ACTIVE PHARMACEUTICAL INGREDIENTS COMMITTEE

GDP for APIs:

"How to do" Document

Interpretation of the EU Guidelines on the Principles of Good Distribution Practice for active substances for medicinal products for human and veterinary use, in parallel with the WHO Guideline Good Trade and Distribution Practices for Pharmaceutical Starting Materials and the relevant chapter of ICH Q7

Version 3 – June 2026

Preamble

The original version of this guidance document has been compiled by a subdivision of the APIC Good Distribution Practice Task Force on behalf of the Active Pharmaceutical Ingredient Committee (APIC) of CEFIC.

Task Force Members:

Dr. Lars Albermann, Merck KGaA
Tom Buggy, DSM
Dario Lopez, Centrient Pharmaceuticals
Dr . Georg Strasser, Janssen Pharmaceutica NV
Dr. Ulrich Kestel, Fareva
Kristina Kos, Teva
Dr. Jelle Van Gauwbergen, Janssen Pharmaceutica NV
Jeffrey Speakman – Evonik
Pierre Krebbers – Aspen pharma
Enno Schweinberger – Siegfried
Martina Rubes – Dipharma
Philippe Lienart – Roquette
Marcel Kamsteeg – Corbion
Philippe Pessina – Sequens
Steven De Strycker – Johnson & Johnson
Anne Lage – Siegfried
Dirkjan Vanzoelen – Ardena
Jeroen Geeven – Ardena
Kai Doderer – Evonik
Vera Branco – Hovione
Erika Vergara – Dow
Ivana Martinovic – TEVA Pharmaceutical Industries Ltd.

With Support and Review from:

Pieter Van der Hoeven, APIC, Belgium
Francois Vandeweyer, Janssen Pharmaceutica NV
Annick Bonneure, APIC Belgium
The APIC Quality Working Group

Table of Contents

Chapter 1 Introduction

1.1 Objective

APIC Good Distribution Practices for Active Pharmaceutical Ingredients "How to do" Document

Historical Background

In the past there have been no separate regulations on GDP for distributors of APIs.
GMP Part II / ICH Q7 for manufacturers of APIs had been the only guidelines partially covering GDP for APIs. They affect primarily the handling of APIs at the manufacturing site, but not distribution outside the site.
The WHO Guide on GTDP for Pharmaceutical Starting Materials has been a reference document with broad acceptance in industry on a voluntary basis.
With the EU Falsified Medicines Directive (Directive 2011/62/EU), the application of GDP for APIs became mandatory. The EU Commission Guideline on principles of Good Distribution Practice of active substances for medicinal products for human use, issued on 19 March 2015, was the first legally binding document specifically addressing distribution activities for APIs. On 2 August 2021, Commission Implementing Regulation (EU) 2021/1280 was issued regarding the distribution of APIs for veterinary medicinal products under Regulation (EU) 2019/6.
In addition, PIC/S issued, in July 2018, a guideline (PI 047-1, 2018) on the principles of Good Distribution Practice of active substances for medicinal products for human use; the requirements in this document are largely identical to those in the EU guideline.

ACKNOWLEDGEMENTS
This document was developed by representatives of member companies of the Active Pharmaceutical Ingredients Committee (APIC).

Purpose of the Document

This document was written by experts from the European industry (CEFIC APIC).

It is essentially an interpretation of "how to" implement the EU Commission Guideline on the principles of Good Distribution Practice (GDP) for active substances for medicinal products for human use, published by the European Commission DG SANCO on 19 March 2015, based on practical experience.

In addition, the following guidelines were taken into account in the preparation of this document: WHO "Good trade and distribution practices for pharmaceutical starting materials – TRS 996, Annex 6"; ICH Q7 / APIC "How to do" Document on ICH Q7; "PIC/S Guide to Good Distribution Practice for Medicinal Products"; and Regulation (EU) 2021/1280 on good distribution practice for active substances used as starting materials in veterinary medicinal products.

This guide provides additional explanatory notes on the EU Commission Guideline on the principles of Good Distribution Practice of active substances for medicinal products for human and veterinary use.

The explanatory notes in this guide reflect the views of the Active Pharmaceutical Ingredients Committee (APIC) and not necessarily those of the European Commission or WHO.

This document does not intend to provide an exhaustive list of "how to" comply with the requirements and recommendations mentioned above.

It provides examples of potential solutions and further detail on how requirements and recommendations can be met and/or interpreted.

The word “should” is used several times in the EU Guideline on the Principles of GDP for APIs. It indicates requirements and recommendations that are expected to apply unless they can be shown to be inapplicable or replaced by an alternative that provides at least an equivalent level of quality assurance. Therefore, “should” does not mean that the requirement does not have to be met simply because it is not phrased as “must”.

This document is intended to be a living document describing current practice and supporting the implementation of the EU Commission Guideline on the principles of GDP for active substances for medicinal products for human and veterinary use. Suggestions and questions from industry or regulators to CEFIC APIC are welcome.

This document has been prepared to provide guidance for companies involved in the distribution of active pharmaceutical ingredients.
Examples based on practical experience are provided to support the application of GDP. However, alternative approaches may also be acceptable.

Regulatory Requirements
Within the EU, according to Article 46 of Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, companies should apply the following measures to prevent the entry of falsified medicinal products into the legal supply chain.
The holder of a manufacturing authorization shall at least be obliged to use only active substances, which have been manufactured in accordance with good manufacturing practice for active substances and distributed in accordance with good distribution practices for active substances. Distributors of active substances may, according to Article 111 of the same directive, become subject to inspections by the competent authority.
Furthermore, the holder of the manufacturing authorization shall verify compliance with good manufacturing practices and good distribution practices by conducting audits at the sites of active substance manufacturers and distributors.

Requirements for veterinary APIs
In general the guideline for veterinary APIs (Implementing Regulation (EU) 2021/1280) does not change the underlying GDP principles established in guideline for human APIs (EU Guidelines on GDP 19 March 2015); rather, it transforms them into binding, harmonised and enforceable legal requirements for the veterinary sector. Many passages of guidelines are identical or at least similar. Both guidelines are applicable for APIs and the scope exclude Intermediates. Most significant difference is the legal status: The 2015 Guideline provides interpretative guidance under Directive 2001/83/EC and allows for flexibility in implementation. By contrast, Regulation (EU) 2021/1280 is adopted under Regulation (EU) 2019/6 and is directly applicable and legally binding in all EEA Member States (including Switzerland). From a content perspective, the requirements for self-inspections under Article 23 of Regulation (EU) 2021/1280 represent the most significant difference.

This document reflects the APIC experts’ interpretation of the following guidelines:

- Guideline (EU) 2015/C 95/01 of 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use
- Implementing Regulation (EU) 2021/1280 of 2 August 2021 as regards measures on good distribution practice for active substances used as starting materials in veterinary medicinal products in accordance with Regulation (EU) 2019/6

In addition, aspects of the following guidelines and documents were also taken into account:

- Falsified Medicines Directive (Directive 2011/62/EU)

- ICH Q 7 (EU GMP Part II): Good manufacturing practice for active pharmaceutical ingredients
- APIC ICH Q7 "How to do"
- ICH quality documents (EU GMP Part II) “Quality Risk Management Q9”
- WHO Technical Report Series (TRS) No. 957, Annex 5 – WHO Good Distribution Practices for Pharmaceutical Products
- WHO Technical Report Series (TRS) No. 996, Annex 6 –WHO good trade and distribution practices for pharmaceutical starting materials
-
- 2013/C 343/01 Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use
- PIC/S Guide to Good Distribution Practice for Medicinal Products

1.2 Regulatory applicability

This document is applicable to the distribution* of active substances for human and veterinary medicinal use in Europe.

**See paragraph 1.2 of the EU Commission Guideline on principles of Good Distribution Practice of active substances for medicinal products for human use and Article 2 (i) Regulation (EU) 2021/1280 for veterinary medicinal products*.

