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AESGP comments on the concept paper on the delegated act for safety features submitted for consultation by the European Commission

GENERAL COMMENTS

AESGP welcomes the opportunity to provide feedback to the concept paper on the delegated act for the safety features introduced by Directive 2011/62/EU[1]. The Directive aims at addressing the public health threat that falsified medicines represent, introducing measures to prevent the entry and supply of falsified medicines in the legal supply chain. AESGP, representing the manufacturers of non-prescription medicines, is fully aligned with the overall objectives of the Directive and strongly supports the European Commission in the effort to ensure that dangerous and ineffective medicinal products do not reach European citizens.

Directive 2011/62/EU stipulates that medicinal products not subject to prescription shall not bear the safety features, unless, by way of exception, they have been listed by the Commission in a delegated act. To AESGP, this represents recognition of the limited falsification risk for non-prescription medicines but does not reduce industry's resolve to ensure consumer safety.

In relation to the possible application of the safety features to non-prescription medicines, clear criteria are set out by the Directive to assess whether products will exceptionally be required to bear the safety features. AESGP welcomes that the exceptional nature of the application of safety features to non-prescription medicines is appropriately reflected in paragraph 84 of the concept paper as well as the European Commission's express intention to remain with the delegated act in line with the spirit of the legislation and the intention of the legislator. This is in any case the fundamental principle underpinning the delegation of powers to the European Commission.

CONCEPT PAPER – CONSULTATION ITEMS

CONSULTATION ITEM N°1
HARMONISATION OF TECHNICAL SPECIFICATIONS

As noted in the concept paper, a harmonised approach in the definition of the characteristics and technical specifications of the serialisation number and carrier may facilitate the implementation of the measure.

The regulation and standardisation of the technical specifications of the serialisation number and carrier will allow the uniform application of the measure across the EU. It

[1] http://ec.europa.eu/health/files/counterf_par_trade/safety_2011-11.pdf

constitutes a far more efficient solution compared to manufacturers using different serialisation methods and actors in the supply chain being required to verify authenticity based on different serialisation methods. By simplifying the verification process, harmonisation through regulation can contribute to the effectiveness of the measure's application and the reduction of implementation costs.

In relation to the anti-tampering device, AESGP agrees with the Commission's position (concept paper, paragraph 10), that manufacturers are best placed to establish how outer packaging is made tamper-proof.

COMPOSITION OF SERIALISATION NUMBER

CONSULTATION ITEM N°2 - MANUFACTURER PRODUCT CODE AND PACK NUMBER

General remark:

Please note that some inconsistencies are presented in the text of the concept paper regarding the use of the terms "serialisation number" and "unique identifier", as the terms are interchangeably used to define different elements of the information that may be included in the safety feature (unique identifier).

AESGP supports the use of an internationally unique product code.

In light of the technical possibility to include additional information in a serialisation number (as shown under paragraph 29 of the concept paper), the number composition proposed under paragraph 21 is restrictive.

In relation to the proposal in paragraph 29 to include the reimbursement number in the unique identifier, another consideration would be to include the reimbursement number in the manufacturer product code (with or instead of the country prefix). In this case, the national reimbursement number could be a worldwide unique number, as this would not be difficult to achieve[2]. The national reimbursement number could then also be the product number.

It should be noted that no 'manufacturer product code' as described in point 2.1.1 of the concept paper is currently in place in a number of EU Member States (including Austria, Belgium, France, Germany, Italy, Portugal and Spain). The introduction of such a number in addition to a serialised or national numbers represents an unnecessary complication in the composition of the unique identifier.

[2] In order to become the product number or be part of the product number, the national reimbursement number issued through a national numbering system (i.e. PZN in Germany, CIP in France) has to be unique worldwide. For this purpose, the institution/agency responsible for numbering has to register with the ISO as an Issuing Agency.

There should be an internationally unique product code that is generated either by the manufacturer or by a national registry.

In relation to the composition proposal for the unique identifier in paragraph 29, this could be presented with the following modification:

Manufacturer Product code (may incl. the prefix of the country and/or the national reimbursement number)	Pack number	National reim-bursement number, unless it is (part of) the manufacturer product code	Expiry date	Batch number

With regard to the composition of the code (data identifier system), this should ensure interoperability with other (existing) data identifier systems such as HIBC, GTIN, etc.

