The International Pharmaceutical Excipients Council

Good Distribution Practices Guide

for Pharmaceutical Excipients

Version 3
2024

This document represents voluntary guidance for the excipient industry and the contents should not be interpreted as regulatory requirements. Alternatives to the approaches in this guide may be used to achieve an equivalent level of assurance for excipient quality.

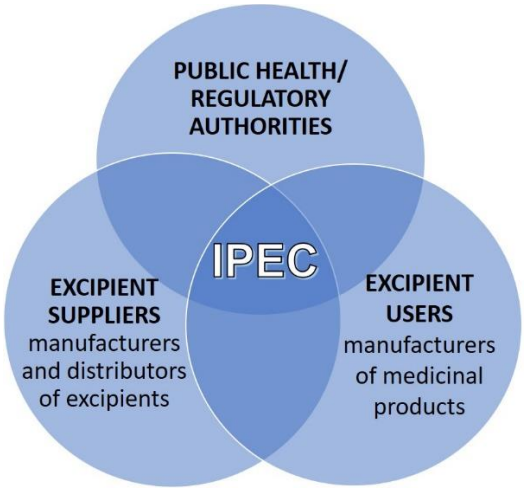
This guide was created to help companies understand current expectations on this topic and is not intended for use by third party certification bodies to conduct audits or to certify compliance with the guide.

FOREWORD

The International Pharmaceutical Excipients Council (IPEC) is an international industry association formed by excipient manufacturers, distributors, and end-users. At the current writing there are regional pharmaceutical excipient industry associations located in the Americas, Europe, Japan, China, and India. IPEC's objective is to contribute to the international excipient standards development and harmonization, provide information useful for new excipient development and introduction, and offer best practice and guidance concerning excipient development.

IPEC has three major stakeholder groups:

1. Excipient manufacturers and distributors, defined as suppliers in this document,
2. Medicinal (drug) product manufacturers, defined as *excipient users* in this document, and
3. Public health and regulatory authorities.



This guide is intended to be voluntary, to indicate best practice, and to be globally applicable. However, it should be recognized that the laws and regulations applying to excipients will vary

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from region to region and country to country. In addition, the rules and regulations are continually evolving. It is the responsibility of the reader to review the most current version of any applicable regulatory requirement. Versions referenced in the guide were based on versions available at the time the guide was published.

In this guide, pharmaceutical excipient(s) will be referred to as excipient(s). This guide may be applied to veterinary medicines, as appropriate and include reference to specific veterinary guidances and regulations.

Throughout the guide, **justification** implies that a decision is made based on scientific, quality and/or regulatory considerations.

This guide has been written to provide guidance for those companies involved in the supply chain of pharmaceutical excipients. Examples based on practical experience are provided to facilitate the application of GDP. However, alternative approaches may be acceptable.

This guide provides additional explanatory notes to:

"Good Trade and Distribution Practices for Pharmaceutical Starting Materials" [1]

The explanatory notes in this guide are the views of The International Pharmaceutical Excipients Council (IPEC) Federation and not necessarily those of the WHO.

This document is a revised version of The IPEC Good Distribution Practices Guide for Pharmaceutical Excipients first published in 2006 and updated in 2017.

*NOTE: Refer to the "International Pharmaceutical Excipients Council Glossary: General Glossary of Terms and Acronyms" for definitions [2]. The first use of a term found in the glossary will be in **BOLD**.*

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ACKNOWLEDGEMENTS

This guide was developed by representatives of the associations which constitute the IPEC Federation (IPEC). The IPEC Federation greatly appreciates the many hours devoted by the core team of individuals and other contributors listed below, to make this guide available to IPEC members and the broader excipient community. Equally, IPEC extends its thanks to the employers of those same contributors who provided the necessary time and resources, without which this guide would not be possible.

IPEC Federation would like to acknowledge the World Health Organisation (WHO) for their extensive efforts in developing the guidelines "*Good Trade and Distribution Practices for Pharmaceutical Starting Materials*" [1] which is valued by the IPEC Federation as a significant step in the development of tools for the improvement of safety and quality of starting materials and finished pharmaceuticals.

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1 INTRODUCTION

1.1 Purpose

GDP is an important element in the **supply chain** management of pharmaceutical **starting materials**. Several incidents in the past were caused by a lack of supply chain security and inappropriate handling of pharmaceutical excipients. This has motivated regulators and the IPEC Federation (**users**, **manufacturers** and **distributors** of pharmaceutical **excipients**) to take action.

The World Health Organization (WHO) published its guideline on *Good Trade and Distribution Practice for Pharmaceutical Starting Materials (GTDP)* in 2003, the scope of which covered both **active pharmaceutical ingredients** (**APIs**) and excipients. The WHO GTDP document provided the general principles to ensure good practices in the pharmaceutical starting materials supply chain. As an explanatory document focusing on pharmaceutical excipients, IPEC first published its ***Good Distribution Practices*** *Guide for Pharmaceutical Excipients*, in 2006. The first revision of this guide was in 2017 and was prompted by the revision of the WHO *Good Trade and Distribution Practices for Pharmaceutical Starting Materials"* [1]. This second, 2024 revision, was prompted by the current regulatory developments in GMPs and GDPs for excipients.

This IPEC Federation document offers a practical approach with examples that provide guidance on the application of the WHO GTDP principles. Where GMP relevant activities are described, references to *The Joint Good Manufacturing Guide for Pharmaceutical Excipients (2022)* (IPEC PQG GMP) [3] and other publications and standards, such as the EXCiPACT® *Certification Standards for Pharmaceutical Excipient Suppliers* [4] and *NSF/IPEC/ANSI 363* - ***Good Manufacturing Practice*** *(GMP) for Pharmaceutical Excipients* [5], are made in order to maintain consistency.

For GDP audits of manufacturers and distributors of excipients please refer to the IPEC *Good Distribution Practices Audit Guide for Pharmaceutical Excipients* [6].

1.2 Scope

This guide is applicable to excipients used in the **manufacture** of medicinal products. Information in the guide may also apply to excipients used in veterinary medicines.

As this document is based on the WHO *Good Trade and Distribution Practice for Pharmaceutical Starting Materials (GTDP) Guideline 2016* [1] it therefore follows the same structure. It is meant to provide guidance in the application of the GTDP specifically applied to pharmaceutical grade excipients. This updated 2024 guide also provides *notes* with practical examples and further explanations, where applicable.

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This document applies to all the different stages of the **distribution**/supply chain of excipients, starting from the point at which an excipient is transferred outside the control of the original manufacturer's material management system, e.g., Enterprise Resource Planning (ERP). It is written mainly for distributors, but it can be applicable for manufacturers and users of excipients if they manage part of the supply chain. Some sections may also be applicable to other parties such as warehousing companies and carriers. The applicability of and responsibility for compliance to these sections should be defined and formalised between the distributor and other parties.

To help the user to identify the sections in the combined WHO and IPEC Guidance (Table 2) applicable to their specific activities, please refer to Table 1 - *Matrix of Applicability*. The matrix differentiates between activities involving warehousing and distribution from those involving additional handling such as distributor bulk storage, repackaging, sampling, or **labelling** activities with excipients, reflecting different levels of control.

For the purpose of this guide “distributor” is a company procuring, importing, holding, supplying or exporting excipients.

A distributor takes possession and/or ownership of the excipient(s), including e.g., repackaging, warehousing and transportation, but does not alter the excipients’ physical and/or chemical characteristics e.g., processing / reprocessing.

For further definitions of terms refer to the *IPEC Federation General Glossary of Terms and Acronyms* [2].

Further processing activities, such as **blending**, mixing, milling, micronisation or any other physical manipulation of pharmaceutical excipients, should also reference the relevant sections of the current version of *The Joint IPEC-PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients (IPEC-PQG GMP)* [3] as well as the *EXCiPACT Good Manufacturing Practices / Good Distribution Practices Standard* [4] or *the NSF/IPEC/ANSI 363 - Good Manufacturing Practices (GMP) for Pharmaceutical Excipients* [5].

