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Delegated Act On Detailed Rules For A Unique Identifier For medicinal Products For Human Use, and Its verification

Response by the Association Of The Dutch Generic Medicines Industry, to the European Commission Concept paper submitted for public consultation (Sanco.ddg1.3(2011)1342823 dated 18-11-2011)

1.Introduction

The Bogin supports the European Union and other initiatives in the fight against counterfeit and falsified medicines. The Directive 2011/62/EU aims to prevent falsified medicines from entering the legal supply chain[1] whilst the real public health problem and threat to patients lies in falsified and counterfeit medicines being dispensed through illegal channels. Moreover there are no exact figures available on falsified medicines in the legal supply chain[2], and there is frequent confusion between the reporting of falsified medicines, counterfeit medicines, and unlicensed products. The scope of falsification and counterfeiting is proven to be a problem that is driven by price and demand[3]. These drivers have also been identified in the health sector, for example a Pfizer-sponsored study[4] demonstrated that the counterfeit medicines market (which is almost exclusively via the internet) is dominated by so-called "lifestyle" medicines and most are counterfeit versions of well-known erectile dysfunction and weight loss products, followed by oncology and influenza[5]. There are no reports or data reporting on counterfeit generic medicines in the EU at all and especially not in the legal supply chain.

Generic medicines are, based on their lower prices and the multisource volumes, unattractive for counterfeiters. Therefore the Bogin supports the adoption of Directive 2011/62/EU as it pursued a risk-based approach to identify products that are at high-risk of being falsified which would require them to be subject to safety features and its verification process. Moreover the co-legislators recognized the low risk of generic medicines being falsified and expressed this in recital 11: *"The scope of these safety features should take due account of the particularities of certain medicinal products or categories of medicinal products, such as generic medicinal products. Medicinal products subject to prescription should as a general rule bear the safety features. However, in view of the risk of falsification and the risk arising from falsification of medicinal products or categories of medicinal products there should be the possibility to exclude certain medicinal products or categories of medicinal products subject to prescription from the requirement to bear the safety features by way of a delegated act, following a risk assessment."*[6]
Paragraph 9 of the Commission's concept paper states the obligation that all medicinal products should in principle be obliged to bear the safety features.

[1] recital 29 - Directive 2011/62/EU
[2] See Annex 1: Parliamentary Questions
[3] OECD, "The Economic Impact of Counterfeiting and Piracy"
[4] Nunwood survey data November 2009. Online consumer survey, participants 14,000 in 14 countries
[5] WHO - fact sheet N° 275
[6] Recital 11 - Directive 2011/62/EU

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To ensure complying with this principle in a cost-effective and cost-proportionate way, products at risk of being falsified should be defined using a robust weighted risk assessment[7] that can ensure a rapid evaluation[8] of the products that are judged by the national competent authorities[9] to be at risk or not at risk of falsification.

The introduction of expensive safety features for low cost medicines while there are no incidents of falsified products reported in the EU legal supply chain is contrary to the principle of cost-effectiveness and proportionality. Moreover it would place an unjustifiable burden on the sustainability of an industry which is a corner stone of healthcare provision in Europe.
The EGA, The European Generic Association, has calculated that the implementation costs for the EU generic industry could reach:€ 1 billion. In addition to this, the costs for running repository systems in the EU for the verification of authenticity of generic medicines would be an additional: € 200,000,000 / year. Taking into account the costs of these investments above and the fact that the life-span of the additional hardware on the production line is only 5 years, the overall costs would be € 500 million per year for the EU generics industry.
Furthermore, the generic medicines industry represents over 60% of the medicines that are dispensed in the Netherlands, while only using less than 15% of the total pharmaceutical budget. At EU level these figures are of about the same magnitude.

If safety features applied to all prescription medicines in the EU, the Commission would not apply the principles of proportionality and cost-effectiveness.

Therefore it is essential that in the delegated act the following principles are adhered to:

- A robust weighted risk assessment to identify high risk products, taking into account the intentions of the co-legislators as indicated in Recital 11, especially regarding generic medicines.
- A cost-effective and cost-proportional solution to prevent falsified items of high risk products from entering the supply chain.

As the generic medicines industry is highly cost-sensitive where API supply and manufacturing alone can account for over 50% of the total cost of a product, the introduction of regulations affecting production costs has a major impact on the overall sustainability of the industry. Such a significant increase in relative production costs for generic medicines especially puts at risk small and medium sized companies.