CONSULTATION ITEM N°3 - ADDITIONAL PRODUCT INFORMATION (BATCH NUMBER, EXPIRY DATE)

As indicated in the concept paper (paragraphs 22-24), the inclusion of the batch number and expiry date in the unique identifier presents certain benefits. AESGP is in favour of the possibility of including the information in the unique identifier on a voluntary basis.

CONSULTATION ITEM N°4 - ADDITIONAL PRODUCT INFORMATION (NATIONAL REIMBURSEMENT NUMBER)

A technical possibility for the inclusion of the national reimbursement number in the serialisation number is presented in our comments on Consultation Item n° 2.

Should the delegated act include provisions for, or references to, the application of the safety features to a reimbursed non-prescription medicine by a Member State for the purposes of reimbursement and for reasons not relating to the product's falsification risk, these should be kept separate from any approach adopted to determine the exceptional inclusion of non-prescription medicines in the 'black list'. A product bearing the safety features in Member States for the purposes of reimbursement alone should not be included in the 'black list' of products required to exceptionally bear the safety features in all Member States.

CONSULTATION ITEM N°5

REGULATION AND TECHNICAL CHARACTERISTICS OF THE CARRIER

Linear barcode

The choice of this barcode would not be optimal as it either requires a lot of space on the packaging or can only include limited information.

2D Data code

A 2D Data code requires comparatively less space on the packaging and can include a sufficient amount of information within one symbol. In addition, not only a defect detection is possible (as is the case with linear barcodes) but also an error correction. Thus it is possible to successfully read out defect symbols.

RFID-transponder

A transponder can include a great deal of information within fixed dimensions. However, it is comparatively expensive. The cost for the RFID-transponders alone can be expected to be higher than the combined cost of printing the safety features and running the repositories system. Other than the cost of the RFID solution, reliability issues associated with this carrier option indicate that it is not appropriate for the safety features.

Based on the above considerations, the 2D Data code option seems to be the optimal choice of carrier. It provides more capacity than the linear bar code and is far more efficient and technically mature compared to RFID.

CONSULTATION ITEM N°6

MODALITIES FOR VERIFICATION - VERIFICATION AT POINTS OF DISPENSATION

AESGP does not see other points of dispensation than the ones described in the concept paper.

The application of the safety features should not affect or be used as an excuse to impede established dispensation and retail methods determined by national policy and regulation.

CONSULTATION ITEM N°7

MODALITIES FOR VERIFICATION - VERIFICATION BY WHOLESALE DISTRIBUTORS

The legislative requirements do not justify the implementation of a 'track and trace' system that would translate in the mandatory and systematic verification of individual packs by all actors in the supply chain.

The systematic verification (and check-out) at the dispensing points may be complemented by voluntary and random authenticity checks by wholesale distributors.

CONSULTATION ITEM N°8

REPOSITORIES SYSTEM - GOVERNANCE

A 'stakeholder governance' structure for the repositories system can be relied upon to provide a more effective and efficient implementation.

The following issues raised in the concept paper should be noted and clarified by the Commission:

- Paragraph 62 refers to a manufacturer obligation to check out a serialisation number. This is only applicable in two cases, namely in the case of re-packaging and replacement of a serialisation number and in the case of destroying the pack after a recall. Otherwise, a manufacturer cannot ensure that the serialisation number is checked out for products dispensed in pharmacies or other end-points in the supply chain.

  To avoid this possible misunderstanding AESGP proposes that the repositories system(s) design ensures that the serialisation number can be checked out during the final dispensing procedure and in the two cases mentioned above.

CONSULTATION ITEM N°9

REPOSITORIES SYSTEM - COMMERCIALLY SENSITIVE INFORMATION

The need to guarantee manufacturers' legitimate interests to protect commercially sensitive information is recognised in the legislation and appropriately identified in the concept paper.

