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COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 10.12.2008
COM(2008) 668 final

2008/0261 (COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending Directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source

{SEC(2008) 2674}

{SEC(2008) 2675}

EXPLANATORY MEMORANDUM

1. BACKGROUND TO THE PROPOSAL

There is an alarming increase in the EU of medicinal products which are falsified in relation to their identity, history or source. These products are from the point of view of EU pharmaceutical legislation illegal insofar as they do not comply with the Community rules for medicinal products. Therefore, in the context of this proposal for an amendment of the pharmaceutical legislation these products shall be referred to as “falsified medicinal products”.

Falsified medicinal products may contain sub-standard or falsified ingredients, or no ingredients or ingredients in the wrong dosage, including active ingredients. They pose a major threat to European patients and European industry and there are strong concerns in the public and amongst policy makers about the steady increase of these products detected in the EU in the last years.

The potential threat to public health is also recognised by the World Health Organisation (WHO), who set up the International Medical Products Anti-Counterfeiting Taskforce ("IMPACT"). IMPACT developed, with active participation of the Community, Principles and Elements for National Legislation against Counterfeit Medical Products, which were endorsed by the IMPACT General Meeting in Lisbon on 12 December 2007. The efforts of IMPACT have been welcomed in the summit declaration of the Group of Eight (G8) on 7 June 2008.

To this adds that the risk profile has changed. The number of falsifications of innovative and life-saving medicines is increasing. Moreover, in order to increase volume, these products are channelled through the lawful supply chain towards the patient. In this way, in 2007, many thousand packs of falsified life-saving drugs have reached patients in the EU.

While there is uncertainty as to the precise number of cases today or in the future, there is a clear trend visible which threatens the high level of protection of public health in the EU. This trend can have disastrous consequences for the trust of the public in the industry and in the policy maker – well comparable to the “food-and-feed crisis” of the 1990’s.

The underlying causes for falsified medicinal products remaining undetected in the lawful supply chain are manifold, but can be reduced to four aspects:

- Falsified medicinal products can not 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 allegedly not being placed on the market; and

- Already the active pharmaceutical ingredients (“API”) entering the manufacturing process may be a falsification of the original API.

The existing provisions of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use¹ are in some respects insufficient to address these concrete causes. In view of the time span between the proposal of changes to Directive 2001/83/EC and their effective implementation, there is a clear need for the Commission to act now.

2. PUBLIC CONSULTATION

In preparation of the impact assessment for this proposal, the Commission had held, from 11 March 2008 to 9 May 2008 a public consultation on “Key ideas for better protection of patients against the risk of counterfeit medicines”. In response to this consultation, the Commission received 128 contributions from stakeholders. Of these, 103 were from industry (pharmaceutical industry, distributors, suppliers of active ingredients, consultants), 15 from citizens, patient (groups), and academics, and 10 from health professionals, pharmacists and health insurers.

Of the 128 stakeholder contributions, in terms of regions, 20 contributions were received from EU-wide associations, 30 from Italy, 14 from the UK, 9 from Germany, 4 each from France and Switzerland, 3 each from Poland and Ireland and the Netherlands, 2 each from Malta, and Denmark, 1 each from Austria, Sweden and Spain, and 18 from non-European third countries. 13 stakeholder contributions were global associations or could not be attributed in terms of region.

30 national and regional authorities profited from this stakeholder-consultation to inform the Commission of their views on the matter.

The respondents unanimously welcomed the initiative stressing that urgent and decisive action was needed, and that the problem of falsified medicinal products is increasing exponentially. Moreover, the “multi-layer” approach by the Commission, based on an identification of the various possible points of entry for falsified medicines was welcomed. A summary of the responses has been published on the Commission website².

3. IMPACT ASSESSMENT

The Commission conducted an impact assessment in accordance with the Commission impact assessment guidelines and published the results in an impact assessment report.

The impact assessment report identifies and assesses policy options to achieve the objective, which is defined as eliminating, by all practical means, the risk of falsified medicines entering the legal supply chain.

¹ OJ L 311, 28.11.2001, p. 67.

² http://ec.europa.eu/enterprise/pharmaceuticals/counterf_par_trade/counterfeit_key.htm

The assessment of the policy options is made against a baseline of “non-action”. For this baseline, various scenarios of the future development of falsified medicines for the period until 2020 have been developed. While these scenarios (and related costs) are by their very nature estimations based on best use of existing data (which is in itself limited), they reveal that societal direct and indirect costs of non action could reach, depending on the scenario, between 9.5bn EUR and 116bn EUR until 2020.