[7] Article 54a(2)(b) - Directive 2011/62/EU
[8] Article 54a(2)(c) - Directive 2011/62/EU
[9] Article 54a(4) - Directive 2011/62/EU

The Bogin also would like to draw the attention to the fact that the application of anti-tampering features requires unprecedented and substantial changes in the production process of all pharmaceutical manufacturers, not only involving costs but significant time delays with risks of medicines shortage. All this reduces patient access to affordable treatment as portfolios of many companies may be reduced. Costs may even be passed on to consumers and payers, which is unethical in times of crisis where there is a high demand for affordable medicines.

2.Consultation item n°1: Please comment on points 1 and 2 (policy options n°1/1 and n°1/2). Where do you see the benefits and disadvantages of each policy option?

Comments Bogin: In principle the Industry should be allowed to follow their own methods of addressing legal requirements. However the system should meet the requirements of the amending Directive 2011/62/EU and be interoperable within the EU member states. So the Commission should establish parameters to ensure interoperability. Cost effectiveness and proportionality are important factors and an impact assessment should be undertaken to guarantee that the most appropriate cost-effective system will be put in place.

3.Consultation item n°2: Where do you see the advantages and disadvantages of the approach set out in point 2.1.1.? Please comment.

Comments Bogin: Whilst there is a need for a regulated harmonization of the technical characteristics of the carrier to ensure inter-operability in the EU, the composition of the serial number should not be harmonized through regulation but should be adjustable to national requirements. Different standards of product coding are used at national level (e.g. PZN in Germany, CNK in Belgium, and GS1 in France). An open code will be required to make the system cost-effective and has no effect on the inter-operability of the system.

Adding a unique identification number to the pack will only be required in case a pack requires identification for authenticity i.e. a high risk product. Including a unique identification number beside the manufacturer product code should suffice.

4.Consultation item n°3: Where do you see the advantages and disadvantages of the approach set out in points (a) and (b) of point 2.1.2? Please comment.

Comments Bogin: Batch number and expiry date will still have to be printed on the pack in order to enable patients to read them. Putting them in a barcode as a part of the serialisation number ,to enable to a machine-readable option, is outside the scope of the Directive and would result in additional costs. It is required that the Commission in "establishing the safety features" gives also "due consideration …… to their cost-effectiveness ". Increasing the cost further would especially be affect small and medium sized companies.

5.Consultation item n°4: Which of the two options set out under point (c) of point 2.1.2 is in your view preferable? Where do you see advantages and disadvantages? Please comment.

Comments Bogin: There is no system in the Netherlands that requires inclusion of a reimbursement number. This is the responsibility of the national authorities in different member states

6.Consultation item n°5: Please comment on the three concepts described under point 2.2. Where do you see the benefits and disadvantages of each of the three concepts. What are the costs for each concept? Please quantify your reply, wherever possible, by listing for example:
- costs for reading devices for the different carriers;
- costs for adapting packaging lines of medicines packaged for the EU market.

Comments Bogin: We should stay within the scope of the Directive. The requirements of this Directive can be met with a (already in use) linear barcode. Therefore the current practice in using a linear barcode is the cost-effective answer and should therefore be the standard.
A 2 D matrix can carry more information, but that is only required if more information has to carry in the barcode. We refer to the EGA response for the effect on the cost factor. We anticipate that scanning equipment that can read both linear and 2D codes is available. It is advisable that the Commission ensures that linear and 2D codes and the scanning equipment used are all compatible and interoperable. RFID is no option because of technical questions and high cost factor.

7.Consultation item n°6: Regarding point 1 (policy option n°2/1), are there other points of dispensation to be considered? How can these be addressed in this policy option?
2. Policy option n°2/2: As in policy option n°2/1, but with additional random verifications at the level of wholesale distributors
3. Policy option n°2/3: As in policy option n°2/1, but with additional systematic verification by the wholesale distributors

Comments Bogin: The system of a unique identifier can only work when there is a reliable verification system in place. Safety features must enable wholesale distributors and persons authorized or entitled to supply medicinal products to the public to verify the authenticity of the medicinal product and identify individual products (Directive 2011/62/EU art. 54o).
Rules for verification are defined in the Directive for re-packagers(i.e. parallel importers).
Attention should be given to the fact that there will be more than one dispensing points: ,distant sales points (internet pharmacies), dispensing doctors, products used by a doctor during patient visits, samples given to doctors , hospitals, home care institutes.

