Comments on the Commission Guidelines on Good Distribution Practice of Medicinal Products for Human Use

Comments from:

Name of organisation or individual
LFB Biomédicaments

1. General comments

General comment
LFB Biomédicaments welcomes the revision of the Guidelines on Good Distribution Practice of Medicinal Products for Human Use and would like to thank the European Commission for the opportunity given to participate to the revision process.

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	**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)*
Point 3.3	Comment: There is no reason to segregate quarantine products from saleable stock. Therefore, we would suggest not to include them in the list of products that should be segregated. Proposed change: "There should be segregated areas designated for the storage of product suspected of falsification, returned products, rejected product and recalled product. The appropriate degree of security should be applied in these areas to ensure that such items remain separate from saleable stock."	
Point 3.4	Comment: There is no justification to keep medicinal products not intended for the Union market in segregated areas. At any time, these products can be identified by their specific article code. Furthermore, regarding GDP requirements, these products follow the same rules as those for products for Union market. Proposed change: Point 3.4 should be deleted.	
Point 3.25	Comment: Crash tests should be performed to ensure procedures are adequately defined. Proposed change: "Procedures to be followed if the system fails or breaks down should be defined. This should include systems for the restoration of data. These procedures should be previously and periodically tested."	
Point 4.8	Comment: Numbering issue: in order to stay in line with the numbering system of the text, please delete the numbering "4.8" of "4.8 Records" (which is described in the following point) and change accordingly the following number sequence. Proposed change: **Records**	

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Point 5 "Operations", "Principle", 2nd paragraph	Comment: Some medicinal products may not have marketing authorisation despite being authorized for distribution. This is the case for example for compassionate use medicinal products or investigational medicinal products. Thus we propose to widen the scope of medicinal products authorised for distribution by a wholesale distributor. Proposed change: "All medicinal products distributed in the EU by a wholesale distributor have to have a marketing authorisation or other authorisation for distribution (e-g Compassionate use authorisation, Investigational Medicinal Products authorisation) granted by the EU or by a Member State. If the product is intended to be exported see below."	
Point 5 "Operations", "Principle", 3rd paragraph	Comment: This point should be completed to describe situations when the distributor should notify the MAH and competent authority. Proposed change: "Any distributor, not being the Marketing Authorisation Holder, who imports a medicinal product from another Member State, outside the scope of a distribution partnership between the distributor and the MAH, shall notify the MAH and the competent authority in the MS to which the medicinal product will be imported of his intention to import that product. All key operations should be fully described in the quality management system in appropriate standard operating procedures."	
Point 5.11	Comment: This chapter seems to describe the case of the distribution of a medicinal product in a Member State where no Marketing Authorisation is granted. In this case, we suggest to be clear that this case can only exist if the competent authority of the Member State has granted a specific authorisation; the only submission of a copy of the marketing Authorisation seems not sufficient. Proposed change Wholesale distributors wishing to distribute or distributing medicinal products in Member State(s) where no Marketing Authorisation is granted (the Marketing Authorisation is granted only in an other Member State) should obtain a	

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	specific authorisation from the competent authorities where the product is intended to be launched.	
Point 5.33	Comment: We propose to specify that it could be not only a person who exports a product. It seems to us important to underline that a person or an entity who exports should have a manufacturing authorisation. Proposed change: "The export of medicinal products falls within the definition of "wholesale distribution"[18]. A person or an entity exporting medicinal products must thus hold a wholesale distribution authorisation or a manufacturing authorisation. This is also the case if the exporting wholesale distributor is operation from a free zone."	
Point 5.34 - c	Comment: The point c seems unclear for us: does the text mean that the supplier mentioned is the supplier of the third country where the product comes from? We would appreciate if you can provide with clarifications on the supplier identity and role. Proposed change: N/A	
Point 5.35	Comment: We propose to detail to whom the rules for document enclosure apply in the case described in that point. Proposed change: "If the medicinal product is supplied to a person in a third country authorized or entitled to supply medicinal products to the public, the rules for document enclosure apply to the entity in Europe who exports in the third country as for supply of the medicinal product established in the EU.[21] "	
Point 6.1	Comment: We would like to take the opportunity of this section to request the notification to the supplier of a complaint about the distribution (e.g. thefts, accidents). Proposed change: "There should be a written procedure in place for the handling of complaints. A distinction should be made between complaints about the quality of a medicinal product and those relating to distribution. In the case of a complaint about the	