1.3 Principles Adopted

This is an international guide. As such it cannot specify all national legal requirements nor cover in detail the particular characteristics of every excipient.

When considering the use of this guide, manufacturers and distributors should consider how it may apply to that specific organization’s product. The diversity of excipients means that some principles of the guide may not be applicable to certain products and processes. The term “should” indicate recommendations that are expected to apply unless shown to be inapplicable or replaced by an alternative that provides at least an equivalent level of **conformance**. Note that “should” does not mean “must” or “shall”.

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This guide includes notes that offer common examples for interpretation and implementation without adding further requirements. Notes are not intended to contain an exhaustive list. They are presented as indented, *italicized* blue text.

2 PHARMACEUTICAL GRADE EXCIPIENTS

Parties involved in the supply chain should be aware that an excipient can only be designated pharmaceutical grade when it is in compliance with pharmacopoeia requirements and other applicable regulatory requirements (if existing for the specific excipient) and is manufactured, repackaged, and handled in accordance with excipient GMP principles e.g., from *IPEC-PQG GMP* [3], *WHO Excipient GMP* [7], *EXCiPACT GMP/GDP* [4] or *NSF/IPEC/ANSI 363 GMP* [5].

Upgrading a different **grade** of the same material, e.g., technical/industrial, cosmetic/personal care or food/feed, to pharmaceutical grade quality, only on the basis of analytical results found to be in conformance with the requirements of a pharmacopeial **monograph**, is not an acceptable practice.

3 GOOD DISTRIBUTION ACTIVITIES FOR PHARMACEUTICAL EXCIPIENTS

The following two tables contain information on:

Table 1: Matrix of Applicability is a high-level overview of relevant Good Distribution Activities and clarifying those sections which apply depending on the activity performed.

Table 2: Applicability for Supply Chain Activities containing IPEC's explanation of the *WHO Good Trade and Distribution Practices for Pharmaceutical Starting Materials* Guideline. A supply chain participant, who exclusively carries out a specific activity, should apply the sections of the document mentioned under the activity. If a company carries out different or additional activities all relevant sections mentioned under all conducted activities should be applied.

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Table 1 Matrix of Applicability

	Warehousing / Distribution (distribution of excipients in original packaging)			Additional Activities				
Activity: / Section:	Transportation of packed excipients	Warehousing (storage of packed excipients)	Reselling packed excipients	Repackaging	Sampling, Testing and Re-testing	Relabelling	Bulk handling / bulk storage	Transportation of bulk excipients e.g. in tank or silo equipment
1. Quality Management	◐	●	◐	●	●	●	●	◐
2. Organization and Personnel	◐	◐	◐	●	●	●	●	●
3. Premises	○	◐	◐	●	●	●	●	◐
4. Procurement, Ware-housing and Storage	○	◐	◐	●	○	◐	●	○
5. Equipment	◐	◐	○	●	◐	○	●	●
6. Documentation	◐	◐	◐	●	◐	●	◐	◐
7. Repackaging and Relabeling	○	○	○	●	◐	◐	◐	○
8. Complaints	◐	●	●	●	◐	●	●	●
9. Recalls	◐	◐	◐	●	○	●	●	○
10. Returned goods	◐	●	●	●	◐	●	●	◐
11. Handling of non-conforming materials	◐	◐	●	●	◐	●	●	◐
12. Dispatch and Transport	◐	○	◐	○	○	◐	○	●
13. Contract activities	●	●	●	●	●	●	●	●

● = applicable ◐ = partly applicable ○ = not applicable

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Table 2 Applicability for Supply Chain Activities

	Good trade and distribution practices for pharmaceutical starting materials (GTDP), WHO Technical Report Series, No. 996, 2016	IPEC Good Distribution Practices Guide for Pharmaceutical Excipients 2024
1. Quality Management		
1.1	Within an organization, quality assurance serves as a management tool. In contractual situations, quality assurance also serves to generate confidence in the supplier. There should be a documented quality policy describing the overall intentions and direction of the distributor regarding quality, which should be formally expressed and authorised by management. The quality policy should clearly indicate that the distributor implements and maintains good trade and distribution practices (GTDP) as described in these guidelines, within the organization and its services.	Parties involved in the excipient supply chain should establish a **Quality Management** System (QMS) to control the quality of their products and services in order to maintain the original quality of the excipient. As an essential pre-requisite for any QMS, the top management should document and sign off a Quality Policy that includes GDP/GMP. A system should be in place to control documents (Document Management System (DMS)) and **data** that relate to the requirements of the applicable QMS. Examples for documented description of the quality management system include Quality Manual, procedures, work instructions. See the *IPEC Excipient Information Package User Guide* [8], the *IPEC Excipient Information Package Templates* [9], and the IPEC *Excipient Information Package User Guide / Sustainability* [10]. Examples for commitment of the organization to applying the appropriate elements of GDP include: tracking quality metrics, GDP certification, presentations, and posters.
1.2	Quality management should include: - an appropriate infrastructure or "quality system", encompassing the organisational 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 independent quality unit (or designee), which is responsible for all quality-related matters;	At a minimum, the QMS should include the following documented elements: - scope of the QMS, - organizational structure; a description of the sequence and interaction between the procedures and departmental functions, and - an independent **quality unit** (or designee), which is responsible for all quality-related matters.

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	Good trade and distribution practices for pharmaceutical starting materials (GTDP), WHO Technical Report Series, No. 996, 2016	IPEC Good Distribution Practices Guide for Pharmaceutical Excipients 2024
	- an appropriate quality risk management (QRM) system to enable a systematic process for the assessment, control, communication and review of risks to the quality of the product. The extent of application of the QRM system should reflect the operations performed; - a validation/qualification system to ensure that the resulting product is capable of meeting the requirements for the specified application; systematic actions necessary to ensure adequate confidence that a material (or service) and relevant documentation will satisfy given requirements for quality – the totality of these actions is termed quality assurance; - a clear documented procedure for selecting, approving, disqualifying and re-approving suppliers of pharmaceutical starting materials and services; - 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; and a system ensuring traceability of products and associated documentation throughout the entire supply chain.	The excipient distributor should conduct risk assessments to identify the risks and opportunities that need to be addressed to: - give assurance that the quality management system can achieve its intended result(s), - enhance desirable effects, - prevent, or minimize, undesirable effects, and - achieve continual improvement. For guidance on risk assessments see *Guidelines of 19 March 2015 on the Formalised Risk Assessment for Ascertaining the Appropriate Good Manufacturing Practice for medicinal Products for Human Use (Text with EEA Relevance (2015/C95/02* [13]. See also: IPEC Risk Assessment Guide for Pharmaceutical Excipients – Part 1: *Risk Assessment for Excipient Manufacturers* [11] *and* *The IPEC Europe How to Document on EU Guidelines on Risk Assessment for Excipients* [12] *PIC/S PI-045-1 Guidelines for the Formalised Risk Assessment for Ascertaining the Appropriate Good Manufacturing Practice for Excipients of Medicinal Products for Human Use* which provides guidelines for implementation [14] *PDA- IPEC Federation Technical Report No.54-6 Formalized Risk Assessment for Excipients*, [15] and *ICH Q9 – Quality **Risk Management** – Scientific Guideline* [16].