Chapter 2 Scope

According to the European Falsified Medicines Directive, Manufacturing Authorization Holders are responsible to use only active substances which have been distributed in accordance with Good Distribution Practices for active substances. This is one significant new requirement in the EU Falsified Medicines Directive.

In the EU framework for human and veterinary medicinal products, the scope relevant to this document can be summarized as follows:

1. For human medicinal products, the EU GDP Guideline applies to the distribution of active substances as defined in Article 1(3a) of Directive 2001/83/EC. For veterinary medicinal products, corresponding GDP requirements apply under Regulation (EU) 2021/1280 (respectively Regulation (EU) 2019/6, Article 4). In both cases, an active substance is a substance or mixture of substances intended to be used in the manufacture of a medicinal product and that, when used in its production, becomes an active ingredient of that product.

2. In view of these guidelines, the distribution of active substances for medicinal products for human & veterinary use (hereafter 'active substances') is defined as procuring, importing, holding, supplying or exporting active substances.

3. Activities consisting of re-packaging, re-labelling or dividing up of active substances are manufacturing activities and as such are subject to the guidelines on Good Manufacturing Practice of active substances.

Chapter 3 General Considerations

This document is based on the EU Commission Guideline on the principles of Good Distribution Practice of active substances for medicinal products for human and veterinary use and therefore follows the same structure.

This APIC document provides guidance on practical approaches, with examples, for applying the principles of the EU GDP guideline for APIs.

The APIC document applies to steps in the distribution/supply chain starting from the point at which an API is transferred outside the control of the original manufacturer's material management system.
Some sections and/or sub-sections of this document may not apply to all parties involved. This document is intended to provide guidance on the application of GDP; however, alternative approaches may be acceptable.
Specific guidance on storage conditions is described in regulatory documents such as USP chapter <659> Packaging and Storage Requirements and the EMEA Guideline on Declaration of Storage Conditions CPMP/QWP/609/96/Rev 2 (EMEA 2007).

Chapter 4 Good Distribution Practices for API

4.1 How to use the "How to do" - Document

The requirements have been interpreted for APIs by APIC, taking into consideration the requirements given in the ICH Q7 / APIC "How to do" Document on ICH Q7. Reference has also been made to WHO Technical Report Series 996 Annex 6 on Good Trade and Distribution Practices for Pharmaceutical Starting Materials.

The interpretation of APIC must be read and considered in conjunction with the requirements of the EU GDP guideline. The references in the other columns should help the user of this document to find the respective paragraphs in the APIC "How to do" document on ICH Q7 and WHO TRS report

The application of the interpretations in this table should always take into consideration the potential inherent risks related to the API and the conditions under which the API is handled and distributed. Risk assessments should be based on sound scientific evaluation and appropriate risk management tools, as referenced, for example, in ICH Q9.

4.2 “How to do” - Document

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
Introduction		
These guidelines are based on the fourth paragraph of Article 47 of Directive 2001/83/EC [(1)]. [(1)] *Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67)*		
They follow the same principles that underlies the guidelines of Eudralex Volume 4, Part II, Chapter 17, with regard to the distribution of active substances and the Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use **(2)** [(2)] *OJ C 343, 23.11.2013, p. 1*		The Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use are referenced to provide an overall definition of good distribution practice; however, the similarity is not fully applicable to APIs.
These guidelines provide stand-alone guidance on Good Distribution Practice (GDP) for importers and distributors of active substances for medicinal products for human use. They complement the rules on distribution set out in the guidelines of EudraLex Volume 4, Part II, and apply also to distributors of active substances manufactured by themselves.		
Any manufacturing activities in relation to active substances, including re-packaging, re-labelling or dividing up, are subject to Commission Delegated Regulation (EU) No 1252/2014 **(3)** and EudraLex Volume 4, Part II. [(3)] *Commission Delegated Regulation (EU) No 1252/2014 of 28 May 2014 supplementing Directive 2001/83/EC of the European Parliament and of the Council with regard to principles and guidelines of good manufacturing practice for active substances for medicinal products for human use (OJ L 337, 25.11.2014, p1*		Repackaging, relabeling, or dividing-up activities performed during distribution are considered GMP-relevant. Therefore, they should comply with the requirements of Commission Delegated Regulation (EU) No 1252/2014 and EudraLex Volume 4, Part II.
Additional requirements apply to the importation of active substances, as laid down in Article 46b of Directive 2001/83/EC.		It is recommended that specific requirements for importing APIs (e.g. national requirements) be defined.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
Distributors of active substances for medicinal products for human use should follow these guidelines as of 21 September 2015.		
Chapter 1 - Scope		
1.1 These guidelines apply to distribution of active substances, as defined in Article 1(3a) of Directive 2001/83/EC, for medicinal products for human use. According to that provision, an active substance is any substance or mixture of substances intended to be used in the manufacture of a medicinal product and that, when used in its production, becomes an active ingredient of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions or to make a medical diagnosis.	**Introduction** The scope of this WHO guidance on Good trade and distribution practices for pharmaceutical starting materials is applicable to any ingredient that is used in the manufacture of a medicinal product, including APIs, excipients and any others.	Transportation companies do not need to be certified by authorities. However, they should follow parts of the GDP guideline relevant to their activities. It is the responsibility of distributors (GDP-certified parties contracting transporters) to verify that the selected transport companies are able to apply these requirements, including a quality system, appropriate personnel, and good documentation practices, in relation to the criticality of their activities.
1.2 For the purpose of these guidelines, distribution of active substances shall comprise all activities consisting of procuring, importing, holding, supplying or exporting active substances, apart from brokering.		This guideline applies only to **distribution activities, including transportation** (i.e. no product container is opened during such activities). The definition of brokering activities provided in the EU guideline is as follows: *All activities related to the sale or purchase of active substances that do not include physical handling and that consist of negotiating independently and on behalf of another legal or natural person.*
1.3 These guidelines do not apply to intermediates of active substances.	Although the API intermediates are not directly in scope of this guideline, the sense of this guideline fits best to API intermediates and might be applied in the general sense to API intermediates (e.g. regarding Supplier qualification, Traceability, Transport conditions, Handling of nonconformities)	The EU guideline does not apply to intermediates or starting materials; it applies only to active substances. According to EU Guideline on GMP for medicinal products for human and veterinary use; volume 4 part 1 chapter 5 *(5.29) supply chain traceability should be established and the associated risks, from active substance starting materials to the finished medicinal product, should be formally assessed and periodically verified. Appropriate measures should be put in place to reduce risks to the quality of the active substance*
Chapter 2 – Quality System Damage management – responsibility for material to be distributed		