These costs of non-action compare against the costs of the chosen policy options. These costs are estimated to be, until 2020, as follows:

- For manufacturers and importers of medicinal products: between 6.8bn EUR and 11bn EUR, depending on the safety technique chosen. The costs for distributors who remove/exchange safety features depend on the extent of their activity. Moreover, depending on the chosen approach, pharmacies are going to bear costs of approx. 157m EUR.
- For wholesale distributors of medicinal products: approx. 280m EUR;
- For wholesale distributors who engage only in export activity: approx. 403m EUR;
- For other traders situated in the distribution chain: approx. 5m EUR;
- For manufacturers of API: approx. 320m EUR. The bulk of these costs is going to fall upon 3rd country manufacturers.

4. LEGAL BASIS AND SUBSIDIARITY

The aim of Directive 2001/83/EC, as well as this proposed amendment, is to establish the functioning of the internal market for medicinal products while ensuring a high level of protection of public health in the EU. The legal basis is thus Article 95 of the Treaty.

To the extent that Directive 2001/83/EC establishes exhaustive rules, Member States are not allowed to “add to” these rules. Moreover, the aim to combat falsified medicinal products 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.

5. AMENDMENTS

In order to address the risk of falsified medicinal products entering the legal supply chain, the Commission proposes a number of amendments to Directive 2001/83/EC. These include:

- Certain obligations for other players than wholesale distributors, who act in the distribution chain. These actors are typically involved in the transactions without actually handling the products (for example, by auctioning or brokering products, cf. Article 1(14) of the proposed amending Directive).

- A legal basis for the Commission to render obligatory specific safety-features (such as a serialisation number or a seal) on the packaging of prescription-medicines (Article 1(8) of the proposed amending Directive).
- A prohibition in principle of manipulating (i.e. removing, tampering with, or over-labelling) safety features on the packaging by actors situated “in-between” the original manufacturer and the last actor in the distribution chain (typically the pharmacist) or end user (doctor/patient).
- Obligatory audits of supplying wholesale distributors of medicinal products in order to ensure reliability of business partners (Article 1(13) of the proposed amending Directive).
- Strengthened requirements for imports of API from third countries if it could not be established that the regulatory framework in the respective third country ensures a sufficient level of protection of human health for products exported to the EU (Article 1(4) of the proposed amending Directive).
- Audits of manufacturers of API (Article 1(3)(a) of the proposed amending Directive).
- Strengthened rules for inspections including increased transparency of inspection results through publication in the EudraGMP database managed by the EMEA (Article 1(15) of the proposed amending Directive).

With regards to the impact on economic operators, the Commission, when choosing the policy options, took care to

- keep any increase of costs for compliance (incl. administrative costs) to the minimum necessary to achieve the aim;
- allow, where possible, for flexibility so that the regulatory framework can be adapted to a changing risk-profile; and
- spread the responsibility amongst *all* actors, i.e. not just the pharmaceutical industry as such but also wholesalers, API-suppliers and importers.

A detailed discussion of the proposed amendments, including an assessment of their socio-economic impact, is contained in the impact assessment report.

6. CONSISTENCY WITH OTHER COMMUNITY POLICIES

The proposal is part of the Community strategy for safe, innovative and accessible medicines, as presented by the Commission in its Communication to the Council, the European Parliament and the European Economic and Social Committee: “Safe, innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector”³. The proposal is also in line with the Commission’s strategic objective to

³ COM(2008) .

protect citizens from health threats as set out in the Commission White Paper “Together for Health: A strategic approach for the EU 2008-2013”.⁴

7. BUDGETARY IMPLICATION

It is proposed to extend the Community-database of GMP⁵-compliant companies to GDP⁶-compliant wholesale distributors (cf. above, point 5, 7th bullet). As set out in the legislative financial statement annexed to the proposal, these IT-related measures are not expected to have budgetary implications.

8. ADDITIONAL INFORMATION

The proposal concerns an EEA matter and therefore extends to the European Economic Area.

⁴ COM(2007) 630 .

⁵ **Good Manufacturing Practices.**

⁶ **Good Distribution Practices.**

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amending Directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission⁷,

Having regard to the opinion of the European Economic and Social Committee⁸,

Having regard to the opinion of the Committee of the Regions⁹,

Acting in accordance with the procedure laid down in Article 251 of the Treaty¹⁰,

Whereas:

- (1) Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use¹¹ lays down the rules for *inter alia* manufacturing, importation, placing on the market, and wholesale distribution of medicinal products in the Community as well as rules relating to active pharmaceutical ingredients used as starting materials.
- (2) There is an alarming increase of medicinal products detected in the Community which are falsified in relation to their identity, history or source. These products usually contain sub-standard or falsified ingredients, or no ingredients or ingredients in the wrong dosage, including active ingredients, thus posing an important threat to public health.
- (3) Past experience shows that such medicinal products are not only marketed through illegal supply chains, but reach the patient via the legal supply chain as well. This poses a particular threat to human health and may lead to a lack of trust of the patient

⁷ OJ C [...], [...], p. [...].

