<18 July 2013>

Submission of comments on:

GMP revision: Chap 3 – Premises and Equipment
GMP revision: Chap 5 - Production
GMP revision: Chap 6 – Quality Control
GMP revision: Chap 8 - Complaints and Product Recall

Comments from:

Name of organisation or individual
BPI – German Pharmaceutical Industry Association

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)*
	Structure of the Table Of Comments (ToC) 1.) File format We doubt that it increases the safety of EMA's IT-structures very much that interested parties are being invited to send their comments using doc(x)-files. Even though it might make life easier when compiling the comments of different stakeholders data and/ or IT-safety should be an issue for the agency, too. We strongly recommend the use of pdf-files instead. 2.) Structure We have found it rather exhausting to use the suggested structure of the ToC and we have severe doubts that this structur will help understanding all comments, since we have rearranged Chapter 8 (see the attached table for Chapter 8). Instead, we suggest the following structure: A | B | C | D | E A - Line number(s) of the relevant text (e.g. Lines 20-23)	

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	B - Stakeholder number (to be completed by the Agency) C - Comment and rationale D - Proposed changes E - Outcome (if applicable) (to be completed by the Agency)	

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)*
Chapter 3 (Premises and Equipment), No. 3.6		*Comment* The toxicological evaluation should not be required for ALL products manufactured. It should only be required for certain hazardous contaminants such as highly sensitizing materials (such as beta lactams), biological preparations containing living organisms, certain hormones, cytotoxics, and other highly active materials. *Proposed change (changes in bold)* 3.6 Cross-contamination should be avoided for all products by appropriate design and operation of manufacturing facilities. The measures to prevent should be commensurate with the risks. Quality Risk Management principles should be used to assess and control the risks. **For the production of particular medicinal products, such as highly sensitising materials (e.g. penicillins), biological preparations (e.g. from live micro-organisms), certain antibiotics, certain hormones, certain cytotoxics or certain highly active drugs risk assessment should include a toxicological evaluation (see Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities). For these particular products dedicated facilities**	

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		are required when they present a risk: a) Which cannot be adequately controlled by operational and/or technical measures or b) Scientific data does not support threshold values (e.g. allergenic potential from highly sensitizing materials such as beta lactams) or c) Threshold values derived from the toxicological evaluation are below the levels of detection. Further guidance including some exemptions could be found in Chapter 5 and in Annex 2, 3, 4, 5 of the EU detailed guidelines on GMP and the guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities.	
Chapter 5 (Production) 5.17		*Comment* If a cross-contamination can be safely excluded, the use of the equipment for the production of medical devices, cosmetics and/ or food supplements shall be permitted. *Rationale* The production of medical devices, cosmetics and/ or food supplements is a usual procedure and does not lead to exceptional problems as long as cross-contamination is prevented and the measures described below are being taken. *Proposed change (in bold)*	

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		The production of non-medicinal products in areas and with equipment destined for the production of medicinal products should only be allowed where the measures described below and in Chapter 3 are sufficient to prevent cross-contamination. **The production of technical poisons shall be treated differently.**	
Chapter 5 (Production) 5.19		*Comment* The toxicological evaluation should not be required for ALL products manufactured. It should only be required for certain hazardous contaminants such as highly sensitizing materials (such as beta lactams), biological preparations containing living organisms, certain hormones, cytotoxics, and other highly active materials. (see also Chapter 3, no. 3.6) *Proposed change (in bold)* A Quality Risk Management approach should be used based upon the potential cross contamination risks prevented by the products manufactured. Factors including: facility/equipment design, personnel flow, physico-chemical characteristics of the active substance, process characteristics, cleaning processes and analytical capabilities relative **to acceptance criteria (e.g. 10 ppm, 1/1000 dosis)** should also be taken into account. … or product family. This may range from … entire manufacturing facility. It may be acceptable …, where justified. The outcome of the Quality Risk Management process should be the basis for determining the necessity for and extent to which equipment and facilities should be dedicated to a particular product or product family. This may range from dedicating specific product contact parts to dedication of the entire manufacturing facility. It may be acceptable to confine	