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
2.1 Distributors of active substances should develop and maintain a quality system setting out responsibilities, processes and risk management principles. Examples of the processes and applications of quality risk management can be found in EudraLex Volume 4, Part III: GMP related documents, ICH guideline Q9 on Quality Risk Management (ICH Q9).	1.2 Quality management should include: - an appropriate infrastructure or "quality system", encompassing the organizational structure, procedures, processes and resources. The size, structure and complexity of the distributor and its activities should be taken into consideration when developing or modifying the quality system; 1.3 The system should cover for example, but not be limited to, the quality assurance principles in these guidelines. 2.2 Individual responsibilities should be clearly defined, understood by the individuals concerned and recorded in writing (as job descriptions or in a contract). Certain activities, such as supervision of performance of activities in accordance with local legislation, may require special attention. Personnel should be suitably qualified, trained and authorized to undertake their duties and responsibilities.	These requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular Chapters 2 and 17). Parties involved in the distribution of APIs should establish a Quality Management System to manage the quality of their products and services and to maintain the original quality of the APIs. As an essential prerequisite for any Quality Management System, top management should establish a corporate quality policy. The parties involved should share responsibility for ensuring that the API provided by the distributor conforms to the mutually agreed specification requirements of the pharmaceutical manufacturer and/or is suitable for its intended use. Quality Risk Management principles should be integrated into the quality management system.
2.2 The quality system should be adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities. It should ensure that: **(i)** active substances are procured, imported, held, supplied or exported in a way that is compliant with the requirements of GDP for active substances;	1.4 All parties involved in the manufacture and supply chain must exercise responsibility to ensure the quality and safety of the materials and products, and that they are fit for their intended use in accordance with their specifications. 2.1 There should be an adequate organizational structure and a sufficient number of personnel should be employed to carry out all the tasks for which the supplier is responsible. 4.1 Materials should be purchased from approved suppliers in accordance with mutually agreed formal specifications.	These requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular Chapters 2 and 17). A system should be in place to control documents and data related to the applicable Quality System requirements. As a minimum, the Quality Manual should include the following elements: - scope of the Quality Management System, - organizational structure, including a description of top management responsibilities, - written procedures, processes, and resources, or references to them, and - a description of the sequence and interaction between procedures and departmental functions. The Quality Management System should also include a procedure to verify that any API supplier or relevant service provider has the capability to consistently meet previously agreed requirements. This may include periodic audits of service providers.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
		Any computerized system used to ensure the required traceability and data integrity should be properly installed, qualified, and controlled.
(ii) management responsibilities are clearly specified;	2.2 Individual responsibilities should be clearly defined, understood by the individuals concerned and recorded in writing (as job descriptions or in a contract). Certain activities, such as supervision of performance of activities in accordance with local legislation, may require special attention. Personnel should be suitably qualified, trained and authorized to undertake their duties and responsibilities.	Requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular chapter 2) Refer to Chapter 3 below for personnel requirements.
(iii) active substances are delivered to the right recipients within a satisfactory time period;	13.4 There should be a written and approved contract or formal agreement between the contract giver and contract acceptor that addresses and defines in detail the responsibilities with respect to GTDP and which party is responsible for which quality measures	Requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular chapter 10.24 and 17) There should be an organization and corresponding processes in place to ensure the product is shipped to the right customer (see also "delivery to customers" item 6.13, 6.14 and 6.15) . Note: The satisfactory timeframe should be defined in the supply agreement or service level agreement, taking into account the need to avoid customer stock shortages (refer to Chapter 6, Operations). Active substances should always be transported in a manner that avoids unjustified periods of storage. (See also Chapter 5, “Glossary of terms”.)
(iv) records are made contemporaneously;	Partially covered by chapter 6.1 6.1 Documents, in particular instructions and procedures relating to any activity that might have an impact on the quality of materials, should be designed, completed, reviewed and distributed with care. Documents should be completed, approved, signed and dated by appropriate authorized persons and should not be changed without authorization. Specifications for materials, including packaging materials, should be available, reviewed and revised on a regular basis.	These requirements are part of good documentation practices, including ALCOA principles. Refer to **Chapter 4** on documentation for more details.
(v) deviations from established procedures are documented and investigated;	11.1 non-conforming materials should be handled in accordance with a procedure that will prevent their introduction or reintroduction into the market. Records covering all activities, including destruction, disposal, return and reclassification, should be maintained.	The conclusions of deviations with impact on the product should be risk based. If there are deviations with potential impact on the product quality (e.g. the storage conditions, damages ….,) the API manufacturer should provide support as needed.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
	11.2 An investigation should be performed to establish whether any other batches are also affected. Corrective and preventive measures should be taken where necessary.	There should be a communication process in place between the customer/distributor and the API manufacturer regarding deviations occurring at distributor level, to ensure that the reporting of the deviation is performed in a timely manner. The responsibility for investigating such deviations should be defined in the relevant contracts (e.g. quality agreements or supply agreements) and aligned with the applicable INCOTERM conditions. The management of deviations and damage during storage and transport should involve all relevant parties in the supply chain.
(vi) appropriate corrective and preventive actions, commonly known as 'CAPA', are taken to correct deviations and prevent them in line with the principles of quality risk management;	Partially covered by chapter 1.9 and 11.2 1.9 A system should be in place for the performance of regular internal audits with the aim of continuous improvement. The findings of the audit and any corrective and preventive actions taken, including verification of their effectiveness, should be documented and brought to the attention of the responsible management. 11.2 An investigation should be performed to establish whether any other batches are also affected. Corrective and preventive measures should be taken where necessary.	Self-explanatory
(vii) changes that may affect the storage and distribution of active substances are evaluated.	Partially covered by chapter 1.2 and 6.1 1.2 Quality management should include - a robust deviation management and change control programme designed to ensure that quality is continually assessed and maintained: these should include a customer notification where appropriate; 6.1 Documents, in particular instructions and procedures relating to any activity that might have an impact on the quality of materials, should be designed, completed, reviewed and distributed with care. Documents should be completed, approved, signed and dated by appropriate authorized persons and should not be changed without	There should be a communication process in place to ensure that any change at distributor level (changes to what has been committed and agreed in the quality agreement) will be assessed by the manufacturer of the API prior to implementing the change and communicated to the customer in a timely fashion.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
	authorization. Specifications for materials, including packaging materials, should be available, reviewed and revised on a regular basis.	
2.3 The size, structure and complexity of the distributor's activities should be taken into consideration when developing or modifying the quality system.	1.2 Quality management should include - an appropriate infrastructure or "quality system", encompassing the organizational structure, procedures, processes and resources. The size, structure and complexity of the distributor and its activities should be taken into consideration when developing or modifying the quality system	An appropriate organization should be in place with an adequate number of resources.
Chapter 3 – Personnel		
3.1 The distributor should designate a person at each location where distribution activities are performed who should have defined authority and responsibility for ensuring that a quality system is implemented and maintained. The designated person should fulfil his responsibilities personally. The designated person can delegate duties but not responsibilities.	1.2 Quality management should include - an independent quality unit (or designee), which is responsible for all quality-related matters	There should be an organization in place to implement and maintain the quality system, with a designated representative at each location. Key quality responsibilities should not be delegated. These responsibilities should be described in writing, for example in the form of a contract or agreement between the relevant parties.
3.2 The responsibilities of all personnel involved in the distribution of active substances should be specified in writing. The personnel should be trained on the requirements of GDP for active substances. They should have the appropriate competence and experience to ensure that active substances are properly handled, stored and distributed.	**2.1**: There should be an adequate organizational structure 2.2: Individual responsibilities should be clearly defined, understood by the individuals concerned and recorded in writing (as job descriptions or in a contract). Certain activities, such as supervision of performance of activities in accordance with local legislation, may require special attention. Personnel should be suitably qualified, trained and authorized to undertake their duties and responsibilities. 2.3 All personnel should be aware of the principles of the appropriate guidelines, including but not limited to GTDP	The organization should be documented in an organizational chart with clear indication of personnel responsible for distribution activities. Levels of authorization should be clearly defined in job descriptions. There should be an adequate number of personnel qualified through appropriate education, training, and/or experience to perform and supervise activities relating to API distribution. A system for planning, documenting, and following up on training should be in place. For personnel directly involved in GDP processes, it is recommended that GDP-focused training be provided.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
3.3 Personnel should receive initial and continuing training relevant to their role, based on written procedures and in accordance with a written training program.	**Chapter 2.2**: Personnel should be suitably qualified, trained 2.4 Personnel should receive initial and continuing training relevant to their tasks. Training should be provided by qualified trainers in accordance with a training programme. The effectiveness of training should be verified where appropriate. Training records should be maintained. All personnel should be motivated to support the establishment and maintenance of quality standards.	Personnel involved should be trained in the handling of the material, taking into account the requirements of the material safety data sheet. Personnel should be trained on GDP principles and on the chapters relevant to their area of responsibility. For transport companies, the training program should be aligned with the activities for which they are responsible. All relevant personnel should receive initial and periodic refresher training commensurate with the potential impact of their activities on the API. Applicable quality standards should form part of a regular training program delivered by qualified personnel, and the training should be documented.
3.4 A record of all training should be kept, and the effectiveness of training should be periodically assessed and documented.	2.4 Personnel should receive initial and continuing training relevant to their tasks. Training should be provided by qualified trainers in accordance with a training programme. The effectiveness of training should be verified where appropriate. Training records should be maintained. All personnel should be motivated to support the establishment and maintenance of quality standards.	Records should be maintained listing the name, address, and qualifications of any contracted service provider and the type of service they provide.
Chapter 4 - Documentation		
4.1 Documentation comprises all written procedures, instructions, contracts, records and data, in paper or in electronic form. Documentation should be readily available or retrievable. All documentation related to compliance of the distributor with these guidelines should be made available on request of competent authorities.	6.10 Records should be kept and must be readily available upon request in accordance with GMP and GSP (Good Storage Practices) * **Guide to good storage practices for pharmaceuticals. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-seventh report. Geneva: World Health Organization; 2003: Annex 9 (WHO Technical Report Series, No. 908)*	Self-explanatory If computerized systems are used at distributor level, then the computer systems should be validated.
4.2 Documentation should be sufficiently comprehensive with respect to the scope of the distributor's activities and in a language understood by personnel. It should be written in clear, unambiguous language and be free from errors.	6.2 Documents should have unambiguous contents: their title, nature and purpose should be clearly stated. They should be laid out in an orderly manner and be easy to check.	Self-explanatory