⁸ OJ C [...], [...], p. [...].

⁹ OJ C [...], [...], p. [...].

¹⁰ OJ C [...], [...], p. [...].

¹¹ OJ L 311, 28.11.2001, p. 67.

in the legal supply chain. The rules contained in Directive 2001/83/EC should be amended in order to respond to this increasing threat.

- (4) The potential threat to public health is also recognised by the World Health Organisation (WHO), who set up the International Medical Products Anti-Counterfeiting Taskforce ("IMPACT"). IMPACT developed, with the active participation of the Community, Principles and Elements for National Legislation against Counterfeit Medical Products, which were endorsed by the IMPACT General Meeting in Lisbon on 12 December 2007.
- (5) Today's distribution network for medicinal products is increasingly complex and involves many players which are not necessarily wholesale distributors as defined in Directive 2001/83/EC. In order to ensure reliability in the distribution chain, pharmaceutical legislation should address all actors in the distribution chain: this includes not only distributors who procure, hold, store and supply products, but also persons who are involved in transactions without handling the products. They should be submitted to proportionate rules in order to exclude, by all practical means, the possibility that medicinal products which are falsified in relation to their identity, history or source to enter the legal supply chain in the Community.
- (6) Directive 2001/83/EC applies also to wholesale distributors which do not place medicinal products on the market but export them. The rules applicable to those wholesale distributors – which apply no matter whether the exported product is intended to be imported, i.e. placed on the market or merely introduced without being imported - should be clarified.
- (7) In order to take account of new risk profiles, while at the same time ensuring the functioning of the internal market for medicinal products, safety features designed to ensure the identification, authentication and traceability of prescription medicinal products should be established at Community level. When introducing obligatory safety features for prescription medicinal products, due account should be taken of the particularities of certain products or categories of products, such as generic medicines. This includes the risk of falsifications in view of their price and past incidences in the Community and abroad, as well as the consequences of falsifications for public health in view of the specific characteristics of the products concerned or of the severity of the conditions intended to be treated.
- (8) Any actor in the supply chain who packages medicinal products has to be a holder of a manufacturing authorization. In order for the safety features to be effective, the manufacturing authorization holder should only be permitted to remove, replace or cover these features under strict conditions.
- (9) These manufacturing authorisation holders should be held strictly liable for damages to patients caused by products placed by them on the market which are falsified in relation to their identity.
- (10) In order to increase reliability in the distribution chain, wholesale distributors should verify, either by themselves or through a body accredited for that purpose, that their suppliers comply with good distribution practices.

- (11) To ensure transparency, a list of those wholesale distributors whose compliance with applicable Community rules has been established after inspection by a competent authority of a Member State, should be published in a Community database.
- (12) Falsified active pharmaceutical ingredients pose the risk of sub-standard active pharmaceutical ingredients. This risk should be addressed. In particular, manufacturers of medicinal products should ensure either by themselves or through a body accredited for that purpose that the supplying manufacturer of active pharmaceutical ingredients complies with good manufacturing practices.
- (13) The manufacture of active pharmaceutical ingredients should be subject to good manufacturing practices irrespective of whether those ingredients were manufactured in the Community or imported. With regard to the manufacture of active pharmaceutical ingredients in third countries, it should be ensured that the rules for the manufacture of active pharmaceutical ingredients intended for export to the Community, including inspection and enforcement, provide for a level of protection of public health equivalent to that provided for by Community legislation.
- (14) In order to facilitate enforcement and control of Community rules relating to active substances used as starting material, the manufacturers or importers of those substances should notify their activity.
- (15) To ensure a similar level of protection of human health throughout the Community, and to avoid distortions in the internal market, the harmonised principles and guidelines for inspections of holders of manufacturing and wholesaler authorisations of medicinal products as well as manufacturers of active substances should be strengthened. This should also help to ensure the functioning of existing mutual recognition agreements which rely on efficient and comparable inspection and enforcement throughout the Community.
- (16) The measures necessary for the implementation of this Directive should be adopted in accordance with Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred by the Commission¹².
- (17) In particular the Commission should be empowered to adopt measures regarding safety features that shall appear on the packaging of medicinal products subject to medical prescription and to adopt detailed rules for medicinal products introduced without being placed on the market. Since those measures are of general scope and are designed to amend non-essential elements by supplementing it, they must be adopted in accordance with the regulatory procedure with scrutiny provided for in Article 5a of Decision 1999/468/EC.
- (18) Since the objective of ensuring the functioning of the internal market for medicinal products, while ensuring a high level of protection of public health against medicinal products which are illegal in view of a falsified identity, history or source, cannot be sufficiently achieved by the Member States, as they cannot adopt individually harmonised measures applicable in the Community and can be better achieved by action at Community level, the Community may adopt measures, in accordance with

¹² OJ L 184, 17.7.1999, p. 23.

the principle of subsidiarity as set out in Article 5 of the Treaty. In accordance with the principle of proportionality, as set out in that Article, this Directive does not go beyond what is necessary in order to achieve that objective.