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		manufacturing activities to a segregated, self contained production area within a multiproduct facility, where justified. **In case of particular medicinal products, such as highly sensitising materials (e.g. penicillins), biological preparations (e.g. from live micro-organisms), certain antibiotics, certain hormones, certain cytotoxics or certain highly active drugs** a toxicological evaluation should be the basis for the establishment of threshold values in relation to the products manufactured (see Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities). Where the toxicological evaluation supports a threshold value, this should be used as an input parameter in risk assessment.	
5.20, 1st paragraph		*Comment/ Rationale* This document/ listing might attract inspectors to use it as a "checklist". Reality in itself might be much more versatile than to be reflected in a paper like this. *Proposed change (in bold)* **The outcome of the Quality Risk Managemnet process should be the basis for determining the necessity for and the extend of** technical and organisational measures to mitigate risks of cross-contamination **which** could include, but are not limited to, the following: ...	
5.26, 1st paragraph		*Comment* Not in all cases a direct purchase from manufacturer of starting materials is beneficial; it is rather an ideal situation. In all cases where small quantities are being ordered, the power to demand specific documents from the manufacturer etc. is much higher in the	

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		case of a trader who orders larger quantities. *Proposed change* ...the supply chain and the associated risks involved. ~~Where possible starting materials should be purchased directly from the manufacturer of the starting material.~~	
5.27, 3rd paragraph		*Comment* The medicinal product manufacturer regularly has no contact and business relation, respectively with the active substance starting materials manufacturers. Thus, it is sufficient that the active substance manufacturer has supply chain and traceability records of the active substance starting materials. And it is the task of the medicinal product manufacturer to check this when performing his audit of the active substance manufacturer. *Proposed change* The supply chain and traceability records for each active substance ~~(including active substance starting materials)~~ should be available and be retained by the EEA based manufacturer or importer of the medicinal product.	
5.27; 4th paragraph		*Comment* Active substance manufacturers regularly have business relations to several medicinal product manufacturers. Every medicinal product manufacturers performs audits acc. to EU-GMP-Guide part II. Thus it should be possible that audit reports can be exchanged among medicinal product manufacturers and accepted after evaluation. This	

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		should be possible without concluding a contract. *Proposed change (in bold)* Audits should be carried out at the manufacturers and distributors of active substances to confirm that they comply with the relevant good manufacturing practice and good distribution practice requirements. The holder of the manufacturing authorization shall verify such compliance either by himself, **another EEA medicinal product manufacturer** or through an entity acting on his behalf under a contract. For veterinary medicinal products, audits should be conducted based on risk.	
5.30		*Comment* The adoption of the batch number assigned by the manufacturer of the starting material can also be appropriate. *Proposed change* Labels should bear at least the following information: - The designated name...applicable;. - a batch number ~~given at receipt~~;	
5.33		*Comment* To avoid double or unnecessary work we strongly suggest the introduction of a risk-based approach here.	
5.33, lit a)		*Comment* If this paragraph would be applicable to all starting materials the need for a full analysis at both the API manufacturers' site as well as at the pharmaceutical company's site might be needed.	

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		Rationale We suggest a wording that emphasizes the need for those examinations based on a risk assessment/ based on the criticality of the APIs. *Proposed change* a) For critical starting materials, a formal agreement…..	
5.33, lit b)		*Comment* Both active substances and excipients belong to starting materials. Whereas the qualification of an active substance manufacturer is based on an audit, excipients manufacturers can also be qualified by other tools/activities. *Proposed changes (in bold)* b) The finished product manufacturer should perform **a verification, which might include** audits ~~at appropriate intervals~~ at the site(s)**,** carrying out the testing (including sampling) of the starting materials in order to assure compliance with Good Manufacturing Practice and with the specifications and testing methods described in the Marketing Authorisation dossier.	
5.33, lit e)		*Comment* The performance of a full analysis is not necessary and will not create a higher level of safety but will only increase the effort at the manufacturer's side of the finished products. *Proposed changes (in bold)* The finished product manufacturer should also perform a**n** ~~full analysis~~ **analysis of critical parameters** at appropriate intervals	