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
4.3 Any alteration made in the documentation should be signed and dated; the alteration should permit the reading of the original information. Where appropriate, the reason for the alteration should be recorded.	No direct requirement, but should be covered by § 6.10 6.10 Records should be kept and must be readily available upon request in accordance with GMP and GSP	Self-explanatory Refer to good documentation practices for data in paper and in electronic form.
4.4 Each employee should have ready access to all necessary documentation for the tasks executed.	No direct requirement, but should be covered by § 2.2 2.2 […] Personnel should be suitably qualified, trained and authorized to undertake their duties and responsibilities.	Self-explanatory
Procedures		
4.5 Written procedures should describe the distribution activities which affect the quality of the active substances. This could include receipt and checking of deliveries, storage, cleaning and maintenance of the premises (including pest control), recording of the storage conditions, security of stocks on site and of consignments in transit, withdrawal from saleable stock, handling of returned products, recall plans, etc.	6.1 Documents, in particular instructions and procedures relating to any activity that might have an impact on the quality of materials, should be designed, completed, reviewed and distributed with care. Documents should be completed, approved, signed and dated by appropriate authorized persons and should not be changed without authorization. Specifications for materials, including packaging materials, should be available, reviewed and revised on a regular basis.	Comment: Written procedures should be in place, and the corresponding processes should be implemented.
4.6 Procedures should be approved, signed and dated by the person responsible for the quality system.	6.1 […] Documents should be completed, approved, signed and dated by appropriate authorized persons and should not be changed without authorization. […]	Self-explanatory
4.7 Attention should be paid to the use of valid and approved procedures. Documents should be reviewed regularly and kept up to date. Version control should be applied to procedures. After revision of a document a system should exist to prevent inadvertent use of the superseded version. Superseded or obsolete procedures should be removed from workstations and archived.	Not detail as such	(APIC 2014): Procedures on document control should be established. A revision history of documents should be readily available. Changes to procedures should be considered in the training program If an electronic system is used to control the revision and approval of SOPs, the system should be validated and should comply with data integrity principles, including audit trail requirements. If a paper-based system is used, it should be managed in a controlled manner under Quality Unit oversight.
Records		

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
4.8 Records should be clear, be made at the time each operation is performed and in such a way that all significant activities or events are traceable. Records should be retained for at least 1 year after the expiry date of the active substance batch to which they relate. For active substances with retest dates, records should be retained for at least 3 years after the batch is completely distributed.	Partially covered by §6.10 6.10 Records should be kept and must be readily available upon request in accordance with GMP and GSP	Comment: Retention periods of documents should be established. The security and methods of archiving and retrieval of such records should be ensured. Record retention schedule and practices for distribution records should be specified in the quality agreement.
4.9 Records should be kept of each purchase and sale, showing the date of purchase or supply, name of the active substance, batch number and quantity received or supplied, and name and address of the supplier and of the original manufacturer, if not the same, or of the shipping agent and/or the consignee. Records should ensure the traceability of the origin and destination of products, so that all the suppliers of, or those supplied with, an active substance can be identified. Records that should be retained and be available include: I. identity of supplier, original manufacturer, shipping agent and/or consignee; II. address of supplier, original manufacturer, shipping agent and/or consignee; III. purchase orders; IV. bills of lading, transportation and distribution records; V. receipt documents; VI. name or designation of active substance; VII. manufacturer's batch number; VIII. certificates of analysis, including those of the original manufacturer; IX. retest or expiry date.	Partially covered by §6.8, 6.3 and 6.4 6.8 Each container should be identified by labelling bearing at least the following information: – the name of the pharmaceutical starting material (including grade and reference to pharmacopoeias where relevant); – if applicable, the International Nonproprietary Name (INN); – the amount (weight or volume); – the batch number assigned by the original manufacturer or the batch number assigned by the repacker, if the material has been repacked and relabelled; – the retest date or expiry date (where applicable); – the storage conditions; – handling precautions, where necessary; – identification of the original manufacturing site; – name and contact details of the supplier. 6.3 Certificates of analysis (COAs) issued by the original manufacturer should be provided. If additional testing is done, all COAs should be provided. COAs should document product traceability back to the manufacturer by naming the original manufacturer and the manufacturing site. COAs should indicate which results were obtained by testing the original material and which results came from skip-lot testing or other testing and should specify the organization responsible for issuing the COA.	Requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular chapter 6.30 and 10.24) Comment: Recommendation: In addition to the records requested by the EU GDP guideline, the quantity of each shipment of each batch should also be retained and be readily available.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
	6.4 Before any material is sold or distributed, the supplier should ensure that the COAs and results are available and that the results meet the required specifications	
	6.3 Certificates of analysis (COAs) issued by the original manufacturer should be provided. If additional testing is done, all COAs should be provided. COAs should document product traceability back to the manufacturer by naming the original manufacturer and the manufacturing site. COAs should indicate which results were obtained by testing the original material and which results came from skip-lot testing or other testing and should specify the organization responsible for issuing the COA. 6.5 The original manufacturer and the intermediaries handling the material should always be traceable and transparent; and this information should be made available to authorities and end-users, downstream and upstream, when requested.	A distributor should not change the original title and data of the CoA or other quality documents. Whenever possible, the original manufacturer's documentation should be used, or transcription of data should be verified. The original manufacturing site should be identified by name or unique identifier on the CoA or any other document agreed upon with the customer Comment: Records should be readily available and should ensure traceability of the supply chain for products/APIs from origin (manufacturer), through suppliers/distributors, to destination (purchaser).
	6.4 Before any material is sold or distributed, the supplier should ensure that the COAs and results are available and that the results meet the required specifications.	API should normally be released according to their specification for shipment. In case of API pending final release testing, API could be shipped under quarantine when authorized by the quality unit, in agreement with customer and according to local legislation. Appropriate controls and documentation should be in place. The process for transfer under quarantine should be defined in a procedure. The Quality Unit of both sites needs to approve shipment under quarantine, and the receiving site must not use the material before a certificate of analysis for the batch in scope has been issued. Before shipment under quarantine, the manufacturing batch record should be reviewed and approved by the Quality Unit.
Additionally:	6.9 Relevant storage and handling information and safety data sheets should be available	--
Chapter 5 – Premises and Equipment		
5.1 Premises and equipment should be suitable and adequate to ensure proper storage, protection from contamination, e.g. narcotics, highly sensitising materials, materials of high pharmacological activity or toxicity, and distribution of active substances. They	3.1 Premises, including laboratory facilities, must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit ef-	Requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular chapter 4) Buildings and facilities used in the distribution of APIs should be located, designed, and constructed to facilitate cleaning, maintenance,