(19) Directive 2001/83/EC should therefore be amended accordingly,

HAVE ADOPTED THIS DIRECTIVE:

Article 1

Directive 2001/83/EC is amended as follows:

1) In Article 1, the following point 17a is inserted after point 17:

‘17a. Trading of medicinal products:

All activities consisting of negotiating independently on behalf of another person the sale or the purchase of medicinal products, or billing or brokering medicinal products, apart from supplying medicinal products to the public, and not falling under the definition of wholesale distribution.’

2) In Article 2, paragraph 3 is replaced by the following:

‘(3) Notwithstanding paragraph 1 and Article 3(4), Title IV of this Directive shall apply to medicinal products intended only for export and to intermediate products and active substances used as starting materials.’

3) Article 46 is amended as follows:

(a) The first subparagraph of point (f) is replaced by the following:

‘(f) to comply with the principles and guidelines of good manufacturing practice for medicinal products and to use as starting materials only active substances, which have been manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials. To this end, the holder of the manufacturing authorization shall verify compliance of the active substances manufacturer with good manufacturing practices by himself or through a body accredited for this purpose by the competent authority of a Member State.’

(b) The following point (g) is added:

‘(g) to inform the competent authority of products he gets knowledge of which are or which are suspected to be falsified in relation to the identity, history or source of products manufactured by him.’

4) The following Article 46b is inserted after Article 46a:

‘Article 46b

(1) Member States shall take appropriate measures to ensure that the manufacture on their territory of active substances used as starting material, including active

substances that are intended for export, complies with good manufacturing practices for active substances.

(2) Active substances used as starting material shall only be imported if:

- (a) they have been manufactured by applying standards of good manufacturing practice at least equivalent to those laid down by the Community; and
- (b) they are accompanied by a written confirmation from the exporting third country that 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 Community, and that the plant is subject to control and enforcement ensuring that those good manufacturing practices cannot be circumvented.

(3) The requirement set out in point (b) of paragraph 2 shall not apply if the exporting country is listed in accordance with Article 111b.'

5) In Article 47, the third paragraph is replaced by the following:

'The principles of good manufacturing practice for active substances used as starting materials referred to in point (f) of Article 46 and in Article 46b shall be adopted in the form of detailed guidelines.'

6) In Article 51, paragraph 1, the following point (c) is added after point (b):

'(c) in the case of products intended to be placed on the market in the Community, that the safety features referred to in point (o) of Article 54 have been affixed on the packaging.'

7) The following Articles 52a and 52b are inserted after Article 52:

Article 52a

Importers and manufacturers of active substances used as starting materials established in the Community shall notify their address to the competent authority of the Member State where they are established.

Article 52b

(1) Notwithstanding Article 2(1), and without prejudice to Title VII, Member States shall ensure that medicinal products not intended to be placed on the market are not introduced into the Community if there are reasons to believe that the products claim a falsified identity, history or source.

(2) The Commission shall adopt the necessary measures for the implementation of paragraph 1. Those measures, designed to amend non-essential elements of this Directive by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 121(2a).'

8) In Article 54, the following point (o) is added:

‘(o) safety features making it possible to ascertain identification, authenticity and traceability of medicinal products, other than radiopharmaceuticals, subject to medical prescription as defined in Title VI.’

9) The following Article 54a is added:

‘Article 54a

(1) The safety features referred to in point (o) of Article 54 shall allow wholesale distributors or pharmacists or persons authorised or entitled to supply medicinal products to the public to perform all of the following:

- (a) verify authenticity by assessing overt, covert, or forensic devices;
- (b) identify individual packs;
- (c) verify whether the outer packaging has been tampered with.

(2) The safety features referred to in point (o) of Article 54 shall not be partly or fully removed or covered-up, unless the following conditions are fulfilled:

- (a) The manufacturing authorisation holder verifies, prior to partly or fully removing or covering-up the safety feature, the authenticity of the product;
- (b) The manufacturing authorisation holder complies with point (o) of Article 54 by replacing the safety feature with a safety feature which is equivalent as regards the possibility to ascertain identification, authenticity and uninterrupted traceability of the medicinal product, and without opening the immediate packaging as defined in Article 1(23);
- (c) The replacement of the safety feature is subject to supervision by the competent authority.

(3) Manufacturing authorisation holders shall be liable for damages in accordance with Council Directive 85/374/EEC caused by medicinal products which are falsified in terms of their identity.

(4) The Commission shall adopt the measures necessary for the implementation of point (o) of Article 54 and of paragraphs (1) and (2) of this Article.