Companies should have access to their own data, yet commercially sensitive information (e.g. information on commercial arrangements between pharmacies and manufacturers) should be protected. Commercial organisations should not be in a position to use the repositories system to gain access to information pertaining to the

commercial activities of competing companies or other actors in the supply chain. Strict controls need to be put in place and be documented to ensure the protection of commercially sensitive information.

CONSULTATION ITEM N°10

REPOSITORIES SYSTEM - PERSONAL DATA PROTECTION & REPACKAGING OF MEDICINAL PRODUCTS

(a) Personal Data protection

The use of the repositories system should ensure that only authentic products are purchased by individuals. The use of the system for commercial activities or purposes other than those stipulated in the legislation cannot be justified.

(b) Re-packaging

The only measure that could be considered as equivalent to the safety features is the replacement of the original unique identifier with a new unique identifier by the re-packager, who would then assume responsibility for the product's authenticity. The replacement requirement should also concern the anti-tampering device.

The delegated act should account for the differences in pack sizes of re-packaged products and include clear provisions to address the need for new identifiers to correspond/be linked to original authentic products.

CONSULTATION ITEM N°11

LISTS OF MEDICINAL PRODUCTS WHICH, IN THE CASE OF PRESCRIPTION MEDICINES ARE EXEMPTED FROM THE OBLIGATION TO BEAR THE SAFETY FEATURES, AND IN THE CASE OF NON-PRESCRIPTION MEDICINES WILL BE REQUIRED TO BEAR THE SAFETY FEATURES

- IDENTIFICATION OF PRODUCTS

It is important to appropriately differentiate between the establishment of the 'black list' and that of the 'white list'. AESGP is exclusively commenting on the 'black list'.

As noted in paragraph 84 of the concept paper, the possibility of exemptions from the general principle laid out in the legislation concerning the 'black list' should be interpreted narrowly.

Based on the legislative requirements and options described in the concept paper, identifying a product by its name and country of marketing authorisation (unless it is a centrally authorised medicine) is the appropriate approach for the construction of the 'black list'. It allows a clear definition of the product concerned and reflects the exceptional character of the measure.

CONSULTATION ITEM N°12

LISTS OF MEDICINAL PRODUCTS WHICH, IN THE CASE OF PRESCRIPTION MEDICINES ARE EXEMPTED FROM THE OBLIGATION TO BEAR THE SAFETY FEATURES, AND IN THE CASE OF NON-PRESCRIPTION MEDICINES WILL BE REQUIRED TO BEAR THE SAFETY FEATURES

- QUANTIFIED APPROACH FOR APPLICATION OF CLASSIFICATION CRITERIA

As noted in the response to Consultation Item 11, the approaches to construct the 'black list' and 'white list' need to be clearly separated. AESGP is exclusively commenting on issues relating to the 'black list'.

A narrow interpretation of the exemptions from the general principle laid out in the legislation for the application of the safety features excludes any notion of a systematic assessment of non-prescription medicines. Any considerations on whether or not to include a non-prescription medicine in the 'black list' should therefore only be made based on the availability of clear evidence of a high falsification risk.

AESGP agrees with the European Commission's position[3] that the approach described under paragraph 87 of the concept paper is not to be understood as a systematic review of medicines but only as a possible approach to the handling of notifications described in Article 54a(4) of the legislation. The notion of a systematic screening for the identification/classification of non-prescription medicines not only goes against the general principles of the legislation, but would furthermore be a resource-consuming and cost-ineffective procedure, requiring the assessment of over 50.000 products[4].

The concept paper in paragraph 87 provides the example of a quantification system for the application of the classification criteria. This type of quantification system as a method to aggregate clearly disparate risk elements to reach an evaluation is highly questionable from a political and methodological perspective. On top of this inherent system limitation, different value-points are arbitrarily attributed to the five criteria laid out in the Directive without any foundation or justification of a correlation between the values attributed and the extent of the contribution of each criterion to the falsification risk.

The indicative numbers provided as an implementation example of the proposed quantification system set an absurdly low threshold of 11 points for non-prescription medicines to be included in the 'black list'. Considering (a) the equally flawed postulation that 2 Euros can be considered as a high price, (b) that high price and high

[3] Position expressed at the technical workshop on the concept paper organised by DG SANCO in Brussels on 20 December 2011. For more information, please refer to the meeting summary circulated by DG SANCO on 11 January 2012.