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
should be suitably secured to prevent unauthorised access. Monitoring devices that are necessary to guarantee the quality attributes of the active substance should be calibrated according to an approved schedule against certified traceable standards.	fective cleaning and maintenance in order to avoid contamination, cross-contamination, mix ups, build-up of dust, dirt or waste and, in general, any adverse effect on the quality of materials. 3.4 Suitable supporting facilities and utilities (such as air control, ventilation and lighting) should be in place and appropriate to the activities performed, in order to avoid contamination, cross-contamination and degradation of the material. Utilities that could affect product quality should be identified and monitored. 3.2 Measures should be in place to prevent unauthorized persons from entering the premises	and operations as appropriate to the type and stage of handling. Where the equipment itself (e.g., closed or contained systems) provides adequate protection of the product, such equipment can be located outdoors. Equipment should be qualified before use to ensure that it is functioning as intended. Defined physical areas or other control systems (e.g. computerized systems) should be in place for activities such as receipt, identification, and quarantine of incoming products. Sufficient warehouse space should be available to allow efficient movement without damaging packaged products and to facilitate cleaning. Appropriate access control for the premises should be ensured. Adequate lighting should be provided in all areas to facilitate cleaning, maintenance and proper operations. *Comment: also applicable to Sections 6.7 and 6.8.*
	4.10 Where special storage conditions are required (e.g. particular temperature, humidity or protection from light) these should be provided, monitored and recorded as appropriate. 4.11 Highly active materials, narcotics, other dangerous drugs and substances presenting special risks of abuse, fire or explosion should be stored in safe, dedicated and secure areas. In addition and where applicable, international conventions and national legislation are to be adhered to 4.12 Special attention should be given to the design, use, cleaning and maintenance of all equipment for bulk handling and storage, such as tanks and silos.	Requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular chapter 7.4) Facilities should also be designed to minimize potential contamination. The risk of contamination and mix up should also be considered in respect to the flow of products and personnel through the buildings or facilities.
	5.1 Equipment must be located, designed, constructed, adapted, qualified, used, cleaned and maintained to suit the operations to be carried out. Its layout, design and use should aim to minimize the risk of errors and permit effective cleaning and maintenance so as to avoid cross-contamination, build-up of dust or dirt and any adverse effect on the quality of materials.	Requirements are also covered by GMP (EudraLex Volume 4, Part II – see in particular chapter 5) A set of current drawings should be maintained for facilities and critical installations (e.g. instrumentation and utility systems). Schedules and procedures (including responsibilities) should be established for the preventive maintenance and calibration program of the facility.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
	5.2 Defective equipment should not be used and should either be removed or labelled as defective. Equipment should be disposed of in such a way as to prevent any misuse. 5.3 The status of the equipment should be readily identifiable. 5.9 Procedures should be in place for the operation and maintenance of equipment. Lubricants and other materials used on surfaces that come into direct contact with the materials should be of the appropriate grade, e.g. food-grade oil, and should not alter the quality of the materials. 5.10 Washing and cleaning equipment should be chosen and used such that it cannot be a source of contamination 5.6 Balances and other measuring equipment of an appropriate range and precision should be available and should be calibrated in accordance with a suitable schedule.	
Chapter 6 – Operations		
Orders		
6.1 Where active substances are procured from a manufacturer, importer or distributor established in the EU, that manufacturer, importer or distributor should be registered according to Article 52a of Directive 2001/83/EC.(1) *(1) Extract from Directive 2001/83/EC- Article 52a* *1. Importers, manufacturers and distributors of active substances who are established in the Union shall register their activity with the competent authority of the Member State in which they are established.* *2. The registration form shall include, at least, the following information:* *(i) name or corporate name and permanent address;* *(ii) the active substances which are to be imported, manufactured or distributed;*	Not detailed as such	

