



**Australian Government**  
**Department of Health**  
Therapeutic Goods Administration

# Sunscreen manufacturing

Demonstrating compliance with the PIC/S guide to GMP, PE009-13

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**TGA** Health Safety  
Regulation



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This guidance is for sunscreen manufacturers who must comply with the *PIC/S Guide to Good Manufacturing Practice for Medicinal Products*.

In Australia, many sunscreens are regulated as therapeutic goods because of their important role addressing public health issues. As such they must comply with the [Therapeutic Goods Act 1989](#), the [Therapeutic Goods Regulations 1990](#) and any other relevant regulatory requirements.

Sunscreens that are regulated as therapeutic goods under the *Therapeutic Goods Act 1989* are referred to as 'therapeutic sunscreens'. Included in this category are:

- primary sunscreens with SPF 4 or more
- secondary sunscreens - except those regulated as cosmetics
- primary or secondary sunscreens with SPF 4 or more that contain an insect repellent
- sunscreens with SPF less than 4 that are exempt from being listed under the *Therapeutic Goods Act 1989* because they come within the exemption in item 8(g) of Schedule 5 of the *Therapeutic Goods Regulations 1990*.

Details on the therapeutic sunscreen regulatory framework are available at [Australian Regulatory Guidelines for Sunscreens](#). To be listed on the ARTG, sunscreens must comply with the Australian and New Zealand sunscreen standard [AS/NZS 2604:2012 Sunscreen products-Evaluation and classification](#).

## This guidance

This guidance explains TGA's interpretation and expectations for compliance by therapeutic sunscreen manufacturers, with specific sections of the PIC/S Guide to Good Manufacturing Practice for Medicinal Products PE009-13 ([PIC/S Guide to GMP](#)).

TGA has adopted the PIC/S Guide to GMP, PE009-13 (excluding Annexes 4, 5 and 14), which took effect on 1 January 2018 with a 12-month [transition plan](#).



This guidance is not mandatory or enforceable under law. It is not intended to be restrictive. It describes a way that a sunscreen manufacturer may operate to demonstrate compliance with the PIC/S Guide to GMP, PE009-13.

This information is provided for guidance only and has been developed on the basis of current knowledge of the subject matter. It should not be relied upon to address every aspect of the relevant legislation.



In this guidance, 'we' refers to the TGA and 'you' refers to manufacturers.

## Related information

For technical requirements, refer to:

- [PIC/S Guide to GMP for medicinal products](#)

Other TGA guidance relevant to sunscreen manufacturing:

- [Manufacturing medicines](#)
- [Data Management and Data Integrity \(DMDI\) Guidance](#)
- [Release for supply of medicines](#)
- [PQRs for listed and complementary medicines](#)
- [Supplier assessment, approval and qualification for listed and complementary medicines](#)
- [Process validation for listed and complementary medicines](#)
- [Medicines labels: Guidance on TGO 91 and 92](#)
- [Uniform recall procedure for therapeutic goods](#)

Other useful guidance:

- WHO heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms ([Annex5, TRS 961](#))
- [CPMP/ICH/381/95](#): ICH Topic Q 2(R1) – Note for Guidance on Validation of Analytical Procedures: Text and Methodology
- [PIC/S recommendation publications](#)

## Further questions

If you have further questions, or you require further clarification of a particular requirement, email the [Manufacturing Quality Branch](#).

## Sections of PE009-13 that apply

The sections of the PIC/S Guide to GMP (PE009-13) that apply to sunscreens will be determined by the nature of your operations and the variety of products or dosage forms you manufacture.

In general, you should follow the principles of Part I of PE009-13, and in addition, all annexes relevant to their operations and dosage forms.

Generally speaking, you should meet the requirements of:

- Annex 8 (sampling)
- Annex 9 (manufacture of liquids, creams and ointments)
- Annex 11 (computerised systems)
- Annex 15 (qualification and validation)
- Annex 19 (reference and retention samples)



- Annex 20 (quality risk management), a voluntary annex; however, the principles outlined in the annex are applicable to the manufacture of therapeutic sunscreens

The following annexes are not usually relevant to sunscreen manufacture: annex 7 and 13.

The following annexes are not relevant to sunscreen manufacture: annexes 1, 2, 3, 6, 10, 12 and 17.

The TGA has not adopted annexes 4, 5, 14 and 16. Annex 18 no longer exists.