Those measures, designed to amend non-essential elements of this Directive by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 121(2a)

When adopting those measures, the Commission shall consider the risk related to products or categories of products and at least all of the following:

- (a) the price and sales volume of the product;

- (b) the number of incidences of falsifications in third countries and within the Community;
- (c) the evolution of those incidences in the past;
- (d) the specific characteristics of the products concerned;
- (e) the severity of the conditions intended to be treated.

On the basis of these criteria, the requirements referred to in points (a) and (b) of paragraph (1) of this Article may be waived for certain products or product categories.

The measures referred to in this paragraph shall take due account of the legitimate interests to protect information of a commercially confidential nature and of the protection of industrial and commercial property rights.'

- 10) In Article 57, the fourth indent of the first paragraph is replaced by the following:
 - '- without prejudice to point (o) of Article 54, identification and authenticity.'
- 11) The heading of title VII is replaced by the following:
 - 'Wholesale distribution and trading of medicinal products';
- 12) In Article 77, paragraph 4 is replaced by the following:
 - '(4) The Member States shall forward to the Agency a copy of the authorization referred to in paragraph 1. The Agency shall enter that information in the Community database referred to in Article 111(6). At the request of the Commission or any Member State, Member States shall supply all appropriate information concerning the individual authorization which they have granted under paragraph 1.'
- 13) Article 80 is amended as follows:
 - (a) Point (e) is replaced by the following:
 - '(e) they must keep records either in the form of purchase/sales invoices or on computer, or in any other form, giving for any transaction in medicinal products received, dispatched or traded at least the following information:
 - date,
 - name of the medicinal product,
 - quantity received, supplied or traded,
 - name and address of the supplier or consignee, as appropriate;';
 - (b) The following points (h) and (i) are added:
 - '(h) they must maintain a quality system setting out responsibilities, processes and risk management;

- (i) they must inform the competent authority of products they receive which they identify as infringing, or they suspect of infringing, either of the following:

– Article 6(1) of this Directive;

– trademark-holder’s rights under Community law, as provided for by Council Regulation (EC) No 40/94 of 20 December 1993 on the Community trademark¹³ or under the law of the Member State where the product has been received.

Moreover, in cases where these infringements or suspected infringements relate to a falsified medicinal product, the holder of the marketing authorisation or of the trademark that has been falsified shall be informed.’

- (c) The following subparagraphs are added:

‘For the purpose of point (b), in the case where the product is obtained from another wholesale distributor, holders of the wholesale distribution authorisation must verify compliance with good distribution practices of the supplying wholesale distributor either by themselves or through a body accredited for that purpose by the competent authority of a Member State.

Where the product is obtained from the manufacturer or importer, holders of the wholesale distribution authorisation must verify that the manufacturer or importer holds a manufacturing authorization.’

- 14) The following Articles 85a and 85b are inserted after Article 85:

‘Article 85a

In the case of wholesale distribution to third countries Article 76, Article 80(c) and (i), and Articles 81 and 82 shall not apply. Moreover, Article 80(b) shall not apply where a product is directly received from a third country.

Article 85b

Persons trading medicinal products shall ensure that the traded medicinal products are covered by a marketing authorization granted pursuant to Regulation (EC) No 726/2004 or by the competent authorities of a Member State in accordance with this Directive. In addition, the requirements set out in Article 80(d) to (h) shall apply.

They shall notify their activity to the competent authority of the Member State where they are established.’

- 15) Article 111 is amended as follows:

¹³ OJ L 11, 14.1.1994, p. 1.

- (a) In paragraph 1, the following subparagraph is added:

‘Inspections shall be carried out in accordance with the guidelines referred to in Article 111a.’

- (b) Paragraph 3 is replaced by the following:

‘(3) After every inspection as referred to in paragraph 1, the competent authority shall report on whether the manufacturer, importer, or wholesale distributor complies with the principles and guidelines of good manufacturing practice and good distribution practices referred to in Articles 47 and 84 or on whether the marketing authorization holder complies with the requirements laid down in Title IX.

The competent authority which carried out the inspection shall communicate the content of those reports to the manufacturer, importer, marketing authorization holder, or to the wholesale distributor who has undergone the inspection.

Before adopting the report, the competent authority shall give the manufacturer, importer, marketing authorization holder, or wholesale distributor concerned the opportunity to submit their comments.’

- (c) Paragraphs 5, 6 and 7 are replaced by the following:

‘(5) Within 90 days of an inspection as referred to in paragraph 1, a certificate of good manufacturing practice or good distribution practice shall be issued to the manufacturer, importer, or wholesale distributor if the outcome of the inspection shows that the person complies with the principles and guidelines of good manufacturing practice or good distribution practice as provided for by Community legislation.

If inspections are performed as part of the certification procedure for the monographs of the European Pharmacopoeia, a certificate shall be drawn up.