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
(iii) particulars regarding the premises and the technical equipment for their activity.		
Receipt		
6.2 Areas for receiving active substances should protect deliveries from prevailing weather conditions during unloading. The reception area should be separate from the storage area. Deliveries should be examined at receipt in order to check that: **(i)** containers are not damaged; **(ii)** all security seals are present with no sign of tampering; **(iii)** correct labelling, including correlation between the name used by the supplier and the in-house name, if these are different; **(iv)** necessary information, such as a certificate of analysis, is available; and **(v)** the active substance and the consignment correspond to the order.	4.3 There should be authorized procedures describing the activities relating to the receipt, storage and distribution of materials. Steps should be taken to ensure and document that the arriving consignment is correct and that the products originate from approved suppliers. Deliveries should be examined to check that containers have not been damaged, altered or tampered with, and that closures and security seals are intact.	Self-explanatory The use of a checklist is recommended to capture the relevant points.
6.3 Active substances with broken seals, damaged packaging, or suspected of possible contamination should be quarantined either physically or using an equivalent electronic system and the cause of the issue investigated.	Partially covered by § 4.2 and 4.3 4.2 Actions should be taken to minimize the risk of falsified or non-conforming materials entering the supply chain. 4.3 There should be authorized procedures describing the activities relating to the receipt, storage and distribution of materials. Steps should be taken to ensure and document that the arriving consignment is correct and that the products originate from approved suppliers. Deliveries should be examined to check that containers have not been damaged, altered or tampered with, and that closures and security seals are intact.	Self-explanatory.
6.4 Active substances subject to specific storage measures, e.g. narcotics and products requiring a specific storage temperature or humidity, should be immediately identified and stored in accordance with written instructions and with relevant legislative provisions.	Partially covered by 4.11 and 4.9 4.11 Highly active materials, narcotics, other dangerous drugs and substances presenting special risks of abuse, fire or explosion should be stored in safe, dedicated and secure areas. In addition, and where applicable, interna-	Self-explanatory The specific storage measures should be written and communicated to relevant personnel.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
	tional conventions and national legislation are to be adhered to. 4.9 The required storage conditions, as specified for the material, should be maintained within acceptable limits at all times during storage. Appropriate checks to confirm that required shipping conditions have been met should be conducted as soon as possible after receipt. The product should be transferred to appropriate storage facilities immediately after checks to be made in the goods receiving area have been conducted.	
6.5 Where the distributor suspects that an active substance procured or imported by him is falsified, he should segregate it either physically or using an equivalent electronic system and inform the national competent authority of the country in which he is registered.	Partially covered by § 4.2 and 4.3, see just before	Self explanatory. It is recommended that the process for notifying the authority be described in a protocol or procedure.
6.6 Rejected materials should be identified and controlled and quarantined to prevent their unauthorised use in manufacturing and their further distribution. Records of destruction activities should be readily available.	Partially covered by § 4.2 and 11.1 4.6 Segregated areas should be provided for the storage of received, quarantined, rejected, recalled and returned material, including materials with damaged packaging. Any system replacing physical segregation, such as electronic segregation based on a computerized system, should provide equivalent security and should be appropriately qualified and validated. 11.1 Non-conforming materials should be handled in accordance with a procedure that will prevent their introduction or reintroduction into the market. Records covering all activities, including destruction, disposal, return and reclassification, should be maintained.	Self explanatory
Storage		
6.7 Active substances should be stored under the conditions specified by the manufacturer, e.g. controlled temperature and humidity when necessary, and in such a manner to prevent contamination and/or mix up. The storage conditions should be monitored and records maintained.	Covered by § 4.9 and 4.10 4.9 The required storage conditions, as specified for the material, should be maintained within acceptable limits at all times during storage. Appropriate checks to confirm that required shipping conditions have been met should	Self explanatory Non controlled storage is considered acceptable supported by a risk assessment and temperature monitoring data of the facility.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
The records should be reviewed regularly by the person responsible for the quality system.	be conducted as soon as possible after receipt. The product should be transferred to appropriate storage facilities immediately after checks to be made in the goods receiving area have been conducted. 4.10 Where special storage conditions are required (e.g. particular temperature, humidity or protection from light) these should be provided, monitored and recorded as appropriate.	Materials should be stored under conditions and for a period that have no adverse effect on their quality and should normally be controlled to ensure the oldest stock is used first. 2013/C 343/01 EUROPEAN COMMISSION Guidelines on Good Distribution Practice of medicinal products for human use state in Chapter 9.2 last paragraph "Provision should be made to minimize the duration of temporary storage while awaiting the next stage of the transportation route." The GDP Group of the ECA Foundation states in its FAQ that "This duration should be specified in company SOPs based on risk assessment. The current industry practice is up to 72 hours storage at temporary facilities. Longer storage periods are classed as long-term storage of product and the facility must have a license to operate." An SOP should be in place to address events that lead to deviations from temporary storage time limits or conditions. The disposition of the product should be determined on the basis of a risk assessment.
6.8 When specific storage conditions are required, the storage area should be qualified and operated within the specified limits.	Partially covered by § 4.10 4.10 Where special storage conditions are required (e.g. particular temperature, humidity or protection from light) these should be provided, monitored and recorded as appropriate	Self explanatory.
6.9 The storage facilities should be clean and free from litter, dust and pests. Adequate precautions should be taken against spillage or breakage, attack by micro-organisms and cross-contamination.	Partially covered by § 4.7 and 4.20 4.7 The storage areas should be kept clean and dry 4.20 Storage areas should be clean and free from accumulated waste and from vermin. A written sanitation programme should be available, indicating the frequency of cleaning and the methods to be used to clean the premises and storage areas	Materials stored in fiber drums, bags or boxes should be stored off the floor and, when appropriate, suitably spaced to permit cleaning and inspection.
6.10 There should be a system to ensure stock rotation, e.g. 'first expiry (retest date), first out', with regular and frequent checks that the system is operating correctly. Electronic warehouse management systems should be validated.	4.16 A default system should be in place to ensure that those materials due to expire first are sold or distributed first (earliest expiry/first out). Where no expiry dates are specified for the materials, the first in/first out principle should be applied	Materials should be stored under conditions and for a period that have no adverse effect on their quality and should normally be controlled to ensure the oldest stock is used first.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
6.11 Active substances beyond their expiry date should be separated, either physically or using an equivalent electronic system, from approved stock and not be supplied.	4.17 A process should be in place to ensure that materials that have reached their expiry or retest date should be withdrawn immediately from saleable stock. Materials with a retest date should be retested according to the appropriate specifications. Materials with an expiry date should not be retested or used after that date.	Self explanatory
6.12 Where storage or transportation of active substances is contracted out, the distributor should ensure that the contract acceptor knows and follows the appropriate storage and transport conditions. There must be a written contract between the contract giver and contract acceptor, which clearly establishes the duties of each party. The contract acceptor should not subcontract any of the work entrusted to him under the contract without the contract giver's written authorization.	Covered with more details upon § 13 Contract activities 13.1 Any activity performed, as referenced in the GMP and GTDP guidelines, delegated to another party, should be agreed upon in a written contract. 13.2 The contract giver should evaluate the proposed contract acceptor's compliance with GTDP before entering into an agreement. 13.3 All contract acceptors should comply with the requirements in these guidelines. Special consideration should be given to the prevention of cross-contamination and to maintaining traceability. 13.4 There should be a written and approved contract or formal agreement between the contract giver and contract acceptor that addresses and defines in detail the responsibilities with respect to GTDP and which party is responsible for which quality measures. 13.5 Subcontracting may be permissible under certain conditions, subject to approval by the contract giver, especially for activities such as sampling, analysis, repacking and relabelling	Self explanatory See APIC quality agreement templates (reference).
Deliveries to customer		
6.13 Supplies within the EU should be made only by distributors of active substances registered according to Article 52a of Directive 2001/83/EC to other distributors, manufacturers or to dispensing pharmacies. Article 52a 1. Importers, manufacturers and distributors of active	Not detailed as such	Recommendation: Official Databases like EudraGMDP database provide a source to check Manufacturing and Import authorizations (MIA's), GMP/GDP certificates and API registrations of registered manufacturers and distributors. These should be checked prior to delivery of APIs to the customer. If none of these documents are available in an official database (e.g. EudraGMDP), for example in the case of brokers or pharmacies, it is recommended that the customer provide them before API dispatch.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
substances who are established in the Union shall register their activity with the competent authority of the Member State in which they are established. 2. The registration form shall include, at least, the following information: (i) name or corporate name and permanent address; (ii) the active substances which are to be imported, manufactured or distributed; (iii) particulars regarding the premises and the technical equipment for their activity.		If the manufacturer holds a GMP certification, no separate GDP certification is required. Particular caution is advised if the company being supplied only has a license to broker. In such a case the "delivery address" should be checked, since a broker is typically not allowed to physically receive pharmaceutical products. .
6.14 Active substances should be transported in accordance with the conditions specified by the manufacturer and in a manner that does not adversely affect their quality. Product, batch and container identity should be maintained at all times. All original container labels should remain readable.	Requirements covered by the § 12 with more details 12.1 Materials should be loaded, unloaded and transported in a manner that will ensure the maintenance of controlled conditions where applicable (e.g. temperature, protection from the environment). The transport process should not adversely affect the materials. Any carrier used for transport should be approved according to a written procedure unless the carrier has been selected by the customer. 12.2 Requirements for special transport and/or storage conditions should be stated on the label and/or in the transport documentation. If the pharmaceutical starting material is intended to be transferred outside the control of the manufacturer's materials management system, the name and address of the manufacturer, quality of contents, special transport conditions and any special legal requirements should also be included on the label and/or in the transport documentation. 12.3 The supplier of the materials should ensure that the contract acceptor for transportation of the materials is aware of and provides the appropriate storage and transport conditions, e.g. through audits. 12.4 Procedures should be in place to ensure proper cleaning and prevention of cross-contamination when liquids (tanks) and bulk or packed materials are transported	Self explanatory Refer to the APIC statement on Good distribution practices for definition of **Product temperature range** when distributing the product under non-controlled temperature.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
6.15 A system should be in place by which the distribution of each batch of active substance can be readily identified to permit its recall.	Requirements covered by the § 9.1 & 9.5 9.1 There should be a system for recalling promptly and effectively from the market, materials known or suspected to be defective 9.5 In the event of serious or potentially life-threatening situations, all customers and competent authorities in all countries to which a given material may have been distributed should be promptly informed of any intention to recall the material	Prior to a recall a notification of the competent authority is required. The recall decision should be in agreement with the competent authority.
Transfer of Information		
6.16 Any information or event that the distributor becomes aware of, which have the potential to cause an interruption to supply, should be notified to relevant customers.	Partially covered under recall procedure, see §9.5 9.5 In the event of serious or potentially life-threatening situations, all customers and competent authorities in all countries to which a given material may have been distributed should be promptly informed of any intention to recall the material	Recommendation: To ensure a continuous supply of the general public with medicinal products, manufacturers need to know as early as possible about anything that has the potential to disrupt the supply chain. Therefore suppliers/distributors must inform their relevant customers if they become aware of any information or event that has the potential to lead to supply disruptions as agreed in the quality agreement.
6.17 Distributors should transfer all product quality or regulatory information received from an active substance manufacturer to the customer and from the customer to the active substance manufacturer.	Partially covered under recall procedure, see §9.2 and 9.5 9.2 The original manufacturer should be informed in the event of a recall. 9.5 In the event of serious or potentially life-threatening situations, all customers and competent authorities in all countries to which a given material may have been distributed should be promptly informed of any intention to recall the material	Self explanatory
6.18 The distributor who supplies the active substance to the customer should provide the name and address of the original active substance manufacturer and the batch number(s) supplied. A copy of the original certificate of analysis from the manufacturer should be provided to the customer.	Covered by § 6.3 and 6.5 6.3 Certificates of analysis (COAs) issued by the original manufacturer should be provided. If additional testing is done, all COAs should be provided. COAs should document product traceability back to the manufacturer by naming the original manufacturer and the manufacturing site. COAs should indicate which results were obtained by testing the original material and which results came from skip-lot testing or other testing and should specify the organization responsible for issuing the COA.	Self explanatory