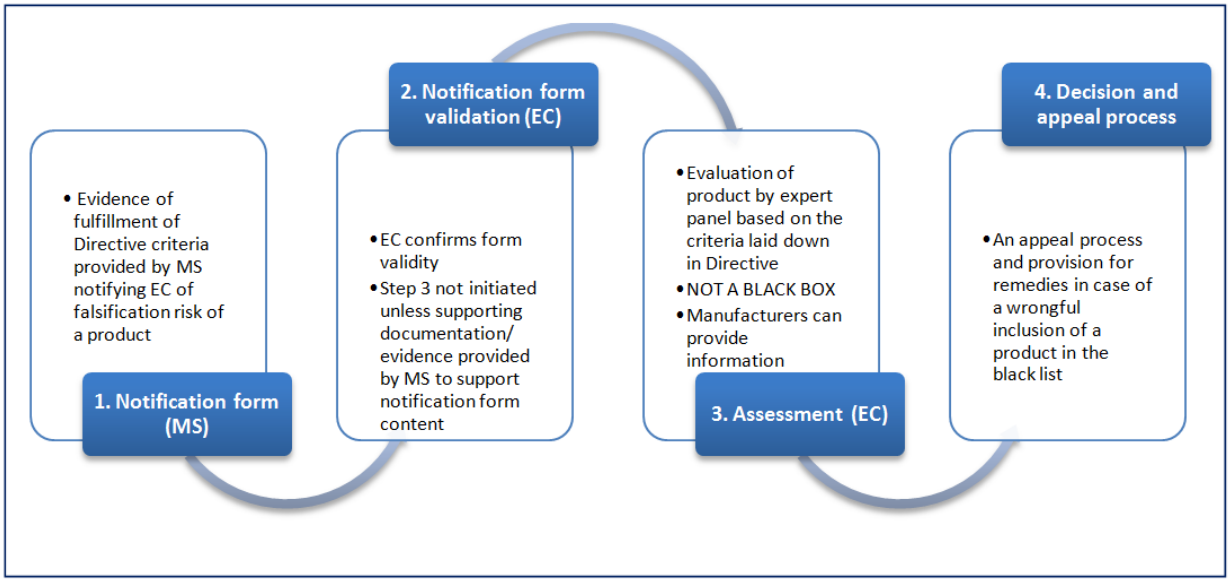
[4] This figure results from data included in the European Commission's Impact Assessment for the proposal on Variations (page 9), which indicates that the total number of marketing authorisations for human medicines in 2006 was 158.999. According to data from the Austrian Agency for Health and Food Safety (AGES), around 32% of medicinal products approved for human use in Austria is available as non-prescription medicines (source). This ratio of prescription to non-prescription medicines can be considered a close and conservative approximation of the European ratio, especially considering that it does not account for the considerable number of homeopathic products.

volume lead to a 10 point accumulation and (c) that the quantification system adds points for the remaining criteria regardless of whether these are fulfilled or not, the following is clear: contrary to the legislation provisions and the intention expressed by the Commission to narrowly interpret the possibility of exemptions (see paragraph 84 of the concept paper), the quantification system, as presented, would in fact result in the majority of non-prescription medicines being required to bear the safety features. Should a system similar to this be eventually adopted in the delegated act, an indicative figure for a threshold that could possibly be considered as being in line with the legislative provisions cannot be lower than 25 points.

In order to provide the appropriate context to the comments above and proposals below, it should be mentioned at this point that currently no non-prescription medicines in the European market satisfy the criteria laid down by the Directive in order to be required to exceptionally bear the safety features (i.e. high-price/volume products addressing severe conditions and for which cases of falsification have been reported in the legal supply chain).