(6) Member States shall enter the certificates of good manufacturing practice and good distribution practice which they issue in a Community database managed by the Agency on behalf of the Community.

(7) If the outcome of the inspection as referred to in paragraph 1 is that the person does not comply with the principles and guidelines of good manufacturing practices or good distribution practices as provided for by Community legislation, the information shall be entered in the Community database referred to in paragraph 6.’

- 16) The following Articles 111a and 111b are inserted after Article 111:

‘Article 111a

The Commission shall adopt detailed guidelines laying down the principles for inspections referred to in Article 111.

Article 111b

(1) The Commission shall, following a request from a third country, list that country by way of a Decision if its regulatory framework for active substances exported to the Community and the respective control and enforcement ensure a protection of public health equivalent to that in the Community. Particular account shall be taken of:

- (a) the country's rules for good manufacturing practices;
- (b) the regularity of inspections of good manufacturing practices;
- (c) the efficacy of enforcement of good manufacturing practices;
- (d) the regularity and rapidity of information supplied by the third country relating to non-compliant producers of active ingredients.

(2) The Commission, in accordance with the procedure set out in Article 121(2), shall adopt guidelines defining in detail the requirements set out in points (a) to (d) of paragraph 1.

(3) The Commission, in cooperation with the Agency and competent authorities of the Member States, shall verify regularly whether the conditions set out in paragraph 1 are fulfilled. The first verification shall take place no later than 3 years after the country has been listed in accordance with paragraph 1.'

17) The following Articles 118a, 118b, and 118c are inserted after Article 118:

'Article 118a

The competent authorities shall issue the accreditation referred to in Articles 46(f) and 80(b) if the applicant can demonstrate that he is competent to carry out verification of compliance with good manufacturing practices or, in the case of wholesale distributors, good distribution practices.

Article 118b

The Member States shall lay down the rules on penalties applicable to infringements of the national provisions adopted pursuant to this Directive and shall take all measures necessary to ensure that they are implemented. The penalties provided for must be effective, proportionate and dissuasive. The Member States shall notify those provisions to the Commission by [insert concrete date 18 months after publication] at the latest and shall notify it without delay of any subsequent amendment affecting them.

Article 118c

Member States, in applying this Directive, shall take the necessary measures to ensure cooperation between competent authorities for medicinal products and customs authorities.'

Article 2

- 1) Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by [insert concrete date 18 months after publication] at the latest. They shall forthwith communicate to the Commission the text of those provisions and a correlation table between those provisions and this Directive.

They shall apply those provisions from [insert concrete date 18 months after publication + one day].

However, the Member States shall apply:

(a) the provisions necessary to comply with Article 1(4) in so far as it relates to Articles 46b(2)(b) and 46b(3) of Directive 2001/83/EC as amended by this Directive from [insert concrete date 24 months after publication];

(b) the provisions necessary to comply with Article 1(6),(8) and (9) from [insert concrete date 48 months after publication].

When Member States adopt those provisions, they shall contain a reference to this Directive or be accompanied by such a reference on the occasion of their official publication. Member States shall determine how such reference is to be made.

- 2) Member States shall communicate to the Commission the text of the main provisions of national law which they adopt in the field covered by this Directive.

Article 3

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

Article 4

This Directive is addressed to the Member States.

Done at Brussels,

For the European Parliament
The President

For the Council
The President

LEGISLATIVE FINANCIAL STATEMENT

1. NAME OF THE PROPOSAL:

Proposal for a Directive of the European Parliament and of the Council amending Directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source

2. ABM / ABB FRAMEWORK

Policy Area(s) concerned and associated Activity/Activities: Enterprise – Internal market, product safety

3. BUDGET LINES

3.1. Budget lines (operational lines and related technical and administrative assistance lines (ex- B..A lines)) including headings:

02.0302

3.2. Duration of the action and of the financial impact:

The action will start in 2012 with a duration of 2 years.

3.3. Budgetary characteristics:

Budget line	Type expenditure	of New	New	EFTA contribution	Contributions from applicant countries	Heading in financial perspective
02.0302	Non-comp	Diff ¹⁴	NO	YES	NO	No 1.a

¹⁴ Differentiated appropriations.

4. SUMMARY OF RESOURCES

4.1. Financial Resources

4.1.1. Summary of commitment appropriations (CA) and payment appropriations (PA)

EUR million (to 3 decimal places)

Expenditure type	Section no.		Year 2012	2013	n + 2	n + 3	n + 4	n + 5 and later	Total
Operational expenditure¹⁵									
Commitment Appropriations (CA)	8.1.	a							
Payment Appropriations (PA)		b							
Administrative expenditure within reference amount¹⁶									
Technical & administrative assistance (NDA)	8.2.4.	c							
TOTAL REFERENCE AMOUNT									
Commitment Appropriations		a+c							
Payment Appropriations		b+c							
Administrative expenditure <u>not</u> included in reference amount¹⁷									
Human resources and associated expenditure (NDA)	8.2.5.	d							
Administrative costs, other than human resources and associated costs, not included in reference amount (NDA)	8.2.6.	e							
Total indicative financial cost of intervention									
TOTAL CA including cost of Human Resources		a+c +d+ e	0.25	0.25					0.5
TOTAL PA including cost of Human Resources		b+c +d+ e	0.25	0.25					0.5

Co-financing details

¹⁵ Expenditure that does not fall under Chapter xx 01 of the Title xx concerned.