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	Good trade and distribution practices for pharmaceutical starting materials (GTDP), WHO Technical Report Series, No. 996, 2016	IPEC Good Distribution Practices Guide for Pharmaceutical Excipients 2024
		Validation means: The documented act of proving that any procedure, process, equipment, material, activity, or system leads to the expected results. - A validation program that is typically performed in the pharmaceutical industry for APIs and drug products (i.e. DQ, IQ, OQ and PQ) may not always be applicable to excipients. See also the IPEC Federation Validation Guide for Pharmaceutical Excipients [17] *Note: see examples in The IPEC PQG GMP (see section on scope and processes of QMS) [3].*
1.3	The system should cover for example, but not be limited to, the quality assurance principles in these guidelines.	*Self-explanatory*
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.	Parties involved should share responsibility for assuring that the excipient conforms to the mutually agreed **specification** and is suitable for its intended use.
1.5	The responsibilities placed on any one individual should not be so extensive as to present any risk to quality. In the event of a supplier having a limited number of staff, some duties may be delegated or contracted out to designated persons who are appropriately qualified. There should, however, be no gaps or unexplained overlaps related to the application of GTDP for pharmaceutical starting materials as described in these guidelines.	There should be an adequate number of qualified personnel available either in-house or a contracted service to carry out all operations in compliance with this guide (refer to 2.2). Delegation of some duties is possible provided that this is not covering key quality processes such as final **batch** release and is documented in the QMS.
1.6	Where electronic commerce (e-commerce) is used, defined procedures and adequate systems should be in place to ensure confidence in the quality of the material and its traceability.	*Self-explanatory*

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1.7	Authorised release procedures should be in place to ensure that when material is released for its intended purpose, it is of an appropriate quality, meets its specifications and is sourced from approved suppliers.	If an excipient is provided in containers originally sealed by the manufacturer, no additional testing or batch release is required. Inspection of the integrity of the packaging (including **labelling**) and tamper evident seals should be carried out. A copy of the manufacturer's quality documentation (e.g., COA) should be made available for each delivery. Material deriving from non-pharmaceutical grades, such as food, cosmetic/personal care, industrial/technical grades, should not be designated as pharmaceutical grade even if tested and confirmed to conform to pharmacopoeial specifications when it is not produced under GMP manufacturing conditions and quality system appropriate for pharmaceutical excipients. Compliance with standards such as EXCiPACT or NSF/IPEC/ANSI 363-2019 provides assurance that the excipient was handled in conformance with an appropriate QMS. If an excipient is repackaged by the distributor, additional testing and batch release should be carried out according to section 7. *Note: see examples in the IPEC PQG GMP guide section 8.4.2.2 [3].*
1.8	Implementation of QRM principles using appropriate tools such as hazard analysis and critical control point (HACCP); inspection and certification of compliance with an appropriate quality system such as applicable International Organization for Standardization (ISO) series, and recognition of compliance with national and/or regional standards by external bodies is recommended. However, this should not be seen as a substitute for the implementation of these guidelines or for conforming, for example, to pharmaceutical GMP and good storage practices (GSP) requirements, as applicable.	*Self-explanatory*
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	Internal audits should be carried out at a frequency based on the status and criticality of the QMS activity, following Quality Risk Management (QRM) principles. Audits and follow-up actions should be conducted in accordance with documented procedures. Audit results should be

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	verification of their effectiveness, should be documented and brought to the attention of the responsible management.	documented and discussed with management personnel having responsibility in the area audited. Furthermore, corrective action and preventive action should be undertaken on the recorded non-conformities, and they should require timely follow-up actions.
2. Organisation and personnel		
2.1	There should be an adequate organisational structure and a sufficient number of personnel should be employed to carry out all the tasks for which the supplier is responsible.	The organisational structure should be formally documented in an organisational chart. There should be an adequate number of personnel, qualified by appropriate education, training and/or experience to perform and supervise activities concerning excipient distribution. Evidence of competence should be made available. There should be a Quality Unit or function that is independent of the operational functions and ensures quality relevant responsibilities e.g. handling of non-conformities, documentation and **traceability** of the excipient distribution activities.
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 authorised to undertake their duties and responsibilities.	Personnel, including external contractors, should be suitably qualified, trained, experienced and authorised to perform their duties and responsibilities. Levels of authorization should be clearly defined and documented, e.g., in QMS, job descriptions, contracts. Records should be maintained listing the name, address, and **qualification**s of any GDP and GMP related contracted service providers and the type of service they provide.
2.3	All personnel should be aware of the principles of the appropriate guidelines, including but not limited to GTDP.	*Self-explanatory*
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	A system for planning, provision and follow-up of regular training should be in place.

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	verified where appropriate. Training records should be maintained. All personnel should be motivated to support the establishment and maintenance of quality standards.	Quality standards applied should be part of a regular, ongoing and documented training program provided by qualified individuals. The extent of training should be dependent upon the company's and the employees' activities. All personnel should receive initial and regular follow-up training. The level of training and its frequency should be determined according to the potential impact of the activities on the excipient. Employees, in addition to Job Curriculum training, should receive appropriate GDP/GMP awareness and refresher training at regular intervals. Examples to verify the effectiveness of trainings include: - asking questions during and/or after the training, - written tests, and - documented observation of a practical demonstration.
2.5	Personnel dealing with hazardous materials (such as highly active, toxic, infectious or sensitizing materials) should be given specific training and should be provided with the necessary protective equipment. Documented policies and procedures for the use of personal protective equipment should be followed to decrease exposure of workers working directly with products and those in the immediate environment.	Personnel should be trained in the handling of the material according to requirement of the product safety data sheet and any applicable national and local legislation. These practices should be in line with hygiene procedures and any conflict between hygiene and safety procedures should be avoided. In case of conflict, safety procedures have priority, and a risk assessment should be performed and documented.
2.6	Personnel who may be exposed to materials from open containers should maintain good hygiene, have no open wounds and should wear appropriate protective garments, gloves, masks and goggles.	Activities exposing the excipient to personnel (e.g., sampling, packing/repacking) should be performed in such a way as to protect the excipient from **contamination**. The following will help to reduce the risk of contamination: - the wearing of clean personal protective equipment as appropriate to the activity (e.g., such as head, face, hand, and arm coverings); adequate washing facilities and supplies should be provided and easily accessible,

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		- the removal or covering of jewellery and other loose items as appropriate to the activity, - the storage and consumption of food, beverage, tobacco products and similar items should take place only in designated areas, - the provision of an adequate and continued personal hygiene and sanitation training program' and - instruction to report to management any health conditions that may have an adverse effect on excipient quality. Employee with an at-risk health condition should be reassigned to work where not exposed to excipient.
3. Premises		*Note: see examples in the IPEC PQG GMP guide section 7.1.4 [3]*
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 minimise the risk of errors and permit effective 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.	The prevention of contamination should be considered in the design of the handling processes and facilities, where the excipient is exposed. Buildings and facilities used in the handling, packaging, testing, or storage of an excipient should be maintained in a good state of repair and should be of suitable size, construction, and location to facilitate cleaning, maintenance, and error free operation, appropriate to the type of processing. All processes associated with the handling of highly sensitizing or toxic products (e.g. herbicides, pesticides etc.) should be located in dedicated facilities or equipment should be strictly separated from that used for excipient manufacture and distribution. If this is not possible, then appropriate measures (e.g. cleaning, inactivation) should be implemented to avoid cross-contamination and the effectiveness of these measures should be demonstrated. There should be adequate facilities for the sampling and testing of packaging components and finished excipients.

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		See also the current '*IPEC-PQG GMP* and EXCiPACT / ANSI 363 for the risk assessment approach to address these requirements. The current guide also references "How to" examples to assist in implementation processes.
3.2	Measures should be in place to prevent unauthorised persons from entering the premises.	*Self-explanatory*
3.3	Premises should be designed, equipped and maintained so as to afford maximum protection against the entry of insects, rodents or other animals. A pest control programme should be implemented and maintained. Its effectiveness should be monitored.	*Self-explanatory*
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.	A documented risk assessment should be conducted to determine the necessary controls for facilities and utilities (e.g. lighting, air control, nitrogen, compressed air, steam, water) that could affect excipient quality.
3.5	If sampling of pharmaceutical starting materials is performed, the sampling area should be separate and in a controlled environment. Sampling should only be performed in a storage area if it can be conducted in such a way that there is no risk of contamination or cross-contamination. Adequate cleaning procedures should be in place for the sampling areas.	*Self-explanatory*
4. Procurement, warehousing and storage		*Note: see examples in IPEC PQG GMP section 8.5.4*
	Note: GSP are applicable in all circumstances in which, and in all areas, where materials are stored.	