In case an OTC product, based on a positive risk assessment, will have to bear the safety features (unique serial number and ant tempering device) one has to consider that in a number of EU member states, like in the Netherlands, those products could be also sold through drogeries (drugstores), supermarkets and petrol stations.
Verification at the point of dispensing is an important aspect, but not covered by the Directive, which does not provide for a pharmacist to check every pack dispensed if it carries a safety feature.

8.Consultation item n°7: Please comment on the three policy options set out in points 1 to 3. Where do you see the benefits and disadvantages? Please comment on the costs of each of these policy options. Quantify your response, wherever possible. This applies in particular to the:
- number of wholesale distribution plants;
- costs for adapting such plants;
- duration of scanning of the serialisation number;
- number of pharmacies, including hospital pharmacies;
- number of medicinal products dispensed by pharmacies and a hospital pharmacy.

Comments Bogin: The Directive is clear about this point for wholesalers (amended article 80): "they must verify that the medicinal products are not falsified by checking the safety features on the outer package, in accordance with the requirements laid down in the delegated acts referred to in article 54a(2)".
The Directive overarching goal is to prevent falsified products to enter the supply chain. To enable for the wholesalers to execute this task it is of great importance that a robust risk assessment should identify the products really being at risk of being falsified. This robust risk assessment will limit the number of products that have to bear the safety features and the unique number and resulting in verification, for both wholesalers and points of dispensing, that will be both reasonable and proportionate.

9.Consultation item n°8: Please comment on the three policy options set out in points 1 to 3. Where do you see the benefits and disadvantages? Please comment on the costs of each of these policy options. Please quantify your reply, wherever possible. This applies in particular to the estimated one-off costs and running costs for a repositories system. Where possible, please provide information on past experiences with a repositories system at individual company level and at national level (taking into account the experiences of Member States and companies).

Comments Bogin: Based on the current available data it is very difficult to have a preference for a certain solution. It will depend on the outcome of this consultation, especially on the final decisions. The number of risk products in the system will be an important factor in the final approach. We think that more information on estimated costs is needed and that a proper impact analysis is needed. We believe that a pan European solution would increase costs. Principally a stakeholder solution should be the first choice, but it can be anticipated that it might result in a system of combining a stakeholder governance with a national governance . Interconnectivity for the different systems has to be secured.

But in any case, as the industry is carrying the cost of the repository system, it is important that the cost contribution is based on the principle of proportionality and thus on the value of the products concerned.

10.Consultation item n°9: Please comment on point 4.1. Are there other items of information which should be taken into consideration when addressing the issue of commercially sensitive information in the delegated act?

Comments Bogin: The focus of the Directive should be leading, all information mentioned in the consultation should be considered confidential and not to be used than other for the purposes of strict the aims of the Directive to prevent falsified medicines entering the legal supply chain.

11.Consultation item n°10: Please comment on points 4.2 and 4.3. What aspects should be taken into consideration in the delegated act?

Comments Bogin: We support the EU Commission concerning article 54a(3)(a) of the Directive 2011/62/EU in personal data protection.

12.Consultation item n°11: Which approach seems the most plausible from your view? Can you think of arguments other than those set out above? Can you think of other identification criteria to be considered?
2. Applying the classification criteria

Comments Bogin: In the Netherlands an extensive discussion took place with all parties, competent authorities and industry, about the risk of falsified medicines and actions to be taken to limit the risk as much as possible. Analysis of the source of falsified medicines identified the source being mainly internet. In the regular supply chain falsifications are very rare. This has resulted that the Dutch Government has started a campaign warning potential buyers against buying medicines via internet. (Note: it must be clear that we are not talking about official approved internet pharmacies) It was also clear that demand was driving the ordering of medicines and that that was limited to a few categories of medicines. (mainly hormone and psychotropic products, products against virus or bacterial infections, products for erectile dysfunction). It can be concluded that falsifications are very rare in the EU legal supply chain. For generic products no falsifications have been reported in the legal supply chain.
Therefore it is essential that a robust weighted risk assessment identifies the products at Risk, and only those products should bear the safety features.
In the Directive it formulated as follows (point 11) :
"The scope of these safety features should take due account of the particularities of certain medicinal products or categories of medicinal products, such as generic medicinal products. Medicinal products subject to prescription should as a general rule bear the safety features.

However in view of the risk of falsification and the risk arising from falsification of medicinal products there should be the possibility to exclude certain medicinal products or categories of medicinal products subject to prescription from the requirement to bear the safety features by way of delegated act, following a risk assessment."

The Directive is clear about its goals and the necessity of a robust the risk assessment. The 6 factors mentioned in the Directive are important criteria, although of a total different weight if it comes to weighing these factors to determine the real risk of falsification of the product.