AESGP supports the adoption of a classification system that effectively reflects the letter and spirit of the Directive. The Directive stipulates that non-prescription medicines are in principle excluded and should only exceptionally be required to bear the safety features. The decision on whether or not to include a non-prescription medicine in the 'black list' should be based on the process and careful consideration of the criteria laid down in Article 54a (2) of the Directive. Moreover, the measure's application should only serve the objective of ensuring that no falsified medicines enter the legal supply chain. To this end, and in line with the legislation, AESGP proposes the process shown in Diagram 1 as the most effective way to identify products requiring attention and assessment in order to determine whether these should be included in the 'black list'. Each step is further explained in the following paragraphs.

Diagram 1. Identification and classification process for exceptional cases of non-prescription medicines assessed to be included in the black list



official documentation and reports substantiating their assertion of a non-prescription medicine being at risk of falsification.

AESGP presents below an example of a notification form that could be used by Member States in the context of the notification process, constructed based on the criteria set out in the Directive.

<table>
<tr><th colspan="4">Notification by Member State</th></tr>
<tr><td colspan="4"></td></tr>
<tr><td>Product name</td><td colspan="3">Manufacturer</td></tr>
<tr><td>INN</td><td colspan="3"></td></tr>
<tr><td colspan="4"></td></tr>
<tr><td>Criteria establishing falsification risk</td><td colspan="3">Supporting evidence
Please note: Notification forms submitted without supporting documentation are considered incomplete and will not be considered</td></tr>
<tr><td rowspan="10">1. Recorded cases of falsification in the legal supply chain</td><td>Case nr.</td><td>Date</td><td>Case description and documentation*</td></tr>
<tr><td>1</td><td></td><td></td></tr>
<tr><td>2</td><td></td><td></td></tr>
<tr><td>3</td><td></td><td></td></tr>
<tr><td>4</td><td></td><td></td></tr>
<tr><td>5</td><td></td><td></td></tr>
<tr><td>6</td><td></td><td></td></tr>
<tr><td>…</td><td></td><td></td></tr>
<tr><td colspan="3">*Please include official documentation (authority case report, confiscation report, border control records).

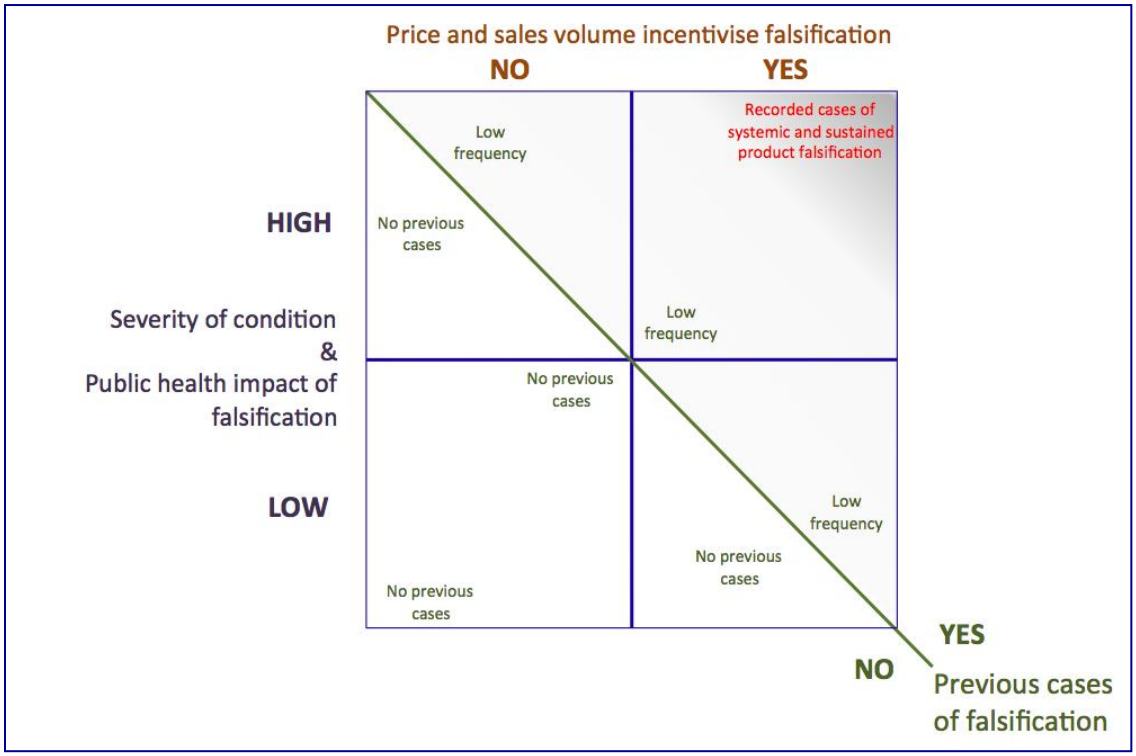
Cases not accompanied by detailed official documentation validating falsification will not be considered in the further assessment process.</td></tr>
<tr><td>2. Severity of conditions intended to be treated</td><td colspan="3">Please explain and submit/attach supporting reports/ documentation concerning:
Condition treated/Indication of use: ……
Consequence of falsification: ……</td></tr>
<tr><td>3. Other potential risks to public health requiring additional safety measures</td><td colspan="3">Please explain falsification consequences on public health and submit/attach supporting reports/ documentation: ……
(any impact related to users to be addressed under point 2):</td></tr>
<tr><td colspan="4">4. Incentives for falsification</td></tr>
</table>