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4.1	Materials should be purchased from approved suppliers in accordance with mutually agreed formal specifications.	*Self-explanatory*
4.2	Actions should be taken to minimise the risk of falsified or non-conforming materials entering the supply chain.	*Self-explanatory*
4.3	There should be authorised 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.	Written procedures should describe receipt of the excipient, its storage, release for shipment and onward dispatch. Some considerations (that may not be applicable in all situations) are: - receipt: adherence to specific transport conditions, visual inspection of the container (packaged or bulk), confirmation of excipient identity from the **label** against documentation, evidence of infestation, - storage: cleanliness of excipient storage area, accuracy of the inventory locator system; monitoring of specific storage conditions if applicable, - proof of product integrity: **verification** of correct material by matching excipient label, its dispatch documentation and potential security features (no damage or tamper evidence), and - dispatch: truck cleanliness, tracking records, cleanliness of containers, and transport equipment, adherence to specific transport conditions.
4.4	Storage areas should have sufficient capacity to allow orderly storage of the various categories of materials.	Excipients should be stored in a manner to protect and maintain their quality (see 4.9 and 4.10) and the integrity of their packaging and labelling. The facility should be organised in a manner to facilitate orderly storage, appropriate segregation and correct selection of designated materials. Different materials and different batches of the same material should not be stored within the same storage location unless appropriate controls are in place. Excipients should be stored in conformance with safety requirements.

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4.5	Receipt and dispatch bays should be equipped with the means to protect materials from adverse environmental conditions. Reception areas should be designed and equipped to allow containers of incoming materials to be cleaned before storage if appropriate. Upon receipt, material should be segregated until released by the quality unit.	Protection from adverse environmental conditions should be considered as a minimum requirement (e.g., roof or shelter) but any specified storage conditions should be met when required to provide suitable protection against deterioration, contamination, and loss of traceability.
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 computerised system, should provide equivalent security and should be appropriately qualified and validated.	See 1.2. For any electronic system e.g., ERP, replacing or in combination with physical segregation it should be demonstrated and documented that the intended segregation rules are consistently applied and that any quarantined, rejected, recalled or otherwise blocked material cannot be selected by the system for production or distribution purposes. Accessing blocked material requires special authorization from the quality unit or defined designee. Quality should review and authorize the fate of the recalled and returned excipient. *Note: For example, if a container is damaged and cannot be resold, Operations can dispose of the material provided it is documented according to company procedures, without the need for Quality oversight.*
4.7	The storage areas should be kept clean and dry.	*Self-explanatory*
4.8	Segregated areas and materials should be appropriately identified.	Segregation can be achieved through either physical or **computer**-controlled **system**s.
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.	*Self-explanatory*

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	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.	An assessment should be conducted to confirm the facility can meet specified conditions. When specified conditions are required to maintain product integrity, records should verify that the requirements are met. Separate environmentally controlled storage areas should be considered where necessary.
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.	*Self-explanatory*
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.	*Self-explanatory* See 5.1.
4.13	Products should be packed in such a way as to avoid breakage, contamination, tampering or theft. The packing should be adequate to maintain the quality of the product during transport. If special shipping conditions have to be met, they should be defined, provided and controlled. The containers in which products are shipped should be sealed and should clearly indicate the authenticity of the product and its supplier.	*Self-explanatory*
4.14	Spillages should be cleaned up as soon as possible to prevent possible cross-contamination and hazard.	*Self-explanatory*
4.15	Provision should be made for the proper and safe storage of waste materials awaiting disposal. Toxic substances and flammable materials	*Self-explanatory* See sections 4.2, 4.4, 4.5 and 4.8.

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	should be stored in suitably designed, separate, closed containers in enclosed areas, taking into account the relevant national legislation.	
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.	*Self-explanatory*
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.	Withdrawals from saleable stock should be quarantined until dispositioned by quality.
4.18	Stock inventory should be checked regularly, at least for quantity, overall condition and retesting or expiration dates. Any discrepancies should be investigated.	*Self-explanatory*
4.19	Controls should be in place to ensure that the correct product is picked, packed and distributed. The material should have an appropriate remaining shelf life. All batch numbers should be recorded.	*Self-explanatory*
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.	There should be records to show when inspections were made, including observations of the findings for vermin and all pest control activities. Materials used for control of vermin should not adversely affect the excipient, should comply with local regulatory agency, if required, for use in food or pharmaceutical facilities, and should be recorded with safety data sheets made available locally to their usage (see also 3.3).
5. Equipment		*Note: see examples in the IPEC-PQG GMP guide section 7.1.3.2 [3].*
5.1	Equipment must be located, designed, constructed, adapted, qualified, used, cleaned and maintained to suit the operations to be carried out.	A qualification procedure and a cleaning and maintenance plan should be in place. The subject activities should be performed and recorded by trained personnel.

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	Its layout, design and use should aim to minimise 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.	
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.	*Self-explanatory*
5.3	The status of the equipment should be readily identifiable.	The status of all equipment should be known such as by signage or logbooks (e.g. to be cleaned, out of order, approved for use etc.).
5.4	Fixed pipework should be clearly labelled to indicate the contents and, where applicable, the direction of flow.	*Self-explanatory*
5.5	All services, piping and devices should be adequately marked, and special attention paid to the provision of non-interchangeable connections or adaptors for dangerous gases, liquids and other materials.	*Self-explanatory*
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.	There should be procedures in place for calibration of balances and other quality critical measuring equipment on a scheduled basis and defined frequency. Calibration records should be maintained. Calibration status needs to be readily available. Provisions should ensure that only equipment within calibration and of an appropriate range and precision can be used. If equipment is found to be out of calibration, the impact to excipient quality since the last calibration should be investigated.
5.7	Dedicated equipment should be used where appropriate when handling and/or processing pharmaceutical starting materials. Where non-dedicated equipment is used cleaning validation should be performed.	When dedicated or non-dedicated equipment coming in direct contact with the excipient is used for excipient handling (e.g., storage tanks, bulk trucks, pipes and hoses, repackaging equipment etc.; see also 7.10), appropriate cleaning procedures and effective cleaning schedules should be maintained and recorded.

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		Dedicated and non-dedicated equipment might require different levels of cleaning procedures and effective cleaning schedules. Cleaning should be defined and justified. Tanker hoses should be blanked off when not in use in order to prevent access to birds, rodents and insects. Non-dedicated equipment should only be re-used for a different excipient following effective cleaning. Cleaning effectiveness should be verified by e.g.: - checking the equipment after cleaning for residues of the previous product and cleaning agents or alternatively, - testing the final rinse after cleaning for residues of the previous product and cleaning agents or, - by testing each batch for residues of the previous product handled with the same equipment in order to avoid contamination and carry-over of previously processed products. See 1.2 In the case that non-dedicated equipment is used without verification of cleaning, then cleaning procedures need to be validated. The full validation program that is typically performed in the pharmaceutical industry for APIs and **drug products** (i.e., DQ, IQ, OQ and PQ) may not always be applicable to excipients. See also the current *'IPEC Validation Guide* [17]
5.8	Closed equipment should be used when possible. If open equipment is used, suitable measures should be taken to prevent contamination.	Measures to be taken to prevent contaminations may be found in the current '*The Joint IPEC-PQG GMP Guide*' [3].
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.	*Self-explanatory*