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
	6.5 The original manufacturer and the intermediaries handling the material should always be traceable and transparent; and this information should be made available to authorities and end-users, downstream and upstream, when requested	
6.19 The distributor should also provide the identity of the original active substance manufacturer to competent authorities upon request. The original manufacturer can respond to the competent authority directly or through its authorised agents. (In this context 'authorised' refers to authorised by the manufacturer.)	Also covered by § 6.5 6.5 The original manufacturer and the intermediaries handling the material should always be traceable and transparent; and this information should be made available to authorities and end-users, downstream and upstream, when requested	Self-explanatory
6.20 The specific guidance for certificates of analysis is detailed in Section 11.4 of Part II of EudraLex Volume 4.	Not detailed as such, limited information detailed in § 6.3 6.3 Certificates of analysis (COAs) issued by the original manufacturer should be provided. If additional testing is done, all COAs should be provided. COAs should document product traceability back to the manufacturer by naming the original manufacturer and the manufacturing site. COAs should indicate which results were obtained by testing the original material and which results came from skip-lot testing or other testing and should specify the organization responsible for issuing the COA.	Self-explanatory
Chapter 7 – Returns, complaints and recalls		
Returns		
7.1 Returned active substances should be identified as such and quarantined pending investigation.	Requirements covered by the § 10.1 10.1 Goods returned to the supplier should be appropriately identified and quarantined. The conditions under which returned goods have been stored and shipped should be evaluated to determine the quality of the returned goods	Returned APIs should be identified as such and held pending resolution. Procedures for holding, labeling, testing, and any processing of the returned API should be defined.
7.2 Active substances which have left the care of the distributor, should only be returned to approved stock if all of the following conditions are met: **(i)** the active substance is in the original unopened container(s) with all original security seals present and is in good condition; **(ii)** it is demonstrated that the active substance has been stored and handled under proper conditions.	Partially covered under § 10.1 and 10.2, with less requirements 10.1 Goods returned to the supplier should be appropriately identified and quarantined. The conditions under which returned goods have been stored and shipped should be evaluated to determine the quality of the returned goods	If one of the conditions is not met, the distributor may return the material to the manufacturer who has to perform investigation and verify the status of the material and decide if the material may be returned in the approved stock. In addition to examination, testing of returned product could be considered based on a risk assessment.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
Written information provided by the customer should be available for this purpose; **(iii)** the remaining shelf life period is acceptable; **(iv)** the active substance has been examined and assessed by a person trained and authorised to do so; **(v)** no loss of information/traceability has occurred. This assessment should take into account the nature of the active substance, any special storage conditions it requires, and the time elapsed since it was supplied. As necessary and if there is any doubt about the quality of the returned active substance, advice should be sought from the manufacturer.	10.2 The quality unit or designee should decide on the disposition of the returned goods following a formal and documented investigation process. Corrective and preventive actions should be taken where appropriate.	
7.3 Records of returned active substances should be maintained. For each return, documentation should include: **(i)** name and address of the consignee returning the active substances; **(ii)** name or designation of active substance, active substance batch number and quantity returned; **(iii)** reason for return; **(iv)** use or disposal of the returned active substance and records of the assessment performed.	Partially covered under § 10.1 and 10.2, with less requirements	Self explanatory Records of returned products should be maintained and should include the name of the APIs and the lot number (or batch number), reason for the return, quantity returned, date of disposition, and ultimate fate of the returned API.
7.4 Only appropriately trained and authorised personnel should release active substances for return to stock. Active substances returned to saleable stock should be placed such that the stock rotation system operates effectively.	Partially covered under § 10.2, with less requirements	Self explanatory
Complaints and recalls		
7.5 All complaints, whether received orally or in writing, should be recorded and investigated according to a written procedure. In the event of a complaint about the quality of an active substance the distributor should review the complaint with the original active substance manufacturer in order to determine whether any further action, either with other customers who may have received this active substance or with the competent authority, or both, should be initiated. The investigation into the cause for the complaint should be conducted and documented by the appropriate party.	Requirements covered by the § 8 8.1 All complaints and other information concerning potentially defective materials must be carefully reviewed according to written procedures that describe the action to be taken and specify the criteria on which a decision to recall a product should be based. Records of complaints should be retained and evaluated for trends at defined intervals. 8.2 Any complaint concerning a material defect should be recorded and thoroughly investigated to identify the	Procedures for holding, labeling, testing, and any processing of the returned APIs or API intermediates should be defined. Complaints and information about possible defects during distribution activities should be systematically documented and investigated, based on a written procedure with assigned responsibilities. Investigations should be formally conducted and written up in a timely manner to establish if the complaint is justified, to identify root cause(s), to define any initial and/or follow up action(s), and the method of communication, e.g. to the customer, original manufacturer, authorities etc.

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
	origin or reason for the complaint (e.g. the repackaging procedure or the original manufacturing process). Corrective and preventive actions should be taken where appropriate and recorded. 8.3 If a defect in a pharmaceutical starting material is discovered or suspected, consideration should be given to whether other batches should be checked. 8.4 Where necessary, appropriate follow-up action, possibly including a recall, should be taken after investigation and evaluation of the complaint. 8.5 The manufacturer and customers should be informed if action is needed following possible faulty manufacturing, packaging, deterioration or any other serious quality problems with a pharmaceutical starting material	Complaint records should be retained and regularly evaluated for trends, frequency and criticality in order to identify possible additional needs for corrective or preventive actions. Investigations should identify whether the reported defect is limited to a single batch of material, or if other batches need to be considered as part of the investigation. Any additional batches implicated should be identified accordingly. The original manufacturer of the API has to be informed about defects with a potential impact on the product quality. For product recalls see section 9.
7.6 Complaint records should include: **(i)** name and address of complainant; **(ii)** name, title, where appropriate, and phone number of person submitting the complaint; **(iii)** complaint nature, including name and batch number of the active substance; **(iv)** date the complaint is received; **(v)** action initially taken, including dates and identity of person taking the action; **(vi)** any follow-up action taken; **(vii)** response provided to the originator of complaint, including date response sent; **(viii)** final decision on active substance batch.	Not detailed as such, limited information detailed in § 9.6 regarding recall information 9.6 All records should be readily available to the designated person(s) responsible for recalls. These records should contain sufficient information on materials supplied to customers (including exported materials).	Self-explanatory Responsibilities on final decision should be specified in the quality agreement.
7.7 Records of complaints should be retained in order to evaluate trends, product related frequencies, and severity with a view to taking additional, and if appropriate, immediate corrective action. These should be made available during inspections by competent authorities.		Self-explanatory
7.8 Where a complaint is referred to the original active substance manufacturer, the record maintained by the distributor should include any response received from	Partially covered under §8.5 8.5 The manufacturer and customers should be informed	Self-explanatory

