EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 December 2011

Submission of comments on the Revised Commission guidelines on Good Distribution Practice of Medicinal Products for Human Use (SANCO/C8/AM/an D(2010) 380358)

Comments from:

Name of organisation or individual
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Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	The EGA welcomes the revision of the EU GDP guideline and the opportunity to provide its comments on the draft EU GDP guideline for medicinal products.	
	The current text refers alternatively to 'distribution' and 'wholesale distribution' as if the two terms were interchangeable. We believe the two terms actually cover very different realities. The draft guideline Introduction text refers to Article 1(17) of Directive 2001/83/EC as amended for the definition of '*Wholesale distribution of medicinal products*' as '*all activities consisting of procuring, holding, supplying or exporting medicinal products, apart from supplying medicinal products to the public*.' However, Directive 2001/83/EC in the recital (35) is also referring to the need '*[…] to exercise control over the entire chain of distribution of medicinal products, from their manufacture or import into the Community through to supply to the public, so as to guarantee that such products are stored, transported and handled in suitable conditions […]*'. Based on the philosophy emphasised in the Falsified Medicines Directive, we believe the draft EU GDP Guideline actually deals with the distribution of medicinal products in a broad sense and we would	

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	therefore recommend that this be carefully defined and that terminology is used taking this broad sense into account (ie, making a clear distinction between general principles and specific requirements for wholesale distribution).	
	The word ‘’vehicle’ is currently undefined however, it is understood as any methods or means of transport, including aircraft. We would recommend that this be clarified in the final text.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
3.4		**Comment:** The physical segregation of medicinal products intended for the EU from those that are not intended for the EU poses tremendous practical feasibility questions. This is particularly critical for supply chain operators such as international manufacturers who carry out distribution. **Proposal:** The EGA proposes to remove section 3.4 from the final guidance text.	
3.9		**Comment:** The requirement to install an alarm system appears very detailed for the purpose of a general guideline on GDP. Additionally, various valid ways may be considered to prevent unauthorized access depending on the situation at stake. **Proposal:** Accordingly, the EGA would propose the following change in the proposed text **"**Prevention measures would usually include, but not be limited to, a monitored intruder alarm system and**/or** appropriate access control."	
3.15		**Comment:** The current wording lacks specificity to indicate that only the relevant equipment used and having an impact on the medicinal product quality must fulfil this requirement.	

		Proposal: We therefore propose the following change to the draft text **"**All equipment used **and impacting on** the storage and distribution of medicinal products …"	
4.8		**Comment:** Editorial comment: This seems to be a title and not a numbered item. **Proposal:** Please clarify accordingly	
5.8		**Comment:** Editorial comment **Proposal:** Suggested change 'Wholesale distributors must ensure they ~~**must**~~ supply medicinal products only to persons who are themselves in possession of the distribution authorisation or who are authorized or entitled to supply medicinal products to the public in the Member State concerned.'	
6.3		**Comment:** The draft GDP guideline has a dedicated section in chapter 6 which deals exclusively with the topic of falsified medicines. We therefore suggest to remove the mention of falsified medicines in this paragraph. Additionally, for clarity purposes, we would expect the guideline to refer to both the Manufacturing Authorisation Holder and the marketing authorisation holder in this paragraph. **Proposal:** Please change the text as proposed hereafter **"**Any complaint concerning a potential product defect ~~**or a**~~	

		~~**potential falsified product**~~ should be recorded with all the original details and investigation results **from the manufacturer and/or marketing authorization holder** ~~**ed**~~. The national competent authority should be notified without delay **by the manufacturer and/or marketing authorization holder**."	
9.1		**Comment:** Regardless of the presence of specific storage conditions for medicinal products on the package, the available data available might imply precautions and specific storage conditions which are not 'translated' as such into packaging information (which is a regulatory defined parameter). Of course, when there are set limits, these must be supported by adequate stability data showing negligible influence on product quality, safety and efficacy. **Proposal:** The proposed wording is as follows: 'The required storage conditions for medicinal products should be maintained during transportation within ~~**the**~~ defined limits' ~~**as described on the packaging information**~~	
9.6		**Comment:** This section refers to the need for procedures for the '***operation and maintenance of all vehicles and equipment*** *involved in the distribution process'.* We recommend that this paragraph refer specifically to the <u>cargo area</u> of a vehicle, not to the vehicle itself. **Proposal:** "*There should be procedures in place for the operation and maintenance of* ***the cargo area of all vehicles*** *and equipment involved in the distribution process, including*	

		cleaning and safety precautions. Particular attention should be paid to the fact that cleaning agents should not have an adverse effect on product quality."	
9.13		**Comment:** **"***In the event that the transportation of medicinal products requires* ***unloading and reloading e.g. at terminals and hubs, these premises should be audited and approved prior to deployment****. Whenever any changes are made to the approved premises or functions, attention should be paid to the continued suitability of the changed premises or functions for their intended use. Particular attention should be paid to temperature monitoring, cleanliness and the security of unguarded intermediate storage facilities."* We foresee major challenges and critical feasibility issues with the implementation of the above requirement. It is in our opinion not realistic to expect manufacturing authorisation holders and / or MAH to audit all terminals at airports and all harbours where medicines transit. Additionally, it appears equally unlikely that airports and harbours representatives will accept such audits to be carried out and moreover, in the event a company would suggest changes and improvements based on findings during their audit, there are no guarantees that these would be taken into account. **Proposal:** The EMA and European Commission should clarify whether EU GDP inspectors will initiate dialogue with customs authorities in airport and harbour storage facilities in view of future authority inspections.	
9.20		**Comment:**	

		"If refrigerated vehicles are used, the temperature monitoring equipment used during transport should be maintained and calibrated at regular intervals or at a minimum of once a year. This includes ***temperature mapping under representative conditions and should take into account seasonal variations****. Customers should be provided with data to demonstrate that products remained within the required temperature storage conditions during transportation, if requested."* We believe that a requirement for mandatory temperature mapping of the cargo area of a transport equipments is superfluous in case temperature monitoring is carried out. Furthermore, the mapping of the cargo area of all refrigerated transport equipments seems a very ambitious goal of which the cost-benefit/overall added valued for patients and medicinal product quality integrity needs to be established. **Proposal:** We recommend that the sentence regarding the mapping is removed and the temperature **monitoring** becomes mandatory. *"If refrigerated vehicles are used, the temperature monitoring equipment used during transport should be maintained and calibrated at regular intervals or at a minimum of once a year.* ***~~This includes temperature mapping under representative conditions and should take into account seasonal variations.~~*** *Customers should be provided with data to demonstrate that products remained within the required temperature storage conditions during transportation, if requested."*	
9.19		**Comment:** The current wording does not seem in line with applicable	

		terms. **Proposal:** Replace **validated** temperature-control systems by **qualified** temperature-control systems '~~**Validated**~~ **Qualified** temperature-control systems (e.g. thermal packaging, temperature-controlled containers, and refrigerated vehicles) should be used to ensure correct transport conditions are maintained between the distributor and customer.'	

Please add more rows if needed.