Chapter 3

Proposal	EIGA proposal
Production Area 3.6 Cross-contamination should be avoided for all products by appropriate design and operation of manufacturing facilities. The measures to prevent cross-contamination should be commensurate with the risks. Quality Risk Management principles should be used to assess and control the risks. Risk assessment should include among other parameters a toxicological evaluation of the products being manufactured (see Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities). Dedicated facilities are required for manufacturing when a medicinal product presents 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 sensitising 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.	***Production Area*** 3.6 Cross-contamination should be avoided for all products by appropriate design and operation of manufacturing facilities. The measures to prevent cross-contamination should be commensurate with the risks. Quality Risk Management principles should be used to assess and control the risks. Risk assessment should include among other parameters a toxicological evaluation of the products being manufactured (see Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities). Dedicated facilities are required for manufacturing when a medicinal product presents 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 sensitising 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, **6** 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. ***Note : Annex 6 on Medicinal Gases should also be listed***

Chapter 8

Proposal	EIGA proposal
Principle …….. 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.	**Principle** …….. All concerned competent authorities should be informed in case of a **serious batch related** 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.
Personnel and Organisation	**Personnel and Organisation**
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.	8.1 Appropriately trained and experienced personnel should be responsible for managing complaint and **batch** 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.
Procedures for handling and investigating complaints including possible quality defects	**Procedures for handling and investigating complaints including possible quality defects**
8.8 When a quality defect investigation is initiated, procedures should be in place to address at least the following: — The description of the reported quality defect. — 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	8.8 When a quality defect investigation is initiated, procedures should be in place to address at least the following: — The description of the reported quality defect. — The determination of the extent of the quality defect. The checking or testing of reference and/or retention samples, **where appropriate,** should be considered as part of this, and in certain

batch production record should be performed. — 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. — 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 other actions. — 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. — The internal and external communications that should be made in relation to a quality defect and its investigation. — The identification of the potential root cause(s) of the quality defect. — 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.	cases, a review of the batch production **and release** record should be performed. — The need to request a sample **or the return (depending on the package)** 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. — 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 other actions. — 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. — The internal and external communications that should be made in relation to a quality defect and its investigation. — The identification of the potential root cause(s) of the quality defect. — 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.
Investigation and Decision Making	**Investigation and Decision Making**
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.	8.14 **Serious batch related** 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.