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5.10	Washing and cleaning equipment should be chosen and used such that it cannot be a source of contamination.	The use and selection of washing and cleaning equipment should be such that the risk of contamination is minimised.
6. Documentation		*Note: see IPEC-PQG GMP guide section 7.5 [3].*
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.	Documentation comprises all written procedures, instructions, contracts, records and data, in paper or in electronic form. Version control of all documents should be maintained with traceability of the revisions. Quality management system documents should be subject to regular review, have a defined owner and be approved by the quality unit before issuance to the appropriate areas (Note 2). If electronic signatures are used, they should be authenticated, provide equivalent security to handwritten signatures, and comply with relevant regulatory requirements. **Data integrity** principles i. e, ALCOA+ should be incorporated throughout the procedures and systems used for managing documentation. Data integrity controls for excipient distribution processes should be commensurate with risks associated with the use of the data. A higher level of control should be implemented where the loss of data integrity could compromise compliance with excipient GDP, impact confidence in excipient quality, cause the failure or rejection of the medicinal product, or pose potential harm to the patient. Data should be traceable throughout the data lifecycle, and changes should be recorded as part of the metadata (i.e. audit trails) Data integrity requirements apply equally to manual (paper) and electronic data. The inherent risks to data integrity may differ depending upon the

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		degree to which data (or the system generating or using the data) can be configured, and therefore potentially manipulated. Data integrity controls for excipients may be different from controls used for Active Pharmaceutical Ingredients (APIs) and medicinal products. *Notes: 1. Examples of how ownership is defined include:* - *name and / or function of the owner identified within the document, and* - *list of procedures with owners for each.* *The owner does not have to be the quality unit.* *2. How can the quality unit review and approve a document?* - *signing off as reviewed and accepted for final draft version, and* - *signing off as final approver.*
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.	A revision history of documents should be readily available. Related documents should be cross-referenced.
6.3	Certificates of analysis (CoA) 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 organisation responsible for issuing the CoA.	If any batch (**lot**) mixing is carried out, CoA from manufacturers is no longer valid and the **supplier** should perform analyses in its own laboratory or at a named and qualified contract laboratory. Batch (lot) mixing is considered a manufacturing process and therefore should follow GMP (see 7.1). See also '*The International Pharmaceutical Excipients Council* ***Certificate of Analysis*** *Guide for Pharmaceutical Excipients* [18].

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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.	*Self-explanatory*
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.	Distribution records of excipient shipments to initial customers should be kept. To facilitate traceability and retrieval, if necessary, distribution records should include: - **batch number**, - customer name and address, - quantity shipped, - shipment date, and - where critical to maintaining excipient quality, conditions were met during transportation to the initial customer.
6.6	Depending upon risk assessment, and in accordance with the national requirements, quality agreements should form the basis of the relationship for all parties involved in the supply chain. The agreements should include mechanisms to allow transfer of information, e.g. quality or regulatory information and change control.	*Self-explanatory* See also '*The IPEC Federation* ***Quality Agreement*** *Guide and Template(s)'* [19].
6.7	Labels applied to containers should be clear, unambiguous, permanently fixed and should be printed in the company's agreed format. The information on the label should be indelible.	*Self-explanatory*
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),	Label generating systems and procedures should be controlled and documented. Appropriate verification and records should be maintained. Information about the original manufacturing site may also be provided in other ways or in other documents.

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	- 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, and - identification of the original manufacturing site; and name and contact details of the supplier.	In case specific storage conditions are required to ensure stability and quality of the excipients, they should be provided on the label.
6.9	Relevant storage and handling information and safety data sheets should be available.	*Self-explanatory*
6.10	Records should be kept and must be readily available upon request in accordance with GMP and GSP (6).	The security and methods of archiving and retrieval of such records should comply with data integrity principles (see 6.1). The record retention period shall not be less than one year past the excipient's expiry or first re-evaluation date. If the manufacturer does not stipulate an expiry or re-evaluation date, the record retention period shall be at least five years from the **date of manufacture**.
7. Repackaging and relabelling		
7.1	Operations, such as combining into a homogeneous batch, repackaging and/or relabelling, are manufacturing processes and are not recommended. In circumstances where they are to be conducted, their performance should be in compliance with GMP. *Note: It is important to note that any party who engages in repackaging or blending of an API is considered to be a manufacturer and must submit appropriate registration documents for such manufacturing. They must also comply with the GMP for APIs as set out in WHO Technical Report Series, No. 957, Annex 2, [11].*	Processes whereby the original container of excipients is opened or removed are critical for excipient quality (e.g. transfer from bulk container to storage tanks/silos or from storage tanks/silos into containers). Under these conditions excipients could be contaminated with other products, lubricants, cleaners or any other foreign matters. To minimise these risks the IPEC-PQG GMP principles should be applied. See IPEC PQG GMP Guide. [3] *Note that the WHO text on the left-hand column references the WHO Technical Report Series, No. 957, Annex 2, as [11].*

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		The IPEC Good Distribution Practices references this as [21] in section VI – References.
7.2	Special attention should be given to the following points: - prevention of contamination, cross-contamination and mix ups; - appropriate environmental conditions for dispensing, packaging and sampling; - security of stocks of labels, line clearance checks, online inspections, destruction of excess batch-printed labels and label reconciliation; - good sanitation and hygiene practices; - maintaining batch integrity (mixing of different batches of the same solid material should normally not be done); - as part of batch records, all labels that were removed from the original container during operations, and a sample of the new label, should be kept; - if more than one batch of labels is used in one operation, samples of each batch should be kept; and maintaining product identity, integrity and traceability.	Special attention should be given to the following points: - contamination, cross-contamination and mix-ups should be avoided by using suitable equipment and procedures, - environmental conditions and repackaging procedures should be designed to avoid contamination and cross-contamination during repackaging and relabelling operations. The need for filtered air, protective clothing and other measures to prevent product contamination and cross contamination should be identified by a risk assessment. Protective clothing for the operators should be clearly defined, - labels should be printed using a controlled system ensuring that all necessary information is correct (see 6.8). Sufficient crosschecks should be installed to ensure accurate data transfer. A procedure should be installed to avoid mislabelling. Printing and usage of labels should be controlled in accordance with documented procedures. All labelling operations (e.g. generating, printing, storage, usage, destruction) should always be recorded. Labelled containers should be inspected, and surplus labels should be destroyed to avoid any misuse. If labels are not printed at time of use, security stock should be controlled and limited access should be defined. Labels bearing batch specific information should be reconciled, - labels of the original manufacturer should not be overlabeled. Any label change needs to be traceable in the batch record, - repackaging and relabelling operations should be carried out in an environment designed to minimise contamination. It should be clearly defined where and how an excipient will be repackaged and relabelled. Personnel involved in repackaging processes should wear clean

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		protective apparel such as head, face, hand, and arm coverings, if necessary and practice appropriate personnel hygiene (e.g. hand disinfection, following health requirements, health monitoring, covering exposed jewellery). Personnel should be trained on any special hygiene requirements. Training should be recorded. Repackaging areas should be regularly cleaned and, if appropriate, sanitised, - where a new batch number is assigned, traceability to the original batch number should be documented. The combination of product number and batch number should allow full traceability. Assigning the same batch number to containers of different batches complying with the same specification is an unacceptable practice (see also 7.4 and 7.5), - a reference to the details of the original label should be kept with the batch record, - one copy of each separate batch of labels used should be kept with the batch record, and - all repackaging and relabelling processes should be designed and carried out to avoid mix-up and carry-over and to ensure full traceability of the excipients upstream to the original manufacturer and downstream to the final customer. Each step should be recorded by responsible personnel, including name of operator, date (and time, if required).
7.3	Upon receipt, packaging materials should be placed in quarantine and should not be used prior to release. There should be procedures for the inspection, approval and release of the packaging materials.	*Self-explanatory*
7.4	When different batches of a material from the same original manufacturing site are received by a distributor and combined into a	Blending of batches or lots of excipients that individually do not conform to specifications, with other lots that do conform (in an attempt to salvage or hide adulterated excipient) is not an acceptable practice.

