EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Wednesday October 26, 2011

Submission of comments on 'Commission Guidelines on Good Distribution Practice of Medicinal Products for Human Use' (EMA/…/…)

Comments from:

Name of organisation or individual
LOGSanté – French National Federation of Pharmaceutical Depositories

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).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	Wholesale is an ambiguous term and may be understood as the activity of the sole wholesaler. We prefer to use "wholesaling" to characterise the activity of all actors, in particular the wholesaler and the depository, providing wholesale activity. However, we have noticed that some chapters concern only wholesalers. Perhaps it would be necessary to have an additional definition on "Wholesaling distribution" encompassing all actors and not the only one on "Wholesale distribution" (art.1 Directive 2001/83/EC). We propose to insert a grid defining which wholesaling actors are concerned by what article. Could you please also clarify the definition of distributor, term which also appears in the guidelines?	

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)*
Chap 1 , Principle		Comment: all actors are concerned by this chapter Proposed change: Wholesaling distributors must maintain a quality system setting out responsibilities, processes and risk management measures in relation to their activities.	
Chap 1, §1.2		Comment: could you clarify whether a responsible person must be on each site of the company or if there is only one per company who can delegate to other persons her (his) responsibilities? Proposed change: A responsible person or her (his) deputies should be appointed by the management for each distribution site, who should have defined authority and responsibility for ensuring that a quality system is implemented and maintained.	
Chap 1, §1.8 iii)		Comment: could you precise what is meant by "right" recipients? Does it mean the designated recipient or the authorized recipient? What are the relevant criteria to determine the "right" recipient and who is responsible for their designation?	

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		Proposed change: NA	
Chap 1, § 1.9		Comment: Could you specify which kind of outsourced activities are concerned? Proposed change (if any): NA	
Chap 2 , § 2.1		Comment: all actors are concerned by this chapter Proposed change: The wholesaling distributor must designate a person as Responsible Person.	
Chap 2, § 2.5 vi)		Comment: Could you specify the respective responsibilities of the Responsible Person of the marketing authorization holder and the responsible person of the depository? How do you position the customers in this context? Are they the recipients or the Principals?	
Chap 2, § 2.5 vii)		Comment: Not all wholesaling actors have the power to authorize such return. Proposed change: vii) authorizing the return to saleable stock of any returned medicines when the Responsible Person is the Principal; or, implementing such decision when the Responsible Person is the subcontractor.	
Chap 2, § 2.5 xi)		Comment:	

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		1) According to the pharmaceutical definition of quarantine the word "decision" is not appropriate for all wholesaling actors. 2) We would like to add the responsibility for the Responsible person to guarantee the GMP validation process that will be used for outsourcing activities. Proposed change : xi) being involved in any decision to quarantine or dispose of returned, rejected, recalled or falsified products when the Responsible Person is the Principal; such decision is implemented by the Responsible Person of the subcontractor. xiii) validate the GMP validation processes for outsourcing activities	
Chap 3 , Principle		Comment: all actors are concerned by this chapter Proposed change: Wholesaling distributors must have suitable and adequate premises, installations and equipment, so as to ensure proper conservation and distribution of the medicinal products.	
Chap 3, § 3.2		Comment: Could explain in which situation these conditions apply? Proposed change (if any): NA	

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Chap 3, § 3.4		Comment: Is this measure in relation to the customs regulations? Can IT segregation be sufficient as stated in chapter 5, §5.24 ? Proposed change (if any): NA	
Chap 3, 3.26		Comment: All actors are concerned by this chapter. According to the terminology in EUDRALEX vol. 4 (GMP), what is meant is not a plan but a protocol; Proposed change: Wholesaling distributors should identify what qualification and/or validation work is necessary to demonstrate control of key aspects of their activities. The scope and extent of such validations should be determined by a documented risk assessment approach. Validation activities should be planned and documented. The protocol should specify acceptance criteria.	
Chap 4, 4.8		Comment: An error has occurred in the sub numbers. Proposed change: replace 4.9, 4.10 and 4.11 by i), ii) et iii).	

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Chap 5 Principle		Comment: Could you explain the use of the word "distributor" in this chapter? Proposed change: NA	
Chap 5 From § 5.1 to 5.7		Comment: Can you confirm that these paragraphs do not concern the depository actor but only Principals? Proposed change: NA	
Chap 5, § 5.8		Comment: Could you confirm that all actors have the requested capacity and are concerned by this chapter? Proposed change: Wholesaling 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.	
Chap 5, § 5.11		Comment: Could you confirm in which case this applies and which actors are concerned? Proposed change: NA	
Chap 5, § 5.17		Comment: Can you confirm that the "other products" do not encompass healthcare products like Medical Devices and/or Dermo-cosmetics and/or clinical nutrition delivered in pharmacies as far as they are all managed under the GDP rules?	