## Quality management (Chapter 1)

### Terminology for quality management

#### Pharmaceutical Quality System (PQS)

In the latest PIC/S Guide to GMP, 'Pharmaceutical Quality System' (PQS) has replaced the term 'Quality Management System'. This is in line with ICH Q10 global harmonisation efforts, PIC/S harmonisation efforts and to align the GMP guide with contemporary principles of quality systems management. The new terminology better reflects the specific design elements and requirements for a quality system used to manage the manufacture of medicinal products.

The PQS approach described is applicable to the manufacture of all therapeutic goods to which the PE009-13 applies.

#### Manufacturing authorisation

The term 'manufacturing authorisation', generally refers to the licence to manufacture therapeutic goods issued by TGA to domestic manufacturers. For manufacturers located overseas, this would refer to the certificate of GMP compliance issued following an inspection.

#### Marketing authorisation

A 'marketing authorisation' is the approval given to supply a therapeutic good in Australia and involves entry on the Australian Register of Therapeutic Goods (ARTG).

The marketing authorisation includes the details of the product in the Australian Register of Therapeutic Goods (ARTG), as well as all other matters in relation to product registration, listing or inclusion agreed in writing between TGA and the sponsor, and any other requirements imposed by a relevant Delegate of the Secretary upon ARTG entry.

Examples of regulatory requirements include, but are not limited to:

- compliance with standards and registered formulations
- special storage and transportation conditions
- shelf life
- packaging and labelling
- batch release testing requirements

The manufacturer is responsible for ensuring their PQS is designed and operated to ensure all relevant requirements of the marketing authorisation are observed during the manufacture of medicines.

## Holder of the marketing authorisation

The holder of the marketing authorisation is the product sponsor.

## Change management

### Regulated changes

Manufacturing changes that affect the product's listed or registered details are termed 'regulated changes' and require an application to vary the marketing authorisation. Please refer to [Australian Regulatory Guidelines for Sunscreens](#).

These requirements are mandatory and are in addition to the requirements of the PIC/S Guide to GMP (PE009-13).

The requirements within the PIC/S Guide to GMP (PE009-13) in relation to change control and risk assessment apply to both regulated and other changes.

### Change control applies to all GMP-related activities

The expectation that change control does not just apply to validation activities, but to all GMP-related activities undertaken by a manufacturer has been clarified (clause 1.4 xii, xiii).

Any changes to existing processes, systems, facilities, equipment, products, documents, etc. should be evaluated through a change control process. The effort and extent of change control processes should be commensurate with the nature of the change and based on risk management principles.

All changes implemented should be verified for their effectiveness following implementation.

## Managing deviations

There are no changes to the expectations for managing deviations and other similar events (Clause 1.4 xiv). However, PE009-13 now provides clarity regarding the expectations for the investigation of deviations, including adequate root-cause-analysis and identification of corrective and preventative actions.

## Release for supply

For more information on release for supply, refer to:

- [Guidance on release for supply](#)

## Senior management responsibilities for GMP and quality management

Particular emphasis is placed on the roles and responsibilities of senior management who have ultimate control over manufacturing facilities and activities (new clauses in PE009-13 (including clause 1.5)). Senior management hold the responsibility to make sure that adequate resources are available (human, financial and physical) in order to ensure that the manufacturing activity is managed appropriately.

It is expected that senior management ensure that an effective PQS is implemented and undertake an active role in the support, development and implementation of the PQS. Under the new PE009-13, senior management are ultimately responsible and accountable for the effectiveness of the PQS.

## Management reviews

Management reviews (clause 1.6) are a basic quality system element designed to collate, evaluate and communicate details of the effectiveness of the PQS to the management group. Management reviews are particularly important in escalating concerns and enabling senior management support with the aim of resolving issues and managing risks. TGA's basic expectations, based on ICH Q10 principles, are that the management review system should include:

- results and findings of regulatory inspections, , audits and other assessments, and commitments made to regulatory authorities
- periodic reviews of management quality, which can include:
  - measures of customer satisfaction such as product quality complaints and recalls
  - conclusions of process performance and product quality monitoring
  - the effectiveness of process and product changes including those arising from corrective action and preventive actions
- follow-up actions from previous management reviews

The management review system should identify appropriate actions, such as:

- improvements to manufacturing processes and products
- provision, training and/or realignment of resources
- capture and dissemination of knowledge

## Management Review of the Pharmaceutical Quality System

Management should have a formal process for reviewing the PQS on a periodic basis. The review should include:

- measurement of achievement of PQS objectives
- assessment of performance indicators that can be used to monitor the effectiveness of processes within the PQS, such as:
  - complaint, deviation, corrective and preventative actions (CAPA) and change management processes
  - feedback on outsourced activities
  - self-assessment processes including risk assessments, trending, and audits
  - external assessments such as regulatory inspections and findings, and customer audits

Monitoring by managers of internal and external factors impacting the PQS can include:

- emerging regulations, guidance and quality issues that can impact the PQS
- innovations that might enhance the PQS
- changes in business environment and objectives

- changes in product ownership

## Frequency of management reviews

TGA inspectors would generally expect reviews to be conducted at least annually (clause 1.6). However, management reviews may be performed more frequently for new operations, sites that have not previously performed management reviews and sites where the initial management review identifies a number of issues that require rectification.