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5.37		*Comment* The detailed listing of all requirements concerning the tech-transfer does not seem to be appropriate here. *Proposed changes (in bold)* **Delete.**	
5.68		Comment This Chapter (Product shortage due to manufacturing constraints) should be cancelled totally. The supply shortage is not within the scope of GMP. *Proposed changes (in bold)* **Delete Chapter 5.68**	
Chapter 6 6.16		*Original* The results obtained should be recorded, trended and checked to make sure that they are consistent with each other. *Comment* Trending and checking of ALL results is not appropriate. *Proposed changes (in bold)* The results obtained should be recorded. **Results of critical parameters should be** trended and checked to make sure that they are consistent with each other.	
Chapter 6 6.7, 3rd bullet		*Comment* Whereas the terms OOS and OOT are defined /well known this does not apply for the term "anomalous". Instead, this will create	

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point		confusion. *Proposed changes (in bold)* Cancel the words "and anomalous results". - a procedure for the investigation of Out Of Specification ~~**and anomalous results**~~ and Out Of Trend results;	
Chapter 6 6.9		*Comment* There is a huge difference between OOS and OOT (during Stability testing). *Proposed changes (in bold)* Some kind~~**s**~~ of data (e.g. tests results, yields, environmental controls) should be recorded in a manner permitting trend evaluation. Any out of trend ~~**or out of specification**~~ data should be addressed and subject to investigation.	
Chapter 6 6.15		*Comment/ Rationale* Not ALL testing/ analytical methods need to be validated, for example pharmacopoeial methods. *Proposed changes (in bold)* **Were necessary, t**esting methods should be validated. A laboratory that is using a testing method and which did not perform the original validation (e.g. the use of a compendial method), should verify the appropriateness of the testing method. All testing operations described in the marketing authorisation or technical dossier should be carried out according to the approved methods.	

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Chapter 6 6.16		*Comment/ Rationale* It is definitely not necessary to trend and check all results. This will create a huge load of data/ paper with no additional benefit. *Proposed changes (in bold)* The results obtained should be recorded**. Results of critical parameters should be** trended and checked to make sure that they are consistent with each other. Any calculations should be critically examined.	
Chapter 6 6.22		*Original* Their in-use shelf life should be established / documented and scientifically justified. The expiry date of unstable reagents and culture media should be indicated on the label, together with specific storage conditions. *Comment/ Rationale* It is definitely not necessary to establish, document or justify the shelf life of NaCl (known as Sodium Chloride). This, again, will create a huge load of data/ paper with no additional benefit. *Proposed changes (in bold)* **For critical substances/ media and/ or those with known stability problems the** ~~Their~~ in-use shelf life should be established / documented and scientifically justified. The expiry date of unstable reagents and culture media should be indicated on the label, together with specific storage conditions.	
Chapter 6		*Comment*	

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6.37 and 6.39		There is no official guideline in place which defines rules and requirements for the transfer of analytical procedures (TAP) and which kind of test have to be performed. Furthermore different types of TAP are possible e.g. TAP without experimental support of the giving lab. *Proposed change* - Prior to transferring a test method, ~~the transferring side should~~ it should be verified that the test method(s) comply... - Identification of standards and samples to be tested ~~by both laboratories~~	
Chapter 8 Principle		Original **Complaints and Product Recall** All complaints and other information concerning potentially defective products must be reviewed carefully according to written procedures. In order to provide for all contingencies, and in accordance with Article 117 of Directive 2001/83/EC and Article 84 of Directive 2001/82/EC, a system should be designed to recall, if necessary, promptly and effectively products known or suspected to be defective from the market. *Rationale* Only in case of severe problem appropriate measures are justified. *Proposed Change (in bold)* Complaints**, Quality Defects** and Product Recalls **To protect public and animal health, a system and appropriate procedures should be in place to record, investigate and review complaints including potential quality defects, and if**	