4a. High price	Price: …… If applicable: Average price of other products with the same API(s): …… Average price of other products in the same therapeutic area: …… Average price of products in the same category (please define as appropriate): …… *Please submit/attach official reports supporting the data provided concerning sales prices.*
4b. High volume	Volume: …… If applicable: Sales volume share compared to other products with same API(s): …… Sales volume share compared to other products in the same therapeutic area: …… Sales volume share compared to other products in a related therapeutic area: …… Sales volume share compared to other products in the same category (please define as appropriate): …… *Please submit/attach official reports supporting the data provided concerning sales volume.*
5. Specific product characteristics increasing the risk of falsification	Please explain and submit/attach related documentation: ……
6. Other	Please explain and submit/attach related documentation: ……

2. Evaluation system (Article 54a 2c) - Notification validation (EC)

The evaluation system should establish that the product under discussion in principle fulfils the criteria laid down by the Directive (i.e. in terms of the classification criteria diagram below, the completed notification form and the evaluation system should establish that a product is positioned in the upper right corner).

Diagram 2. Black list classification criteria for non-prescription medicines



Upon receiving the notification (completed notification form and accompanying supporting documentation), the European Commission should assess whether it is adequately supported by evidence and thus merits further action.

Notification validation by the European Commission					
Member State:	Product name:				
Manufacturer:	INN:				
	MS notification based on the following criteria		Evidence/documentation submitted to support claim		
	Yes	**No**	**Yes**	**No**	**n/a**
1. Recorded cases of falsification in the legal supply chain	x		x		
2. High severity of conditions intended to be treated	x		x		
3. Other potential risks to public health requiring additional safety measures	x		x		
4. Incentives for falsification					
4a. High price	x		x		
4b. High volume	x		x		
5. Specific product characteristics increasing risk of falsification	x		x		
6. Other					

An incomplete notification form or one not accompanied by supporting documentation/evidence can only mean that Member States either do not find the evidence collection process worthwhile, or that this evidence simply does not exist. Either case clearly indicates a low or non-existent falsification risk and justifies the rejection of the notification by the European Commission.

The European Commission should only consider notifications for which the Member States provide adequate documentation supporting that the Directive's criteria to include a non-prescription medicine in the 'black list' are fulfilled. Under this condition, the European Commission should initiate the next step of the process, as described below.

