakeholder consultation closed. Vote in Standing Committee.
11	85d	**Awareness raising**	Conducting or promoting information campaigns on the dangers of falsified medicinal products	Continuously ongoing	In cooperation with the European Medicines Agency and Member States http://ec.europa.eu/health/human-use/videos/index_en.htm
12	118a	Report to the Council and the European Parliament	Overview of transposition measures on the rules on **penalties** applicable to infringements of the national provisions adopted pursuant to the Directive	By 2 January 2018	-
13	3 of Directive 2011/62/EU	Report to the Council and the European Parliament	Trends of falsifications	See Article 3 of Directive 2011/62/EU.	-
14	121a	Report	In respect of the delegated powers conferred to the Commission	By June 2015.	Covers all delegated powers given in Directive 2001/83/EC.

Annex 3: Deliverables EMA – Overview and state of play

Topic	Relevant provision in Directive 2001/83/EC	Output	State of play, Comments
EU database for API, distributors, GMDP certificates, non-compliance	111(6),(7), 52a(7), 77(4), 40(4); 111a, 2nd paragraph.	Extension of existing EudraGMP database	A common format for 5 new documents connected to the new content of the database has been agreed and published as part of the Compilation of Community Procedures in May 2012. http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004706.pdf The extension of the database to accommodate new information required by the FMD (GDP certificates, Wholesale authorisations and active substance manufacturers, importers and distributor registration) was launched in April 2013 (on-line version) and May 2013 (XML version). Member States have started to populate these new modules.
MS to share information with EMA on inspections.	111(1), 2nd sentence		Information on conducted GMP inspections is already shared through EudraGMP. The database now extends this to GDP inspections. For planned GMP inspections see below.
MS and EMA to cooperate in the coordination of inspections in third countries	111(1), 3rd sentence	Planning module for EudraGMP application	Planning module launched in December 2012 provides a tool for this purpose. Over 80 planned inspections have been uploaded by Member States to date. In addition, an inspection programme in cooperation with MS in the context of Article 46b(4) of Directive 2001/83/EC has been ongoing from July 2013.
Online information on legislation on falsified medicines	85c(5)	Amendments on the website of the Agency	Some information on falsified medicines is already on the Agency's website (http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp&mid=WC0b01ac058002d4e8). Work is underway to expand this section. In addition, work in cooperation with the European Commission and Member States has started, in order to create the new EMA webpages requested by the FMD as regards on-line sales of medicines.

Annex 4: Correction of GDP Guidelines of 7 March 2013
Guidelines on Good Distribution Practice of Medicinal Products for Human Use (draft)
(The pdf is in the list of ducuments of the 71th meeting.)

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