More frequent reviews may be required for sites with larger and more diverse manufacturing operations.

## Quality manual development

A Quality Manual (or equivalent document) is required to be written and maintained (clause 1.7 in PE009-13).

Your quality manual or equivalent should be established and contain the description of the PQS including:

- the quality policy
- the scope of the PQS
- identification of the PQS processes, as well as their sequences, linkages and interdependencies. Process maps and flow charts can be useful tools to facilitate depicting PQS processes in a visual manner
- management responsibilities within the PQS

## Product distribution expectations

When products are distributed, minimise any risk to product quality and take account of 'good distribution practice' (GDP) (clause 1.8 (ix)).

TGA does not currently inspect the wholesale distribution of therapeutic goods that have been released for supply.

For sunscreens, sponsors and manufacturers hold **shared responsibility** for ensuring that products are stored, distributed and subsequently handled so that quality is maintained throughout their shelf life. Quality or technical agreements should clearly identify the responsibilities of manufacturers and Australian sponsor, where they are separate entities.

TGA inspections do include an evaluation of the transport conditions for starting materials, bulk and packed medicines between sites of manufacture and clause 1.8 (ix) would apply in these circumstances.

GDP in the case of Australia would be limited to the application of transport requirements specified in Annex 15 of the PIC/S guide to GMP and not necessarily any other official GDP guideline.

## Product Quality Reviews (PQRs)

Manufacturers of sunscreens are expected to generate PQRs in accordance with GMP requirements (clause 1.10).

For more information see our guidance on [Product Quality Reviews](#), because the guidance for listed and complementary medicines also applies to sunscreens.

## All authorised products require PQRs

'All authorised products' in clause 1.10 refers to all products manufactured, within the reviewed time period, under a manufacturing authorisation. This implies that domestic manufacturers are expected to conduct PQRs for all medicinal products manufactured under the manufacturing licence and overseas manufacturers are expected to conduct PQRs for all medicinal products for which a GMP clearance is granted.

## Export-only medicine PQRs

The PQR requirements for export only products are the same as the PQR requirements for all authorised products.

## Supply chain traceability for active substances in PQRs

As part of your PQR, manufacturers of finished sunscreens should have a clear understanding of the approved suppliers of active substances, and each entity and their responsibility in the supply chain between the site of manufacture and receipt (clause 1.10(i)).

For guidance on the evaluation of supply chains for active materials used in sunscreens see [Supplier assessment, approval and qualification](#).

## Frequency of PQRs

It is important that you perform a review of all relevant elements of clause 1.10 on at least a yearly basis; however, where very few batches of one product are manufactured in one year, or no manufacturing takes place, it may also be acceptable to perform a full PQR on a two yearly basis providing a rationale is documented and scientifically justified.

Manufacturers and sponsors are expected to maintain vigilance over elements of clause 1.10 that do not directly relate to manufacturing activities, e.g. results of ongoing stability, returns, recalls and complaints that may provide information regarding products available in the market, for periods where very few batches of one product are manufactured in one year, or no manufacturing takes place.

## Grouping of products for PQR

Grouping of products is when one PQR is prepared for a group of products. Grouping for the preparation of PQRs is acceptable for sunscreen products and should take consideration of the following:

- a similar base formulation
- the same dosage form
- the same active ingredients
- a similar SPF rating
- been manufactured using similar equipment

## **Shared responsibility for PQRs between manufacturers and the sponsor**

Preparation of PQRs is a shared responsibility between the sponsor and the manufacturer(s) of a product. Manufacturers and sponsors should design and implement effective systems to ensure that PQR reports and relevant data are supplied, compiled and reviewed. Responsibilities in relation to PQRs should be clearly defined within quality or technical agreements between parties.

Each manufacturer in the supply chain is expected to generate and hold PQRs relevant to the specific manufacturing step they are undertaking. These are expected to be supplied to the sponsor and available for review during inspections of manufacturing sites.