¹⁶ Expenditure within article xx 01 04 of Title xx.

¹⁷ Expenditure within chapter xx 01 other than articles xx 01 04 or xx 01 05.

If the proposal involves co-financing by Member States, or other bodies (please specify which), an estimate of the level of this co-financing should be indicated in the table below (additional lines may be added if different bodies are foreseen for the provision of the co-financing):

EUR million (to 3 decimal places)

Co-financing body								
	Year	n + 1	n + 2	n + 3	n + 4	n + 5 and later	Total	
.....	n							
	f							
TOTAL CA including co-financing	a+c +d+ e+f							

4.1.2. *Compatibility with Financial Programming*

- Proposal is compatible with existing financial programming (explanation annexed).
- Proposal will entail reprogramming of the relevant heading in the financial perspective.
- Proposal may require application of the provisions of the Interinstitutional Agreement¹⁸ (i.e. flexibility instrument or revision of the financial perspective).

4.1.3. *Financial impact on Revenue*

- Proposal has no financial implications on revenue
- Proposal has financial impact – the effect on revenue is as follows:

EUR million (to one decimal place)

		Prior to action	Situation following action					
Budget line	Revenue	[Year n-1]	[Year n]	[n+1]	[n+2]	[n+3]	[n+4]	[n+5]
	<i>a) Revenue in absolute terms</i>							
	<i>b) Change in revenue</i>	Δ						

4.2. Human Resources FTE (including officials, temporary and external staff) – see detail under point 8.2.1.

Annual requirements

	Year n	n + 1	n + 2	n + 3	n + 4	n + 5 and
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¹⁸ See points 19 and 24 of the Interinstitutional agreement.

Total number of human resources

5. CHARACTERISTICS AND OBJECTIVES

5.1. Need to be met in the short or long term

The EudraGMP database shall be amended by a chapter for persons introducing medicinal products and by a chapter on wholesale distributors.

This is a relatively simple IT-task, as the actual database (listing all manufactureres and importers) is already available. It is therefore merely an extension of the existing database to more actors handling medicinal products.

5.2. Value-added of Community involvement and coherence of the proposal with other financial instruments and possible synergy

Value added is a facilitated inspection of wholesale distributors and of persons introducing medicinal products. This helps to ensure thorough enforcement of the respective requirements for these actors in the EU.

5.3. Objectives, expected results and related indicators of the proposal in the context of the ABM framework

To add to the existing database for manufacturers and importers of medicinal products an additional chapter on introduction and wholesale distribution.

5.4. Method of Implementation (indicative)

Show below the method(s) chosen for the implementation of the action.

- Centralised Management*
 - directly by the Commission
 - indirectly by delegation to: EMEA
- executive Agencies
- bodies set up by the Communities as referred to in art. 185 of the Financial Regulation
- national public-sector bodies/bodies with public-service mission
 - Shared or decentralised management*
 - with Member states
 - with Third countries
 - Joint management with international organisations (please specify)*

Relevant comments:

6. MONITORING AND EVALUATION

6.1. Monitoring system

The effectiveness of the database can be monitored by assessing its usability. There are various working groups which would assess this effectiveness, such as the working group of enforcement officers.

6.2. Evaluation

6.2.1. Ex-ante evaluation

An ex-ante evaluation, assessing impacts of this measures and possible alternatives is contained in the impact assessment submitted together with the Commission proposal in Inter-Service Consultation. The impact assessment concludes that transparency of results of inspections contributes to efficient surveillance by competent authorities in the Member States as well as to the reliability of commercial actors.

The impact assessment board supported the impact assessment. The final opinion is available here: http://ec.europa.eu/governance/impact/cia_2008_en.htm.

6.2.2. Measures taken following an intermediate/ex-post evaluation (lessons learned from similar experiences in the past)

6.2.3. Terms and frequency of future evaluation

Ongoing in view of the continuous use of the electronic portal by the economic actors.