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	homogeneous batch, the conformity of each batch with its specification should be confirmed before it is added.	A batch can only be homogenous when conforming excipient is mixed. Mixing to form a homogeneous batch is a manufacturing step therefore should be verified and documented.
7.5	Only materials from the same manufacturing site, received by a distributor and conforming to the same specifications, can be mixed. If different batches of the same material are mixed to form a homogeneous batch it should be defined as a new batch, tested and supplied with a batch certificate of analysis. In such cases the customer should be informed that the material supplied is a mixture of manufacturers' batches.	See also 7.1. The blending process should be verified to ensure that it will not impact the quality of the excipient. The blended excipient should be tested to ensure conformance to the specification and to provide data for the Certificate of Analysis (CoA). Blending should not be used to dilute contamination. Blending should also not be used where the performance of the resulting excipient could be impacted.
7.6	In all cases, traceability back to the manufacturer should be documented by identifying the original manufacturer of the specific batch of the material and its manufacturing site.	The quality documents required to accompany deliveries to assure traceability should be subject to an agreement between the distributor and final customer.
7.7	If batches are combined or mixed, the oldest batch should determine the expiry or retest date assigned to the combined or mixed batch.	*Self-explanatory* See 6.3 clarifying GMP and analytical testing requirements for mixed batches.
7.8	If the integrity and quality of the batch is maintained during repackaging and relabelling, then the original CoA of the original manufacturer should be provided. If retesting is done, both the original and the new CoA should be provided as long as the batch integrity is maintained. The batch referred to on the new CoA should be traceable to the original CoA.	If retesting is required, the analytical methods used by the original manufacturer and/or pharmacopoeia methods should be applied. Pharmacopeial methods should be verified by the lab in which tests are performed and non-pharmacopeial methods validated. Where other methods are applied, these should be agreed upon between both parties and documented on the CoA and/or the excipient specification. See also the IPEC Federation Guideline '*The IPEC Certificate of Analysis Guide for Pharmaceutical Excipients*' [].
7.9	Repackaging of materials should be carried out using approved packaging materials for which the quality and suitability have been	*Self-explanatory*

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	established as being equal to or better than those of the original container.	See 7.21 *WHO GTDP guide* for implication on stability studies [1].
7.10	The reuse of containers should be discouraged unless they have been cleaned using a validated procedure. Recycled containers should not be used unless there is evidence that the quality of the material packed in them will not be adversely affected.	The use of new containers is recommended for repackaged excipients. Alternatively, use of dedicated containers in a closed loop is considered an acceptable practice. If containers are reused, then procedures should be based on risk assessment taking into account e.g. the usage of seals, removal of labels, handling and cleaning (see also 5.7). There should be a procedure defining the specific conditions of reuse that should be shared between the supplier and customer.
7.11	Materials should be repackaged only if efficient environmental control exists to ensure that there is no possibility of contamination, cross-contamination, degradation, physicochemical changes and/or mix-ups. The quality of air supplied to the area should be suitable for the activities performed, e.g. there should be efficient filtration.	Environmental conditions should be established by risk assessment. Valuable information may be obtained from the original manufacturer or relevant standards (e.g. EU Guideline on the risk assessment to determine appropriate GMPs for excipients, ISO 14644, Annex 1 to EU-GMP Part I) or compendial monographs and relevant general chapters(see also 2.6).
7.12	Suitable procedures should be followed to ensure proper label control.	Procedures should be implemented to ensure that the correct quantity of labels are printed and issued, and that the labels contain the correct information (see 6.8). The procedures should also define that any excess labels are immediately destroyed or returned to a controlled storage area and actions recorded. Repackaging and relabelling facilities should be inspected immediately prior to use, ensuring that all materials that are not required for the next repackaging operation have been removed. The outcome of this inspection should be recorded.
7.13	Containers of repackaged material and relabelled containers should bear both the name of the original manufacturing site and the name of the distributor/repacker.	If agreed upon with the pharmaceutical customer, information about the original manufacturing site may also be provided in other ways or in other documents.
7.14	Procedures should be in place to ensure maintenance of the identity and quality of the material by appropriate means, both before and after repackaging operations.	Additionally, these procedures should include documented traceability both downstream and upstream. *Note: Such procedures may include e.g.:*

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		- *Labelling* - *Sampling* - *Analytical testing* - *Line clearance* - *Packaging instructions* - *Equipment cleaning* - *Environmental controls* - *Pest control* - *Maintenance* - *Method validation* - *Calibration*
7.15	Each batch of repackaged material should be tested to ensure that the material conforms to documented specifications.	Special consideration should be given to those properties that might be affected by the repackaging. Such properties and a sampling plan that includes the number of samples, from where the samples will be taken and the method of sampling may be identified by a risk assessment and included in a testing regime for samples from filled containers. *Note: Typical parameters to consider may include e.g.:* - *Water content* - *pH* - *Visual inspection* - *Colour* - *Id.* - *Purity* - *Potential impurities* - *Contaminants*

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7.16	There should be a procedure to ensure that appropriate repackaging documentation, in addition to the test results, is evaluated prior to release of the repackaged material.	Each repackaging operation should be recorded with name and date of the relevant operators.. Typically, a checklist and/or form-sheet is used. This record should be evaluated by the quality unit together with the test results prior to the release of the repackaged batch for distribution.
7.17	Sampling, analytical testing and batch release procedures should be in accordance with GMP.	In the case where excipients are to be sampled, tested and released the following principles should be applied. Sampling activities should be conducted under conditions in accordance with a defined sampling method, using approved procedures and sampling tools designed to minimize the risk of contamination, including cross-contamination. Data integrity principles, i.e., ALCOA+, should be incorporated throughout laboratory procedures and systems to always maintain data integrity (see 6.1). Laboratory controls should be established, requiring complete data derived from tests deemed necessary to ensure conformance with specifications and standards. Records (see 6.1) of these controls should include: identification and traceability of samples, i.e., a description of the sample including material name, batch number, identity of sampling and testing personnel, sampling date, test methods, test equipment used, raw data, calculations, and test results. Laboratory reagents, solutions, and reference standards may be purchased or prepared internally. There should be documented procedures for the labelling, handling, use, and storage of laboratory reagents, solutions, and reference standards. Procedures should also be available for the preparation and standardization of internally prepared materials. Purchased materials should be verified on receipt.

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		Purchased and internally prepared materials should be stored appropriately and labelled with the name, concentration, and expiry or re-evaluation date. Purchased materials, once opened, should also be labelled with the remaining usage period. Records for the preparation and standardization of reagents, solutions, and reference standards should be maintained and include at a minimum: identity of the prepared material; identity, quantities, and batch numbers of **components** used in the preparation, name of preparer, equipment used for preparation, date of preparation, expiry or re-evaluation date of the prepared material. When secondary reference standards are used, there should be a documented procedure for their qualification against primary reference standards. This procedure should include requirements for preparation, testing, approval, use, and storage. Expiry or re-evaluation periods should be defined for secondary reference standards. For secondary reference standards with re-evaluation periods, requalification should be performed according to a documented procedure. The quality unit or defined designee is responsible for the release of the re-packaged excipient. There should be a procedure to ensure that appropriate re-packaging documentation, in addition to the test results, is evaluated prior to release of the finished excipient. Excipient shipped to the customer prior to quality unit release should follow a documented quarantine-shipping process that includes acknowledgement by the customer. For re-packaged excipient batches, a CoA containing results acquired from testing should be made available. See the IPEC Certificate of Analysis Guide for Pharmaceutical Excipients for details on the suitable contents of a certificate of analysis.