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	quality of a medicinal product, the manufacturer and/or marketing authorisation holder should be informed without delay. In case of complaint about the distribution of a medicinal product, the supplier and Marketing Authorisation Holder should be informed without delay."	
Point 6.3	Comment: We propose the Marketing Authorisation Holder is also informed of such a complaint. Proposed change: Any complaint concerning a potential product defect or a potential falsified product should be recorded with all the original details and investigated. The national competent authority and the Marketing Authorisation Holder should be notified without delay.	
Points 6.9 and 6.10	Comment: For rare medicinal products, dealing with serious diseases for which the quantities to be administered are difficult to predict, it may be useful to return the medicinal product after five days. Therefore we would like to propose to add a new section, located between sections 6.10 and 6.11. Proposed change: new section: "Rare medicinal products dealing with serious diseases for which the quantities to be administered are difficult to predict can be return to saleable stock in more than within five days of original dispatch providing: - pharmaceutical traceability is ensured by the customer and approved by the supplier and Marketing Authorisation Holder, and - customer demonstrates the medicinal products have been stored within the authorised storage conditions in qualified premises throughout the entire time and the transportation performed according to the supplier and Marketing Authorisation Holder recommendations, and - the Qualified Person supplying the medicinal products approves the return. These operations should be fully described in appropriate standard operating procedures."	

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Chapter 7: "Contract Operations", "Principle"	Comment: This part of the GDP concerns some parts of the distribution flow which are not directly managed by the wholesaler. In the specific case of the exportation of products, the entity or person falls within the "wholesale distribution" as stated point 5.33 (p18). Consequently it must hold a distribution authorisation (or a manufacturing authorisation). But this exportation entity can outsource activities, which are not its direct activity. Of course those parts of the logistic flow must be assessed by the contract giver for the part of the flow subcontracted, but it is not relevant that the contract acceptor (such as freight forwarders or handlers) must hold a distribution authorisation and all associated obligations. Proposed change: When outsourcing activities a written contract should be drawn up. Both the contract giver and the contract acceptor must hold a distribution authorisation for distribution 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. A contract acceptor not dealing with distribution activities (such as transportation) does not require a distribution authorisation.	
Point 7.6	Comment: We propose to stipulate in case the Contract Acceptor decides to pass to a third party any of the work entrusted to him, he will then be responsible to perform the corresponding audit. 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 an audit of the third party. The audit of the third party should be performed by the Contract Acceptor who decides to pass to a third party a part of the work entrusted to him. The Contract Acceptor is responsible of all the activities according to the contract with the Contract Giver. Arrangements made between the Contract Acceptor and any third party should ensure that the wholesale distribution information is made available in the same way as between the	

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	original Contract Giver and Contract Acceptor.”	
Point 9 “Principle”	Comment: We would like to draw your attention on the management of the customs clearance operations. Proposed change: Please add the following “The storage environment for customs clearance remain under the responsibility of local authorities”	
Point 9.12	Comment: We understand the need of a maximum time limit for waiting next stage of transportation. Nevertheless, we propose to set this time limit according to an appropriate assessment, as a pre-defined time limit of 24 hours for all medicinal products seems not to be supported by any data. Accordingly, there is no need to request a distribution authorisation for premises of transportation hub where refrigerated products wait the next stage of the transportation route. Proposed change: “Where transportation hubs are utilised in the supply chain, a maximum time limit should be set according to an appropriate assessment to await the next stage of the transportation route. 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. “	
Point 9.13	Comment: In the event described by this point, the need is to obtain the confirmation that the premises have been qualified. Thus there is no need to perform an audit prior to deployment in case data are provided on demand. 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 evaluated 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	

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	temperature monitoring, cleanliness and the security of unguarded intermediate storage facilities."	
Point 9.16	Comment: International regulations should avoid any duplication of labels. Proposed change: "Containers should bear labels providing sufficient information on handling and storage requirements and precautions to ensure that the products are properly handled and secured at all times. The containers should enable identification of the contents of the containers and the source. Labelling should follow international regulations in order to be harmonised."	
Point 9.16	Comment: Information regarding the expiry date of the insulated boxes should be added on labels. Proposed change: "Containers should bear labels providing the expiry date of the insulated boxes, sufficient information on handling and storage requirements and precautions to ensure that the products are properly handled and secured at all times. The containers should enable identification of the contents of the containers and the source."	
Points 9.19	Comment: If the distribution is properly validated, customers should not need to obtain temperature data for each delivery. 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."	
Point 9.20	Comment: This chapter describes that validated temperature-control systems should be used to ensure transport conditions. If the transport systems are validated, why is it required to provide temperature data to customers? In the case of exportation to a third country, and in case of	

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	agreement between both parties, it could be given a green light by the distributor (or the manufacturer) based on the assessment of the temperature data through the logistic flow (transport release instead of temperature data). Proposed change: "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."	
Point 10.4 4th bullet point	Comment: In order to stay in line with comments we provide on chapter 5, we would like to widen the scope of concerned products to products having a marketing authorisation or an equivalent authorisation. Proposed change: "- procedure for ensuring that medicinal products brokered have a marketing authorisation or an equivalent authorisation."	