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		Proposed change: NA	
Chap 6, § 6.9 ii)		Comment: time to return the products should be adjusted to the specificity of the products. Proposed change: ii) medicinal products returns from a customer not holding a wholesale distribution authorisation should only be returned to saleable stock if they were returned within the appropriate period of time from original dispatch;	
Chap 6, § 6.9 iii)		Comment: NA Proposed change: iii) it is stated that the medicinal products have been transported, stored and handled under proper specified/predefined conditions;	
Chap 6, § 6.9 v)		Comment: spelling mistakes Propose change: v) the distributor has reasonable evidence that the product was supplied to that customer and the batch number of the dispatched product is known, that a copy of the original delivery note is attached and that there is no reason to believe that the product has been falsified.	
Chap 6, § 6.10		Comment: Could you define low temperature? Proposed change: NA	
Chap 7 Principle		Comment: Could you define the scope of the outsourcing	

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		activities described in this chapter? We understand that this chapter applies to the relation between the Principal and the depository. Proposed change: When outsourcing activities a written contract should be drawn up. When products are physically handled by the contract acceptor, both the contract giver and the contract acceptor must hold a distribution authorisation for warehousing activities. The written and signed contract should cover all wholesale distribution activities and clearly establish the duties and responsibilities of each party. Written contracts should be established for any activity likely to impact on GDP related activities.	
Chap 7, §7.5		Comment: all actors and not only the wholesaler are concerned. Proposed change: The Contract Acceptor carrying out activities falling under the definition of wholesaling distribution of medicinal products is a wholesale distributor. As such, he is subject to all obligations for wholesaling distribution of medicinal products.	
Chap 7, §7.6		Comment: the control of the third party may not require an audit which is a rather heavy procedure.	

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		Proposed change: The Contract Acceptor should not pass to a third party any of the work entrusted to him under the contract without the Contract Giver's prior evaluation and approval of the arrangements and a validation procedure of the third party.	
Chap 7,§ 7.9		Comment: In the light of chapter 7 principle, should we consider that service providers such as "pest control" or "cleaning" must hold a pharmaceutical authorization, or does such principle shall not apply to the present paragraph?	
Chap 7, § 7.10		Comment: Because of both, the level and the availability of resources needed for an audit, we should distinguish two situations: audit and simple visit Proposed change: The contracts should permit the Contract Giver to visit the Contract Acceptor at any time and audit him within the appropriate delay as established contractually between the two parties.	
Chap 9, Principle, last paragraph		Comment: Such process can be achieved with a GMP validation procedure. Proposed change: NA	
Chap 9, §9.5		Comment: The awareness of delivery drivers for specific	

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		behavior with respect to pharmaceuticals may be attained without having necessarily recourse to a training procedure for all drivers; especially if we take into consideration that such training would require heavy resources. Proposed change: Delivery drivers (including contract drivers) should be made aware of the relevant areas of GDP.	
Chap 9, § 9.11		Comment: Do you imply that the carrier must have a pharmaceutical authorization ? In reference to art. 81 EEC and art 43 EEC we feel the need to keep the transport market for pharmaceuticals open but are of course also aware of the necessity to secure transport operations. We therefore suggest the following solution: the wholesaling distributor who is the forwarding agent must have to select the carrier through a GMP validation procedure previously approved and validated by his Responsible Person (see chapter 2, §2.5, xiii). This validation process taken from GMP must consist of 3 steps: 1) process design 2) process qualification 3) continued process verification Each of these steps has to be approved and signed by the RP Proposed change: If transportation is sub-contracted to a third party then the	

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		sub contractor should be selected and habilitated for pharmaceutical transportation by the contractor applying the GMP validation procedure. In addition the contractors should be fully aware of all relevant conditions applicable to the storage and transportation of medicinal products.	
Chap 9, § 9.12		Comments: 24 hours may be problematic because deliveries in one day are not the general policy. Domestic deliveries are generally covered within 2 days. The deliveries that should transit on hubs may correspond to all Friday's shipment plus the remainder of those shipped on Thursday. We should also take into account a possible increase in the delay due to bank holiday or traffic restrictions. Proposed change: Where transportation hubs are utilized in the supply chain for domestic deliveries, a maximum time limit of normally 5 working days should be set to await the next stage of the transportation route. For the other deliveries the lead time should correspond to the products' requirements. Where medicinal products are held on the premises for longer than this defined time limit, the hub will be deemed to be acting as a storage site and required to obtain a wholesale distribution authorisation. For refrigerated product any storage at a transportation hub for any period of time would require that premises to hold a wholesalers distribution authorisation.	
Chap 9, &9.13		Comments: all hubs may have unloading and reloading activities and each relevant carrier has an average of 50 hubs	

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		per country which would make the obligation of auditing and approving before deployment rather impossible to achieve. We suggest to establish beforehand a list of the most critical hubs (according in particular to flow levels) to be audited according to the process design and continued process verification (see chap 9, §9.11) Proposed change: 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 by implementing a selection procedure according to criticity level, risk management process and an audit protocol. 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.	
Chap 9, §9.19		Comments: We would like this first paragraph to be clarified. We should guarantee that products are maintained in the right temperature during transportation. For that purpose we apply GMP validation process to determine what means and controls should be used. On request by the customer, prior to shipment, a temperature	

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		data registration could always be provided even in the case the continuous verification process would not require to use such method. Proposed change: Validated 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. On customer's request, prior to shipment, a temperature data should be provided to demonstrate that products remained within the required temperature storage conditions during transit. .	
Chap 9,§9.21		Comment: Cool-packs should also be validated prior to their use Proposed change: If cool-packs are used in insulated boxes, they need to be located such that the product does not come in direct contact with the cool-pack. Staff must be trained on the procedures for assembly of the insulated boxes (seasonal configurations) and on the re-use of cool-packs. Cool packs should be validated by a specific procedure prior to their use.	
Chap 10, Principle		Comment: could you please tell us who are targeted under the	

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		definition of broker?	

Please add more rows if needed.