In point 83 the price of a medicine is being set at a level of 2 € as being a high price . It is unclear what is meant, for instance a tablet, a package with how many tablets. The weighing of these criteria are discussed under consultation item no. 12.
We do not understand the remark in point 84 that the possibility of exemptions should not be "interpreted to narrowly". This looks to contradict the text and the spirit of the Directive 2011/62/EU. The Bogin is of the opinion that the Directive should be followed and that the risk assessment results in a white or black listing. The Bogin is of the opinion that as there is no report of generic medicines being falsified in the EU legal supply chain, and point 11 mentions generic medicinal products as a category of products, these medicinal product should be on the white list. If in the future a specific generic medicinal product would fall in the high risk category it should be taken of the white list.

The Bogin would also to bring forward the argument that the risk analysis should be done at product basis, on the given name that is a part of the registration dossier for obtaining the marketing authorisation.
In point 85 is stated "the EU-scope of the unique identifier is non-optional: a medicinal product which falls within the scope must bear the unique identifier. A medicinal product that falls outside the scope must not have to bear the unique identifier." The Bogin does not understand this point. Ads it is clear that a product at high risk will be in the system, we cannot understand why a manufacturer cannot decide to apply unique identifier if the manufacturer wishes to do so. There is no justification for this limitation in the text of the Directive 2011/62/EU.

13.Consultation item n°12: Please comment on the quantified approach set out above.

Comments Bogin: Falsifying medicinal products is a criminal act. Producers of falsified medicinal products are risking people's lives and are criminals. It is essential that the risk assessment really identifies products at risk. The falsified products as mentioned before are mainly entering via internet and the illegal supply chain and these specific categories of products are of special interest. It is important to understand the drivers for producers of falsified medicines: the first driver is demand.
The proposed method and accumulation of points leads in almost all cases, also for a number of OTC products, to be including the majority of medicinal products in the system. As mentioned in the previous consultation item no. 11 considering 2 € as a high price, especially without even referencing to a quantity or package size, is not realistic.

The order of importance of weighing the risk factors should be in the following order:

(1) Frequency of reported incidents , (2) Price, (3) Product characteristics, (4) Volume, (5) Seriousness of disease,(6) other potential risk{first to be specified!)

We support the proposal of the EGA for weighing the different criteria

Figure 1: Weighted Risk Assessment:

1. Frequency or previous incidents of medicinal products found falsified in the legal supply chain: If a product has been found counterfeited, this is the highest weighted risk factor.
   a) High risk: counterfeits reported in the EU legal supply chain
   b) Medium risk: counterfeits reported in other highly regulated countries in the legal supply chain
   c) Low risk: counterfeits reported in third countries in the legal supply chain
   d) No risk: no counterfeits reported