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7.18	Only official pharmacopoeial methods or validated analytical test methods should be used for the analysis. Where alternatives to the test methods specified in a monograph are used to provide test results, those alternative methods should be demonstrated to be suitable and equivalent.	For control of key parameters during repackaging and or full retesting of excipients, official pharmacopoeia methods or methods validated against the pharmacopoeia methods should be used. Otherwise, the original manufacturer's analytical methods are recommended. Non-compendial, including in-house, analytical test methods should be demonstrated to be at least equivalent to those in the compendia. The responsibility for monitoring the current pharmacopeia or official compendium should be assigned, including material monographs, general notices and mandatory general chapters. The methods used should be listed on the CoA and/or the excipient specification accompanying the excipient or made available to the customer by other documents. These documents should also reference any contract laboratory that is used to perform analyses. The CoA should identify which tests have been performed on the individual batch and which tests have been performed via **skip batch (lot) testing** or reduced testing (see 6.3).
7.19	Out-of-specification test results should be investigated and documented.	Investigation and documentation of out-of-specification (OOS) test results should be carried out according to a written procedure (see 11). Results obtained by retesting may only be used to replace original test results if a documented investigation concludes that the original results are erroneous due to an assignable root cause. When there is no assignable root cause, the OOS procedure should define: - criteria for retesting and the use of retest sample results, - criteria for re-sampling, - which techniques are to be used and under what circumstances.

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		Retesting may not be necessary when product is released under a different specification. However, an OOS investigation should still be performed and documented. Original and retest data should be included in the investigation report, including when the sample is suspected of not being representative of the material from which it was taken. *Note: Examples of assignable root cause that invalidates original results include:* - *sampling error (e.g., pulled from wrong tank, used uncleaned sampling device),* - *test equipment settings were incorrect,* - *wrong weight of sample used in analysis, and* - *wrong analytical procedure used.*
7.20	Samples of pharmaceutical starting materials in appropriate quantities should be kept for at least one year after the expiry or retest date, or for three years after distribution is complete.	If excipients are repackaged, processed or packaged from bulk, retained samples representative of the excipient batch should be kept. The retention period should be justified and based on the expiry or re-evaluation date. The sample size should be the amount required to perform two complete analyses. The retained samples should be stored in a secured location, readily retrievable and in conditions consistent with the recommended storage conditions for the finished excipient. Retained samples should be maintained in a packaging format that does not alter the product. *Note: Reasons for using more protective packaging for retained samples are e.g.:* - *to ensure the results obtained at testing are on a sample that has not changed during storage,*

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		- *because finished packaging sizes may not be practical for sample storage, and* - *because samples for microbiological testing need to be stored in specialized containers*
7.21	The repacker and relabeller should ensure that the stability of the material is not adversely affected by the repackaging or relabelling. Stability studies to justify assigned expiration or retest dates should be conducted if the pharmaceutical starting material is repackaged in a container different from that used by the original manufacturer. It is recognised that some excipients may not need additional stability studies.	Stability and expiration dating of excipients are primarily the responsibility of the excipient manufacturer. If an excipient is transferred to another container type or repackaged by the supplier, stability and **shelf life** (retest or expiry period) considerations should be taken into account, including storage and transport conditions. The type of container, **primary packaging materials** and storage conditions used by the repackaging site should be taken into account when shelf life (retest or expiry period) is defined for excipients. The recommended expiration date provided by the original manufacturer should not be extended without demonstrating stability to justify an extended shelf life (retest or expiry period). In such a case the type of container and storage/transport conditions should be clearly defined. If the need for special storage conditions exists (e.g., protection from light, heat), such restrictions should be indicated on the label. See *The IPEC Stability Guide for Pharmaceutical Excipients* [20].
8. Complaints		
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.	There should be a documented procedure for management of customer complaints. This procedure should include at a minimum: - receiving and documenting the complaint, - investigating the complaint, - the timeline an investigation should be completed in, - criteria for involvement of the original excipient manufacturer, and

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		- concluding and documenting the investigation, identifying:
		  o root cause,
		  o whether the complaint is justified,
		  o impact on other excipients (see 8.3 and 11), and
		  o corrective and / or preventive actions as needed (see 1.9 and 11).
		- responding to the customer and, as appropriate, other parties as required.
		Records of complaints, complaint investigations, and resulting actions should be maintained. Complaints should be regularly evaluated for trends, including recurrence and criticality, in order to identify needs for corrective or preventive actions.
		Note: The procedure for management of customer complaints may also be applied to complaints from internal customers, i.e., intra-company or inter-departmental complaints.

8.2	Any complaint concerning a material defect should be recorded and thoroughly investigated to identify the 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.	*Self-explanatory (see 8.1)*
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.	Investigations should identify whether the reported defect is limited to a single batch. It needs to be considered as part of the investigation if other batches of the same excipient or other excipients could be impacted. Any impacted batches and/or excipients should be identified and labelled (e.g. “under quarantine”) accordingly (see 4.6). If an excipient that could be impacted has already entered the supply chain, it should be considered as part of the investigation. Depending on the type of control (electronic or manual), the excipient may have to be segregated.

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8.4	Where necessary, appropriate follow-up action, possibly including a recall, should be taken after investigation and evaluation of the complaint.	For product recalls see 9.
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.	Communication should be performed upstream to the supplier (manufacturer or any other party selling the excipient) and also downstream to the customer(s) in case they may have received excipient which could be impacted.
9. Recalls		
	Note: In some regions / countries regulatory authorities may have specific definitions for these terms. *In this document "recall" has the same meaning as "retrieval".*	
9.1	There should be a system for recalling promptly and effectively from the market, materials known or suspected to be defective.	Functions involved in the supply chain should implement written procedures to manage excipient **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 parties to be involved in the process (e.g. Quality Assurance, sales, logistics, competent authorities), - define the communication process, documentation and its recording, and - describe how reconciliation discrepancies should be addressed.
9.2	The original manufacturer should be informed in the event of a recall.	If the original manufacturing is found to be contributing to the root cause the original manufacturer should be notified
9.3	There should be detailed written procedures for the organisation of any recall activity. These procedure(s) should be regularly reviewed and updated.	*Self-explanatory*

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9.4	All recalled materials should be stored in a secure area while their fate is decided.	*Self-explanatory* See 4.6
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* See 9.1
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* See 9.1
9.7	The effectiveness of the arrangements for recalls should be evaluated at regular intervals.	Effectiveness should be demonstrated by a so called “mock” recall. A mock recall is a simulated exercise to evaluate the traceability system in excipient distribution and to ensure that the excipient can be returned in case of any adverse problem. Mock recalls should be conducted on a regular basis.
10. Returned Goods		
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 excipients should be identified as such and held under quarantine pending their disposition. There should be written procedures for holding, labelling, testing, and any handling of the returned excipient. Records of returned excipients should be maintained and should include the name of the excipient and the batch (lot) number, reason for the return, quantity returned and the customer from whom it was returned. The impact on excipient quality of the conditions under which returned excipient has been stored and shipped, when not under control of the distributor, should be evaluated by the Quality Unit or designee prior to any movement to return goods to saleable inventory.

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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.	The disposition of the returned excipient, e.g. disposal, destruction, reintroduction to the market, downgrading/reclassification, should be determined by the responsible function based on risk assessment of the returned goods. Elements of the risk assessment may include: - the excipient is in the original unopened container(s) with all original security seals present and is in good condition, - it is demonstrated that the excipient has been stored and handled under defined conditions, e.g. based on written information provided by the customer, - the remaining shelf-life period is acceptable, - the excipient has been examined and assessed by a person trained and authorised to do so, and - no loss of information/traceability has occurred. Records of the Quality Unit's or designee confirmation should be maintained and include, at a minimum, if returned to inventory. This is not required if the material is downgraded or disposed - name of the excipient, - batch (lot) number, - reason for return, - quantity returned, - identification of customer who returned the excipient, - any evaluation that was performed, and - final disposition of the returned excipient.
11. Handling of non-conforming materials		
11.1	Non-conforming materials should be handled in accordance with a procedure that will prevent their introduction or reintroduction into the	Special care should be taken when non-conforming or expired materials are provided to external organisations for destruction. Such activities

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	market. Records covering all activities, including destruction, disposal, return and reclassification, should be maintained.	should be supervised or covered by evidence of destruction preventing the material from reappearing in the market.
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.	The investigation should include the following: - determination of the root cause, - determination of whether a single or multiple batches are affected, - determination of whether a different material is affected, - determination of preventive / corrective actions to prevent the recurrence of the problem, including assignment of responsibilities and timelines for implementation, - determination of measures to establish the effectiveness of the actions taken; and - detailed documentation. The quality unit or designee should review and approve the results of this investigation.
11.3	The disposition of the material, including downgrading to other suitable purposes, should be documented.	*Self-explanatory*
11.4	Non-conforming materials should never be blended with materials that do comply with specifications.	It is not acceptable to blend contaminated or adulterated batches to reduce the contamination or adulteration below an acceptable or detectable limit.
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.	Transport conditions and the equipment to be used should be defined according to the characteristics of the excipient. This requires an understanding of the conditions (e.g. temperature, humidity and exposure to light over time) that may adversely affect excipient quality characteristics. If any special transport conditions are required, they should be monitored and recorded.