7. ANTI-FRAUD MEASURES

8. DETAILS OF RESOURCES

8.1. Objectives of the proposal in terms of their financial cost

N/A

8.2. Administrative Expenditure

8.2.1. Number and type of human resources

N/A

8.2.2. Description of tasks deriving from the action

Initiating work on an extension of the existing database to wholesaler distributors and persons introducing medicinal products

8.2.3. Sources of human resources (statutory)

When more than one source is stated, please indicate the number of posts originating from each of the sources

- Posts currently allocated to the management of the programme to be replaced or extended
- Posts pre-allocated within the APS/PDB exercise for year n
- Posts to be requested in the next APS/PDB procedure
- Posts to be redeployed using existing resources within the managing service (internal redeployment)
- Posts required for year n although not foreseen in the APS/PDB exercise of the year in question

8.2.4. *Other Administrative expenditure included in reference amount (XX 01 04/05 – Expenditure on administrative management)*

EUR million (to 3 decimal places)

Budget line (number and heading)	Year 2012	Year 2013	Year n+2	Year n+3	Year n+4	Year n+5 and later	TOTAL
-------------------------------------	--------------	--------------	-------------	-------------	-------------	-----------------------------	-------

1 Technical and administrative assistance (including related staff costs)

Executive agencies¹⁹

Other technical and administrative assistance

- *intra muros*

- *extra muros*

Total Technical and administrative assistance

8.2.5. *Financial cost of human resources and associated costs not included in the reference amount*

EUR million (to 3 decimal places)

Type of human resources	Year n	Year n+1	Year n+2	Year n+3	Year n+4	Year n+5 and later
-------------------------	--------	----------	----------	----------	----------	-----------------------

Officials and temporary staff
(XX 01 01)

Staff financed by Art XX 01
02 (auxiliary, END, contract
staff, etc.)

(specify budget line)

Total cost of Human Resources and associated costs (NOT in reference amount)

Calculation– *Officials and Temporary agents*

¹⁹ Reference should be made to the specific legislative financial statement for the Executive Agency(ies) concerned.

Reference should be made to Point 8.2.1, if applicable

...

Calculation– *Staff financed under art. XX 01 02*

Reference should be made to Point 8.2.1, if applicable

...

8.2.6. *Other administrative expenditure not included in reference amount*

EUR million (to 3 decimal places)

	Year n	Year n+1	Year n+2	Year n+3	Year n+4	Year n+5	TOTAL
						and later	

XX 01 02 11 01 – Missions

XX 01 02 11 02 – Meetings & Conferences

XX 01 02 11 03 – Committees²⁰

XX 01 02 11 04 – Studies & consultations

XX 01 02 11 05 - Information systems

**2 Total Other Management
Expenditure (XX 01 02 11)**

**3 Other expenditure of an
administrative nature** (specify
including reference to budget line)

**Total Administrative expenditure,
other than human resources and
associated costs (NOT included in
reference amount)**

Calculation - *Other administrative expenditure not included in reference amount*

...

Annex

²⁰ Specify the type of committee and the group to which it belongs.

The Legislative Financial Statement is based on the fact that the legislative proposal, if adopted, will require the European Medicines Agency (“EMA”) to adapt the IT arrangements of the present EudraGMP database to include other actors in the distribution chain, in particular wholesale distributors.

This measure is not expected to have an additional financial impact on the Community budget for the following reasons:

- The costs of the measure are with 500 000 EUR over two years relatively modest (below, a);
- The EMA has had, in recent years, a high budget surplus (below, b); and
- There is a possibility for EMA to re-programme its telematics budget for the expected entry into force date of 2012 (below, c).

a) At the outset, it has to be highlighted that the costs for the measure are relatively minor. They amount to 500 000 EUR over a period of 2 years (2012 and 2013). This is a conservative estimation of the costs. As the measure concerns in practice a mere adaptation of the IT system to an extended scope of the existing EudraGMP database, the costs may even be lower.

b) The EMA budget was €163 million in 2007. The Community contribution has increased from €15.3 million in 2000 to €41 million in 2007. The remainder of the increase of the budget over time has been covered by fees charged by the EMA (estimated at 77% of total income in 2008 and based on Council Regulation (EC) No 297/95 as amended by Commission Regulation No 312/2008 of 3 April 2008). Fee revenues are anticipated to further increase in the coming years in line with the general increase in the number of centrally authorised products. It should be noted that, based on fee income, the EMA budget has run at a surplus in recent years and use has been made of the carry-over facility. Indeed, in 2006 the surplus was superior to €8 million.

c) The current EMA programming for telematics "development costs" (as included in the EMA Telematics Master Plan) provides for the following budget:

Year	2008	2009	2010	2011	2012	2013	Total for period
Total IT annual budget (m EUR to one decimal place)	12.6	11.9	13.1	13.1	12.8	10.4	74.1

As set out above, extending the EudraGMP database is likely to incur costs of maximal 500 000 EUR over 2 years. These costs are going to emerge in 2012 for the database to be live once the proposal is adopted, transposed, and applied thereafter.

It is therefore reasonable to require the EMA to re-programme these one-off costs from its existing telematics budget.