3. Assessment for classification/inclusion in the 'black list'

The assessment of non-prescription medicines by the European Commission in order to determine whether these should bear the safety features should:

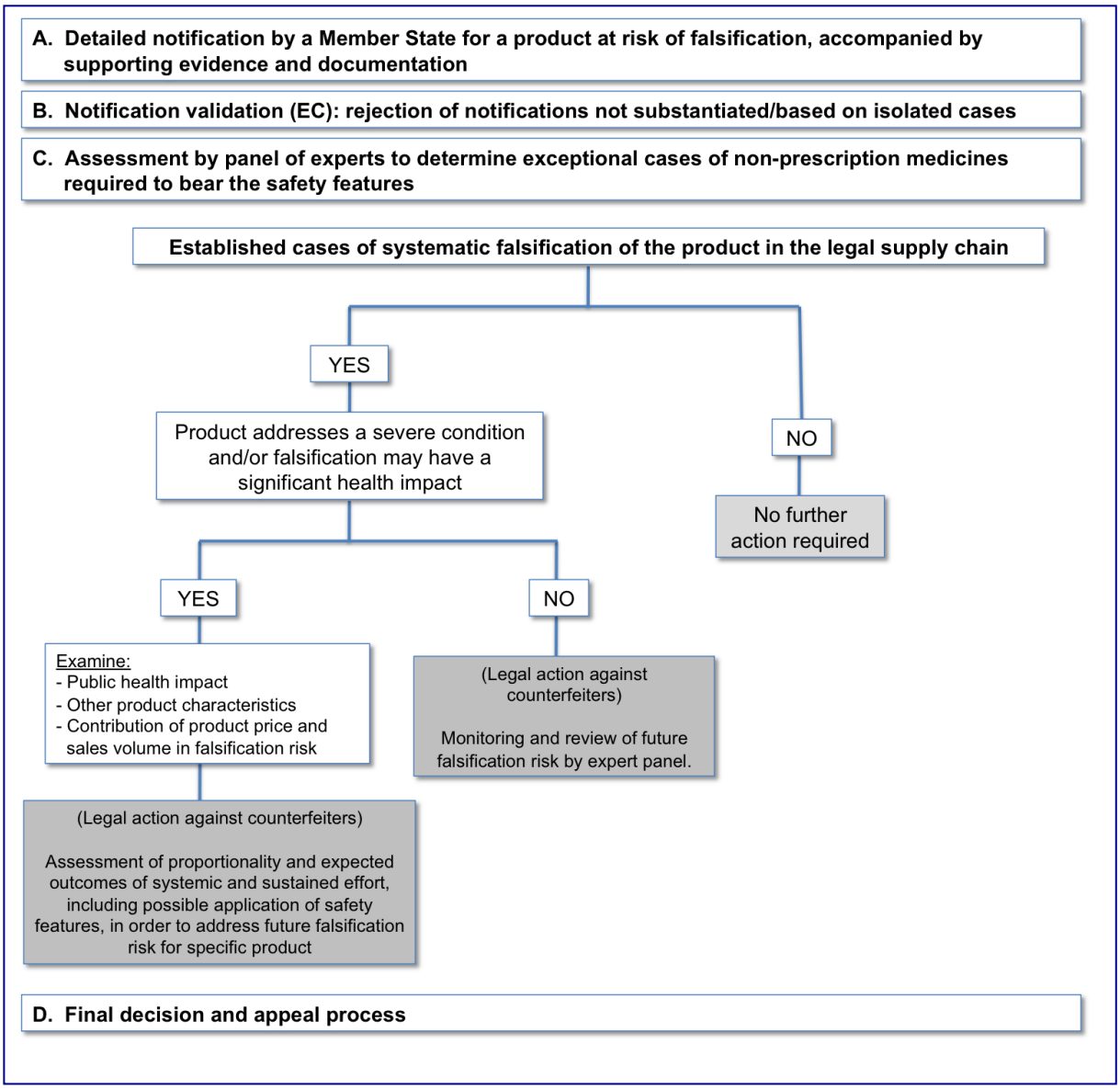
a. follow the legislative provisions
b. be conducted in a cost-effective manner without sacrificing patient safety.

As clearly shown with the example of the concept paper's quantification system, an arbitrary method to aggregate disparate risk elements is not only unscientific[5], but furthermore fails to faithfully, effectively and efficiently serve the legislation's objectives.

AESGP supports a rational and evidence-based assessment of non-prescription medicines that actually fulfil the legislation requirements to exceptionally bear the safety features and therefore go through the first two steps of the process (i.e. Member State completing and European Commission validating a notification of falsification risk) as described above. This approach follows a decision process based on, and covering, all the criteria laid down by the Directive (see Diagram 3).