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		necessary, to effectively and promptly recall medicinal products for human or veterinary use and investigational medicinal products from the distribution network. Quality Risk Management principles should be applied to the investigation and assessment of quality defects and to the decision-making process in relation to product recalls and other risk-reducing actions. Guidance in relation to these principles is provided in Chapter 1. **All concerned competent authorities should be informed in case of a quality defect (faulty manufacture, product deterioration, detection of falsification, non-compliance with the marketing authorisation or product specification file, or any other serious quality problems) with a medicinal or investigational medicinal product which may result in the recall of the product or an abnormal restriction in the supply.** **In case of outsourced activities, a contract should describe the role and responsibilities of the manufacturer, the Marketing Authorisation Holder and/ or Sponsor and any other relevant third parties in relation to assessment, decision-making, and dissemination of information and implementation of risk-reducing actions relating to a defective product. Guidance in relation to contracts is provided in Chapter 7.**	
Chapter 8.1 and 8.9		*Original* 8.1 A person should be designated responsible for handling the complaints and deciding the measures to be taken together with sufficient supporting staff to assist him. If this person is not the Qualified Person, the latter should be made aware of any complaint,	

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		investigation or recall. 8.9 A person should be designated as responsible for execution and co-ordination of recalls and should be supported by sufficient staff to handle all the aspects of the recalls with the appropriate degree of urgency. This responsible person should normally be independent of the sales and marketing organisation. If this person is not the Qualified Person, the latter should be made aware of any recall operation. *Proposed Change* 8.1. Appropriately trained and experienced personnel should be responsible for managing complaint and quality defect investigations and for deciding the measures to be taken to manage any potential risk(s) presented by those issues, including recalls. These persons should be independent of the sales and marketing organisation, unless otherwise justified. If these persons do not include the Qualified Person who is involved in the certification for release of the concerned product, the latter should be made formally aware of any investigations, any risk-reducing actions and any recall operations, in a timely manner *Rationale* Marketing and Sales Dept. shall not be excluded from the process. 8.2 Sufficient personnel and resources should be made available for the handling, reviewing and investigation of complaints and quality defects and for implementing any risk-reducing actions. Sufficient	

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		personnel and resources should also be available for the management of interactions with competent authorities. 8.3 The use of inter-disciplinary teams should be considered, including appropriately trained Quality Management personnel. 8.4 In situations in which complaint and quality defect handling is managed centrally within an organisation, the relative roles and responsibilities of the concerned parties should be documented. Central management should not, however, result in delays in the investigation and management of the issue.	
Chapter 8.2.		*Original* Procedures for handling and investigating complaints including possible quality defects 8.2 There should be written procedures describing the action to be taken, including the need to consider a recall, in the case of a complaint concerning a possible product defect. *Proposed Change* 8.5 There should be written procedures describing the actions to be taken upon receipt of a complaint. All complaints should be documented and assessed to establish if they represent a potential quality defect or other issue. 8.6	

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		As not all complaints received by a company may represent actual quality defect issues, complaints which do not indicate a potential quality defect should be documented appropriately and communicated to the relevant group or person responsible for the investigation and management of complaints of that nature, such as suspected adverse events. 8.7 There should be procedures in place to facilitate a request to investigate the quality of a batch of a medicinal product to support an investigation into a reported suspected adverse event. 8.8 When a quality defect investigation is initiated, procedures should be in place to address at least the following: i. The description of the reported quality defect. ii. The determination of the extent of the quality defect. The checking or testing of reference and/or retention samples should be considered as part of this, and in certain cases, a review of the batch production record should be performed. (Risk based, where necessary) iii. The need to request a sample of the defective product from the complainant and, where a sample is provided, the need for an appropriate evaluation to be carried out. The distribution information for the batch(es) in question. The assessment of the risk(s) posed by the quality defect. (Risk based, where necessary) iv. The decision making process that is to be used concerning the potential need for risk-reducing actions to be taken in the distribution network, such as batch or product recalls, or	

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		other actions. (Risk based, where necessary) v. The assessment of the impact that any recall action may have on the availability of the medicinal product to patients/animals in any affected market and the need to notify any such impacts to the relevant authorities if life-saving drugs are concerned. vi. The internal and external communications that should be made in relation to a quality defect and its investigation. vii. The identification of the potential root cause(s) of the quality defect on the base of a risk assessment. The need for appropriate Corrective and Preventative Actions (CAPAs) to be identified and implemented for the issue, and for the assessment of the effectiveness of those CAPAs on the base of a risk assessment.	
Chapter 8 8.3		*Original* Investigation and Decision Making 8.3 Any complaint concerning a product defect should be recorded with all the original details and thoroughly investigated. The person responsible for Quality Control should normally be involved in the study of such problems. *Proposed Change* 8.9 The information reported in relation to possible quality defects should be recorded, including all the original details. The validity and extent of all reported quality defects should be documented and	