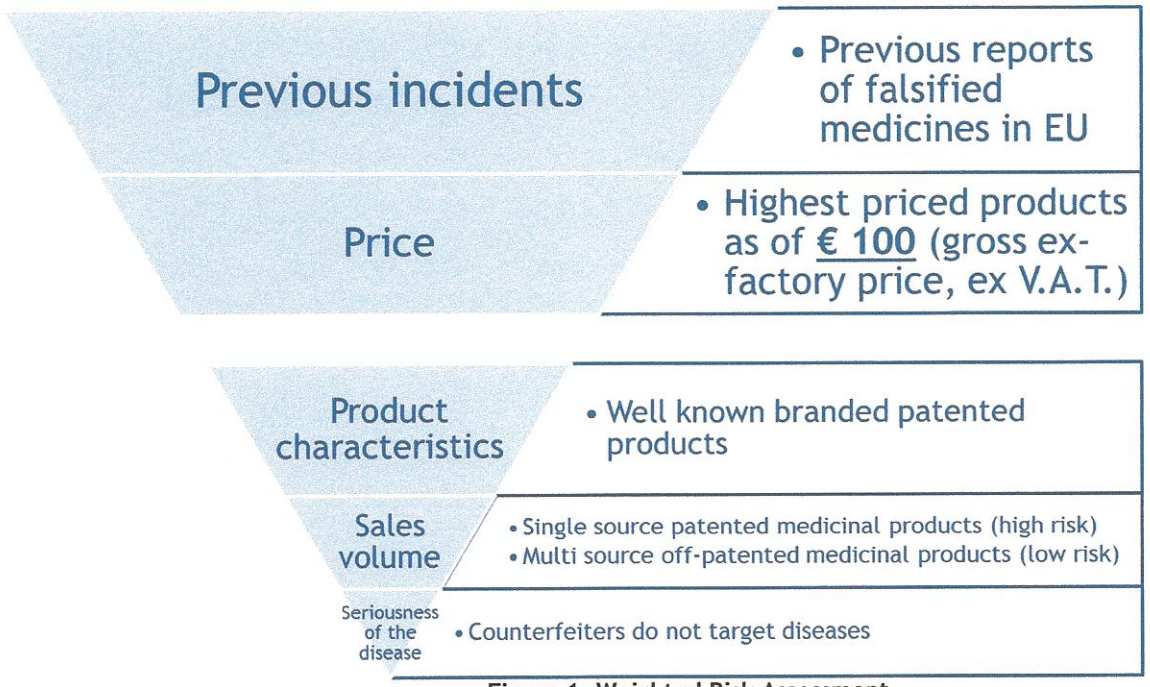
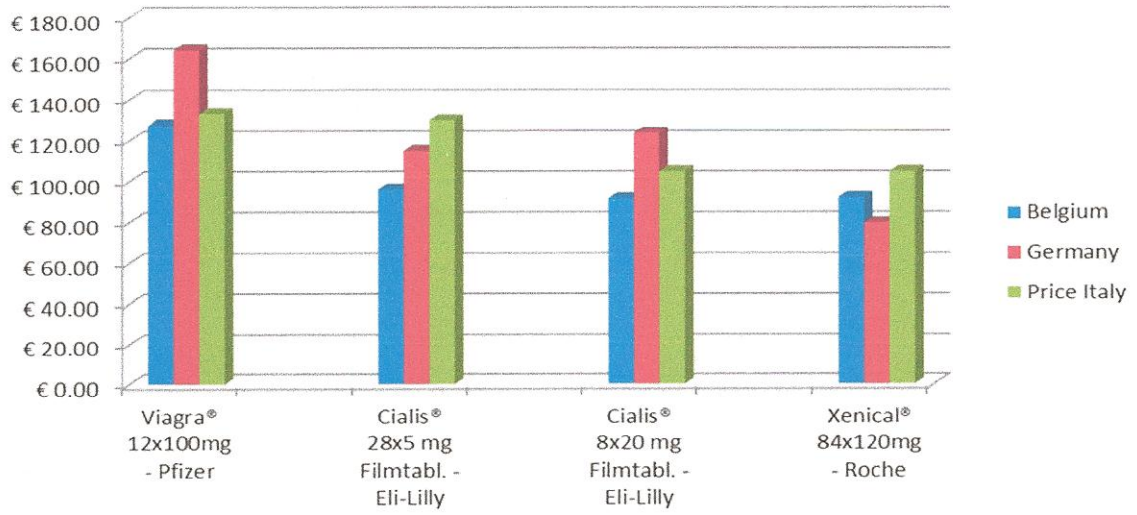


Figure 1: Weighted Risk Assessment

2. Price: Counterfeiting is mostly driven by price. See below a table of products that have been found counterfeited. The EGA therefore considers products below € 2 as low priced and € 100 as highest priced products.



3. Product characteristics: Well-known branded patented products are at a higher risk of being counterfeited. At the time of writing, evidence again shows that counterfeiters are targeting high-priced branded patented products. For example in the USA, recently more counterfeits are found of Avastin[10®]

4. Sales volume
   a) Single source patented medicinal products are high risk
   b) Multi-source off-patent medicinal products are low risk

5. Seriousness of the disease: this is not a driver for counterfeiters however for matters of patient safety, lifesaving products should be graded the highest.

As the concept paper points out in paragraph 6: since the impact assessment for the proposal for Directive 2011/62/EU, the figures may now be partially outdated; the EGA would like to confirm that still no falsified generic medicines have been found in the EU legal supply chain. The difference between falsified medicines and IP infringement also needs to be noted.

[10] http://in.reuters.com/article/2012/04/04/avastin-fake-idINDEE8330EU20120404

14.Consultation item n°13: Please raise any other issue or comment you would wish to make which has not been addressed in the consultation items above.

Comments Bogin: It is essential that the implementation of the delegated act is done in effective and thorough way. The time table mentioned is essential. It is however essential that cost-effectiveness and cost-proportionality plays an important role. An updated analysis of the current status with respect to falsified medicines situation is appropriate. The first impact analysis is from 2008 and an update impact analysis seems appropriate, especially with respect to the fact that all measures should be proportionate and cost effective.