[5] In order to construct a system similar to the quantification system presented in the concept paper, an exhaustive collection and analysis of data concerning the entire pharmaceutical sector (prescription-only and non-prescription medicines) would be required. Only then would it be possible to scientifically determine and appropriately weigh risk factors such as high price and volume, special characteristics and falsification impact. This data collection and analysis would not overlap with the process related to the set up of the serialisation system, which to a large extent requires different information. It would be an additional, onerous and costly exercise aiming at confirming what has already been clearly established by the legislation, i.e. that prescription medicines are in principle required to bear the safety features while non-prescription medicines are exempt.

Diagram 3. Notification, notification validation and classification assessment process to determine exceptional cases of non-prescription medicines to be included in black list



By establishing some common-sense ground rules prior to undertaking a resource-consuming data collection and analysis, the decision process demonstrated in Diagram 3 leads to an effective and efficient assessment of the falsification risk.

For example:

- As non-prescription medicines are in principle excluded from the requirement to bear the safety features, it is difficult to assume that the legislator intended for an assessment of non-prescription products for which no prior falsification case was reported to be carried out. It is therefore only reasonable and falls well within the legislative provisions not to examine the inclusion in the black list of products for which no (or only isolated) cases of falsifications have been

reported in the European market. In case of falsification of specific products in non-EU countries, a clear cause and effect link concerning the application of the measure and the possible reduction of the falsification risk should be established before examining the other criteria to determine the product's inclusion in the black list.

- In cases where systematic falsification of a non-prescription medicine is established, the impact of the legal/criminal proceedings against the counterfeiters of the falsified products found in the legal supply chain should be considered in the decision process. For example (as demonstrated in Diagram 3):
    - When cases of systematic falsification are reported for a product that does not address a severe condition and whose falsification does not present a significant health impact, an expert panel responsible for the 'black list' classification should have the possibility to monitor the case and review it based on the outcome and impact of the criminal proceedings against the counterfeiter(s) prior to deciding whether the case merits further assessment.

Should the notification by the Member State and its validation by the European Commission establish the systematic falsification of a product that (a) addresses a severe condition and/or (b) has a significant health impact, then a comprehensive assessment covering the criteria laid down by the legislation should be launched.

The risk and impact of a product's falsification cannot be determined through a political process. The assessment should rely on evidence and be conducted through on a scientific level. Therefore the assessment process for non-prescription medicines as presented under point C in Diagram 3 should be performed by a panel of experts. The panel's composition should be multidisciplinary in order to reflect the assessment process requirement to evaluate and address different elements relating to identifying and mitigating a product's falsification risk. For example, the panel should be able to provide legal expertise as well as expertise in the areas of risk assessment, crime prevention, packaging, medicine and pharmacology. Additionally, manufacturers of products under examination should participate in this process as they can provide invaluable information and take immediate action, when required.

The data requirements to properly conduct the assessment will clearly depend on the falsification cases reported and the specific product falsification-related characteristics. The assessment procedure should have the necessary flexibility to determine when and which additional information and evidence should be gathered in order to determine how to best ensure patient safety. However, the assessment procedure should be transparent. Under no circumstances should the procedure and the use of the decision process described in Diagram 3 result in a black box where decisions are delivered without being supported by sound and clear evidence.

4. Final decision and appeal process

An appeal process should be put in place in order to prevent products being wrongly proposed for inclusion in the 'black list' and to ensure the possibility of effective redress. Manufacturers should be in a position to review a proposal for inclusion in the 'black list'. In case the decision is based on false information or on conditions of which the manufacturer can provide evidence that they no longer exist, then a mechanism should be available to reverse the decision. Provision should also be made for remedial action for losses or damages due to the wrongful inclusion of a product in the 'black list'.

CONSULTATION ITEM N°13
OTHER ISSUES

- The voluntary application of safety features to non-prescription medicines as well as the notification for assessment by manufacturers concerning proprietary or competing/competitors' products should not be allowed. Any effort to use the legislation to gain a competitive advantage over competitors goes beyond the legislative provisions and is against the legislation's objectives.

Brussels, 25 April 2012