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		Carriers need to be qualified in accordance with written procedure as part of the supplier approval process. If the carrier has been selected by the customer, carrier qualification is the responsibility of the customer. For any bulk transport equipment that has direct product contact, the material of construction should be reviewed to ensure it does not adversely affect product quality including valves, fittings and gaskets, i.e. tankers, bulk ISO containers, hoses etc.
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.	If any special transport conditions are required, they should be discussed and formally agreed between supplier, carrier and customer prior to shipment. If agreed upon with the carrier and/ or customer, information about the original manufacturer may also be provided in other ways or on other documents than the labels (e.g., CoA). Any special transport and/or storage conditions should be referenced on the container label. See also 6.8. *Notes* *1. Defined transportation conditions may be applicable, e.g., in the case of excipients for which transportation conditions outside recommended storage conditions have the potential to result in deterioration of the excipient.* *2. Examples of defined transportation conditions include:* - *temperature,* - *humidity,* - *light,* - *atmosphere, and* - *sanitary (e.g., odourless, free from pest infestation).* - *visibly clean*

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		3. Examples of how transportation conditions may be provided include: - *container label,* - *shipping documents,* - *product specification, and* - *safety data sheet.*
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.	The supplier of the excipient should provide the contract acceptor with information about any special conditions required for transport and/or storage conditions, or equipment to be used. The ability of the contract acceptor to comply with these requirements should be evaluated as part of the initial qualification process (see 12.1). Where special requirements are identified, these should be discussed and included in a written procedure between supplier of the excipient and the contract acceptor (e.g. in a Service Level Agreement) or in case of usage of owned equipment in a written internal procedure.
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.	There should be an agreement defining the specific conditions (e.g. handling, sealing, cleaning, restricted or segregated cargo) between supplier of the excipient and the contract acceptor (e.g. in a Service Level Agreement) or in case of usage of owned equipment in a written internal procedure. For bulk see also 12.5, 12.7, 12.8, 5.8 and 7.7. Transport conditions need to ensure that contamination of the outer packaging material is avoided, especially when shipping less than full truckload quantities.

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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.	Best practice for bulk transport is to use dedicated equipment and defined handling processes. If this is not possible: - the type of transport and ancillary equipment (e.g. seals, fittings, hoses, pumps) should be specified. The materials used should be compatible with the transported excipients. Possible incompatibilities between sealing materials or hoses and the excipient transported should be taken into account especially for solvents, - consideration has to be given to equipment that is exclusively used for transporting similar products, - changes to bulk transport equipment and supplies should be controlled, evaluated and finally approved by the contract giver, and - adequate cleaning and previous cargo procedures have to be in place and records kept of all cleaning activities.
12.6	Packaging materials and transportation containers should be suitable to prevent damage to the pharmaceutical starting materials during transport.	*Self-explanatory*
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.	When dedicated or non-dedicated equipment coming in direct contact with the excipient is used for transporting excipients (e.g. bulk trucks, hoses, couplings), appropriate cleaning procedures and effective cleaning schedules should be maintained and recorded. Dedicated and non-dedicated equipment may require different levels of cleaning procedures and effective cleaning schedules. See section 5.8. When cleaning is required, equipment should only be used again after verification of the cleaning efficiency by way of a written statement and other means if necessary.

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		When non-dedicated equipment is used for transporting excipients in bulk consideration has to be given to previous cargoes. A list of restricted or acceptable previous cargoes should be formally communicated to and agreed upon with the transport companies or in case of owned equipment included in an internal procedure. Documented evidence of previous cargo carried (up to 3 previous loads) should be provided.
12.8	Steps should be taken to prevent unauthorised access to the materials being transported.	Consideration should be given to security aspects through a risk analysis. Additional measures can include tamper evident seals on bulk and individual containers and/or transport units. Examples of tamper evident seals are the closure of the packaging system and could be represented by security tapes with company logo, all special seals or locks to protect the closure of a packaging container or transport container.
12.9	General international requirements regarding safety aspects (e.g. prevention of explosion and of contamination of the environment) should be observed.	Local requirements for transportation of dangerous goods such as ADR, IMDG, 49 CFR, IATA, and ADG should be followed. In addition, packaging materials and transportation containers should also be adequate for the transport securing method used (such as "EU Cargo Securing Guidelines"). See 7.13.
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.	Delegated responsibilities should be agreed in writing (see 13.4) and where appropriate, training should be provided for the delegated activities. Contracts should include requirements for **change control**.
13.2	The contract giver should evaluate the proposed contract acceptor's compliance with GTDP before entering into an agreement.	The evaluation should be based on risk assessment and could include an audit of the contract acceptor's premises, equipment and quality management system. Audit reports of qualified third-party audit organisations may be acceptable.

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	Good trade and distribution practices for pharmaceutical starting materials (GTDP), WHO Technical Report Series, No. 996, 2016	IPEC Good Distribution Practices Guide for Pharmaceutical Excipients 2024
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.	*Self-explanatory*. See 12.4 for the prevention of cross-contamination.

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.	Formal agreements include technical, service level or quality agreements. The responsibility for the quality ultimately remains with the contract giver, and control measures should be defined.
		Note: Examples for controls of outsourced operations and services include:
		- *specific agreed controls and procedures, based on outcome of risk assessment, e.g.,*
		  ○ *review of records and approval of operations or services by the contract giver, and*
		  ○ *on-site presence of the contract giver during execution of outsourced activity.*
		- *review and approval for use of cleaning agents and pest control materials,*
		- *inspections of the service provider's operations and / or services, and*
		- *periodic audits of the service provider.*

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.	*Sub-contracting for manufacturing type activities (e.g. sampling, testing, re-packaging and relabelling) should be approved by the contract giver and agreed upon in writing between the parties. Sub-contracting activities are subject to change control. Sub-contracted activities need to comply with applicable GMP and GDP requirements.*

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[6] IPEC Good Distribution Practices Audit Guide for Pharmaceutical Excipients

[7] Good Manufacturing Practices: Supplementary Guidelines for the Manufacture of Pharmaceutical Excipients; World Health Organisation, WHO Technical Report Series, No 885, 1999

[8] IPEC Excipient Information Package - User Guide

[9] IPEC Excipient Information Package - Templates

[10] IPEC Excipient Information Package User Guide – Sustainability

[11] IPEC Risk Assessment Guide for Pharmaceutical Excipients Part 1 – Risk Assessment for Excipient Manufacturers

[12] IPEC Europe ‘How-To’ Document Guidelines of 19 March 2015 on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use (OJ 2015/C 95/02)

[13] Guidelines of 19 March 2015 on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use (Text with EEA relevance) (2015/C 95/02)

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[15] PDA-IPEC Federation Technical Report No. 54-6 Formalized Risk Assessment for Excipients

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[17] IPEC Federation Validation Guide for Pharmaceutical Excipients

[18] IPEC Federation Certificate of Analysis Guide for Pharmaceutical Excipients

[19] IPEC Quality Agreement Guide and Template(s)

[20] IPEC Stability Guide for Pharmaceutical Excipients

[21] Good Manufacturing Practices for Active Pharmaceutical Ingredients; World Health Organisation, WHO Technical Report Series, No. 957, 2010

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