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		assessed in accordance with quality risk management principles in order to support decisions regarding the degree of investigation and action taken.	
Chapter 8 8.4 & 8.8		*Original* 8.4 If a product defect is discovered or suspected in a batch, consideration should be given to checking other batches in order to determine whether they are also affected. In particular, other batches which may contain reworks of the defective batch should be investigated. *Proposed Change* 8.10 If a quality defect is discovered or suspected in a batch, consideration should be given to checking other batches and in some cases other products, in order to determine whether they are also affected. In particular, other batches which may contain portions of the defective batch or defective components should be investigated. (Risk based, where necessary) 8.11 Quality defect investigations should include a review of previous quality defect reports or any other relevant information for any indication of specific or recurring problems requiring attention and possibly further regulatory action Risk based, where necessary 8.12 The decisions that are made during and following quality defect investigations should reflect the level of risk that is presented by the quality defect as well as the seriousness of any non-compliance with	

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		respect to the requirements of the marketing authorisation/ product specification file or GMP. Such decisions should ensure that patient and animal safety is maintained in a timely manner, in a way that is commensurate with the level of risk that is presented by those issues. 8.13 As comprehensive information on the nature and extent of the quality defect may not always be available at the early stages of an investigation, the decision-making processes should still ensure that appropriate risk-reducing actions are taken at an appropriate time-point during such investigations. All the decisions and measures taken on the base of a risk assessment and as a result of a quality defect should be documented. *Original* 8.8 The competent authorities should be informed if a manufacturer is considering action following possibly faulty manufacture, product deterioration, detection of counterfeiting or any other serious quality problems with a product *Proposed Change* **Fits better into this (sub)paragraph** 8.14 Quality defects should be reported in a timely manner by the manufacturer to the Marketing Authorisation Holder/ Sponsor and all concerned Competent Authorities in cases where the quality defect may result in the recall of the product or in an abnormal restriction in the supply of the product if life-saving drugs are concerned.	

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Chapter 8 8.7		*New* Root Cause Analysis and Corrective and Preventative Actions 8.15 An appropriate level of root cause analysis work should be applied during the investigation of quality defects. In cases where the true root cause(s) of the quality defect cannot be determined, consideration should be given to identifying the most likely root cause(s) and to addressing those on the base of a risk assessment. *Original* 8.7 Special attention should be given to establishing whether a complaint was caused because of counterfeiting. *Proposed Change* 8.16 Special attention should be given **on a risk based approach** to establishing whether a **quality defect** relates to falsification. 8.17 Where human error is suspected or identified as the cause of a quality defect, this should be formally justified and care should be exercised so as to ensure that process, procedural or system-based errors or problems are not overlooked, if present. Risk based, where necessary 8.18 Appropriate corrective and/or preventative actions (CAPAs) should be identified and taken in response to a quality defect. The	

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		effectiveness of such actions should be monitored and assessed. Risk based, where necessary 8.19 Quality defect records should be reviewed and trend analyses should be performed **on a risk based approach** regularly for any indication of specific or recurring problems requiring attention.	
Chapter 8 8.10		*Original* **Product Recalls and other potential risk-reducing actions** 8.10 There should be established written procedures, regularly checked and updated when necessary, in order to organise any recall activity. *Proposed change* 8.20 There should be established written procedures, regularly **reviewed** and updated when necessary, in order to **undertake** any recall activity **or implement any other risk-reducing actions**. 8.21 Any retrieval of product from the distribution network as a result of a quality defect should be regarded and managed as a recall **on a risk based approach**.	
Chapter 8 8.11 – 8.16		*Original* 8.11 Recall operations should be capable of being initiated promptly and at any time.	