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
the original active substance manufacturer, including date and information provided.	if action is needed following possible faulty manufacturing, packaging, deterioration or any other serious quality problems with a pharmaceutical starting material.	
7.9 In the event of a serious or potentially life-threatening situation, local, national, and/or international authorities should be informed and their advice sought.	Requirements covered by the § 9 but also § 8.5 with additional requirements 9.1 There should be a system for recalling promptly and effectively from the market, materials known or suspected to be defective. 9.5 In the event of serious or potentially life-threatening situations all customers and competent authorities in all countries to which a given material may have been distributed should be promptly informed of any intention to recall the material. 8.5 The manufacturer and customers should be informed if action is needed following possible faulty manufacturing, packaging, deterioration, or any other serious quality problems with a pharmaceutical starting material.	Additionally the original manufacturer of the API should be informed about the situation Confirmed complaints related to distribution with product quality impact should be communicated upstream to the manufacturer and also downstream to the customer(s) in case they may have received product with the same batch number.
7.10 There should be a written procedure that defines the circumstances under which a recall of an active substance should be considered.	Requirements covered by the § 9.3 and additional requirements with the §9.7 9.3 There should be established written procedures for the organization of any recall activity; these should be regularly checked and updated. 9.7 The effectiveness of the arrangements for recalls should be evaluated at regular intervals	There should be established written procedures for the organization of any recall activity; implemented system should be frequently tested on functionality (mock recall) The effectiveness of recall arrangements should be evaluated on a regular basis through mock recalls. A mock recall is intended to evaluate the traceability system for material distribution and to confirm that the product can be retrieved in the event of an adverse issue. Functions involved in the supply chain should implement written procedures to manage API recall (retrieval) promptly and effectively. The procedure should: - describe how the process of recall (retrieval) should be managed, based on the risk involved, - describe a decision making process with defined responsibilities, - define the functions involved in the process (e.g. Quality Assurance, sales, logistics, competent authorities etc.) - define the steps needed to retrieve the product

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
		Recalled, quarantined, rejected, or returned products should be identified and controlled under a quarantine system designed to prevent their unauthorized distribution and use in manufacturing or for sale
7.11 The recall procedure should designate who should be involved in evaluating the information, how a recall should be initiated, who should be informed about the recall, and how the recalled material should be treated. The designated person (cf. Section 3.1) should be involved in recalls.	Not detailed as such	Self-explanatory In case of a recall in addition agents, brokers, distributors should transfer all quality or regulatory information received from an API or intermediate manufacturer to the customer and from the customer to the API or intermediate manufacturer.
Chapter 8 – Self inspections		
8.1 The distributor should conduct and record self-inspections in order to monitor the implementation of and compliance with these guidelines. Regular self-inspections should be performed in accordance with an approved schedule.	Requirements covered by the § 9.5 1.9 A system should be in place for the performance of regular internal audits with the aim of continuous improvement. The findings of the audit and any corrective and preventive actions taken, including verification of their effectiveness, should be documented and brought to the attention of the responsible management.	Internal audits should be carried out on a regular basis to determine whether the Quality Management System complies with the GDP guidelines and to support continuous improvement. Audits and follow-up actions should be conducted in accordance with documented procedures. Different areas and functions should be audited. Audit results should be documented and discussed with the management personnel responsible for the audited area and, where relevant, with company management. Corrective and preventive actions should be taken in response to non-conformities identified. Ongoing oversight of plans and actions should be performed by the company's Quality department and senior management. The auditor should be independent of the area being audited, knowledgeable in the subject under inspection, and experienced in audit techniques.
Additional WHO transport guidance	**12. Dispatch and transport**	
	12.1 Materials should be loaded, unloaded and transported in a manner that will ensure the maintenance of controlled conditions where applicable (e.g. temperature, protection from the environment). The transport process should not adversely affect the materials. Any carrier used for transport should be approved according to a written procedure unless the carrier has been selected by the customer.	See 6.14 of EU GDP

EU Guidelines on GDP 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use	WHO TRS N°996, 2016 annex 06	APIC Comments taking into account ICHQ7 / additional requirements
.	12.2 Requirements for special transport and/or storage conditions should be stated on the label and/or in the transport documentation. If the pharmaceutical starting material is intended to be transferred outside the control of the manufacturer's materials management system, the name and address of the manufacturer, quality of contents, special transport conditions and any special legal requirements should also be included on the label and/or in the transport documentation	Covered by § 6.14 of EU GDP
	12.3 The supplier of the materials should ensure that the contract acceptor for transportation of the materials is aware of and provides the appropriate storage and transport conditions, e.g. through audits.	Covered by § 6.14 of EU GDP
	12.4 Procedures should be in place to ensure proper cleaning and prevention of cross-contamination when liquids (tanks) and bulk or packed materials are transported.	Covered by § 6.14 of EU GDP
	12.5 The bulk transport of pharmaceutical starting materials requires numerous precautions to avoid contamination and cross-contamination. The best practice is to use dedicated equipment, tanks or containers.	
	12.6 Packaging materials and transportation containers should be suitable to prevent damage to the pharmaceutical starting materials during transport	
	12.7 For bulk transport, validated cleaning procedures should be used between loadings, and a list of restricted previous cargoes must be supplied to the transport companies	
	12.8 Steps should be taken to prevent unauthorized access to the materials being transported	
	12.9 General international requirements regarding safety aspects (e.g. prevention of explosion and of contamination of the environment) should be observed.	

Chapter 5 – Glossary of terms

Terms	Definition
Batch	A specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval.
Batch number	A unique combination of numbers, letters and/or symbols that identifies a batch (or lot) and from which the production and distribution history can be determined.
Brokering of active substances	All activities in relation to the sale or purchase of active substances that do not include physical handling and that consist of negotiating independently and on behalf of another legal or natural person.
Calibration	The demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements.
Consignee	The person to whom the shipment is to be delivered whether by land, sea or air.
Contamination	The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, or active substance during production, sampling, packaging or repackaging, storage or transport.
Distribution of active substances	All activities consisting of procuring, importing, holding, supplying or exporting of active substances, apart from brokering.
Devia	Departure from an approved instruction or established standard.
Expiry date	The date placed on the container/labels of an active substance designating the time during which the active substance is expected to remain within established shelf life specifications if stored under defined conditions, and after which it should not be used.
Falsified active substance	Any active substance with a false representation of: a/ its identity, including its packaging and labelling, its name or its components as regards any of the ingredients and the strength of those ingredients; b/ its source, including its manufacturer, its country of manufacture, its country of origin; or c/ its history, including the records and documents relating to the distribution channels used.
Holding	Storing active substances.
Procedure	A documented description of the operations to be performed, the precautions to be taken and measures to be applied directly or indirectly related to the distribution of an active substance.

Procuring	Obtaining, acquiring, purchasing or buying active substances from manufacturers, importers or other distributors.
Quality risk management	A systematic process for the assessment, control, communication and review of risks to the quality of an active substance across the product lifecycle.
Quality system	The sum of all aspects of a system that implements quality policy and ensures that quality objectives are met (ICH Q9).
Quarantine	The status of materials isolated physically or by other effective means pending a decision on the subsequent approval or rejection.
Retest date	The date when a material should be re-examined to ensure that it is still suitable for use.
Supplying	All activities of providing, selling, donating active substances to distributors, pharmacists, or manufacturers of medicinal products.
Signed (signature)	The record of the individual who performed a particular action or review. This record can be initials, full handwritten signature, personal seal, or authenticated and secure electronic signature.
Transport (transportation)	Moving active substances between two locations without storing them for unjustified periods of time.
Validation	A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting pre-determined acceptance criteria. One of the common validations in the context of GDP is the validation of the transport. If a transport validation is applicable the following aspects might be considered: - Outcome of the transport risk assessment - Parameters to be assessed (Temperature, humidity, light exposure) - Packaging configuration during transportation - Modes of transport (e.g. road, air, sea) - (Transport routes (typically not defined in detail)) - Planned transport duration - Seasonal considerations (winter, summer) - Monitoring the transport with corresponding dataloggers