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		Proposed change 8.22 Recall operations should be capable of being initiated promptly and at any time. In certain cases recall operations may need to be initiated to protect public or animal health prior to establishing the root cause(s) and full extent of the quality defect *Original* 8.13 The distribution records should be readily available to the person(s) responsible for recalls, and should contain sufficient information on wholesalers and directly supplied customers (with addresses, phone and/or fax numbers inside and outside working hours, batches and amounts delivered), including those for exported products and medical samples. *Proposed change* 8.23 The batch/product distribution records should be readily available to the persons responsible for recalls, and should contain sufficient information on wholesalers and directly supplied customers (with addresses, phone and/or fax numbers inside and outside working hours, batches and amounts delivered), including those for exported products and medical samples 8.24 In the case of investigational medicinal products, all trial sites should be identified and the countries of destination should be indicated. In the case of an investigational medicinal product for which a marketing authorisation has been issued, the manufacturer of the	

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		investigational medicinal product should, in cooperation with the sponsor, inform the marketing authorisation holder of any quality defect that could be related to the authorised medicinal product. The sponsor should implement a procedure for the rapid unblinding of blinded products, where this is necessary for a prompt recall. The sponsor should ensure that the procedure discloses the identity of the blinded product only in so far as is necessary. All aforementioned actions should be taken on the basis of **on a risk based approach.** 8.25 Consideration should be given following consultation with the concerned Competent Authorities, as to how far into the distribution network a recall action should extend, taking into account the potential risk to public or animal health and any impact that the proposed recall action may have. The Competent Authority should also be informed in situations in which no recall action is being proposed for a defective batch because the batch has expired (such as with short shelf-life products.). All aforementioned actions should be taken on the basis of **on a risk based approach.** *Original* 8.12 All Competent Authorities of all countries to which products may have been distributed should be informed promptly if products are intended to be recalled because they are, or are suspected of being defective. *Proposed change/ Rationale*	

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		Fits better into this (sub)paragraph 8.26 All concerned Competent Authorities should be informed in advance in cases where products are intended to be recalled. For very serious issue (i.e. those with the potential to seriously impact upon patient or animal health), rapid risk-reducing actions (such as a product recall) may have to be taken in advance of notifying the Competent Authorities. Wherever possible, attempts should be made to agree these in advance of their execution with the concerned Competent Authorities. 8.27 It should also be considered whether the proposed recall action may affect different markets in different ways, and if this is the case, appropriate market-specific risk-reducing actions should be developed and discussed with the concerned competent authorities. The risk of shortage of an essential medicinal product which has no authorised alternative should be considered before deciding on a risk-reducing action such as a recall. Any decisions not to execute a risk-reducing action which would otherwise be required should be agreed with the competent authority in advance.	
Chapter 8 8.14		*Original* 8.14 Recalled products should be identified and stored separately in a secure area while awaiting a decision on their fate. *Proposed change* 8.28 Recalled products should be identified and stored separately in a	

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		secure area while awaiting a decision on their fate. A formal disposition of all recalled batches should be made and documented and the rationale for the disposition of recalled products (or any reworked versions of them) should be documented and discussed with the relevant competent authority. The extent of shelf-life remaining for any reworked batches that are being considered for placement onto the market should also be considered.	
Chapter 8 8.15		*Original* 8.15 The progress of the recall process should be recorded and a final report issued, including reconciliation between the delivered and recovered quantities of the products. *Proposed change* 8.29 The progress of the recall process should be recorded and a final report issued, including reconciliation between the delivered and recovered quantities of the concerned products/batches.	
Chapter 8 8.16		*Original* 8.16 The effectiveness of the arrangements for recalls should be evaluated regularly. *Proposed change* 8.30 The effectiveness of the arrangements in place for recalls should be periodically evaluated to confirm that they remain robust and fit for use. Such evaluations should extend to both within office-hour	

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)*
		situations as well as out-of-office hour situations and, when performing such evaluations, consideration should be given as to whether mock-recall actions should be performed. This evaluation should be documented and justified 8.31 In addition to recalls, there are other potential risk-reducing actions that may be considered in order to manage the risks presented by quality defects. Such actions may include the issuance of cautionary communications to healthcare professionals in relation to their use of a batch that is potentially defective. These should be considered on a case-by-case basis and discussed with the concerned competent authorities **on the basis of on a risk based approach.**	