The full PQR containing all relevant sections from all manufacturers should be held and reviewed by authorised persons performing the release for supply step. Sponsors are also expected to have access to the PQRs, to ensure product compliance with the marketing authorisation.

## **Quality risk management**

### **Quality risk management is mandatory**

It is a mandatory requirement for you to have an operational quality risk management system in place to ensure that the evaluation of a risk to product quality is based on a sound, scientific basis and that risk assessments are appropriately documented (clauses 1.12 and 1.13).

Annex 20 is voluntary and provides guidance only on Quality Risk Management tools that may be applied by a manufacturer when assessing the risk to product quality.

## **Personnel (Chapter 2)**

### **Senior management responsibilities for personnel**

Particular emphasis is placed on the roles and responsibilities of senior management who have ultimate control over manufacturing facilities and activities in new clauses of PE009-13 (including clause 2.1). Senior management are accountable for ensuring appropriate resources are available to support the relevant manufacturing activities.

### **Personnel qualifications**

#### **Necessary qualifications for staff**

'Necessary qualifications' means having the education, training, experience and skills, or any combination of these elements, that will ensure that staff can perform assigned duties and functions at an acceptable level (clause 2.1).

#### **Qualification requirements for an authorised person**

There are no minimum qualification requirements for authorised persons specified within Australian legislation. However, in accordance with GMP, senior management should ensure that person(s) undertaking the role of authorised person have the education, training, experience

and skills or any combination of these elements to ensure that they can perform the role of the authorised person.

In general an authorised person should be able to demonstrate the following competencies:

- knowledge of the requirements of GMP applicable to the dosage forms for which they are responsible
- a comprehensive understanding of the manufacturing methods and controls for the specific dosage form(s) for which they are responsible
- knowledge of the regulatory requirements relevant to the dosage forms manufactured by their site. In particular, knowledge of the marketing authorisation requirements for the specific products for which they are responsible
- working knowledge of the PQS implemented at their manufacturing site

## **Expectations for training and language**

### **Training requirements**

Training and assessment should be carried out by persons with relevant training, qualifications and experience in the subject matter (clauses 2.10 to 2.14).

Training should be given to all people affected by significant change in the PQS, for example when SOPs or methods of manufacture change. The requirement for initial and ongoing training should be reflected in procedures, and training records should be generated and kept.

There are a number of people who have a direct bearing on quality outcomes. These include senior management, contractors, consultants and casual employees. Therefore, appropriate training and assessment should be provided and recorded.

### **Language requirements**

You should define language requirements or standards and ensure personnel are proficient in the required language for their allocated tasks, particularly in relation to documenting and recording. Procedures employed to overcome identifiable deficiencies should also be documented.

## **Role of consultants**

### **Management of consultants**

Where you engage a consultant to assist in operations, it is important that adequate records are kept and maintained, including:

- contracts between the manufacturer and consultant outlining the scope of services
- up-to-date copies of each consultants curriculum vitae
- job descriptions outlining roles, responsibilities, delegations and authorisations
- training records for local PQS procedures relevant to their role

It is your responsibility to assess consultants and to ensure that they have adequate education, training, and experience, or any combination thereof, relevant to the services for which they are engaged.

## Controlled document approval

Consultants are permitted (where defined by agreements) to write, review and approve documents within the PQS. However, the licence holder ultimately remains responsible for the content of, and adherence to, authorised procedures within their PQS and cannot delegate or discharge the overall responsibility for the accuracy and content of documents signed by the consultants.

# Premises and equipment (Chapter 3)

## Environmental controls

### Starting material environment for sampling

The physical requirements for the area being used to sample non-sterile starting materials are described in clause 3.9. In order to protect the sampled material from contamination, this sampling would be expected to be carried out in an appropriately clean and controlled environment.

During sampling operations, consider the following:

- interior surfaces of the sampling area should permit easy and effective cleaning
- only one material at a time should be taken into the sampling area to prevent cross contamination back into any primary starting material container
- materials should only be opened in the controlled environment of the sampling area
- if sampled materials have fine particles and/or generate dust there should be adequate containment/dust extraction controls in place
- appropriate cleaning and area clearance should be in place



Sampling of starting materials in an open warehouse would **not** be allowed.

### Primary packaging materials for non-sterile products environment for sampling

Physical requirements for the area being used to sample primary packaging material for non-sterile products are described in clause 3.9. As product-contact components, primary packaging materials should be sampled within an environment that adequately protects the packaging from contamination.





Sampling of primary packaging materials in an open warehouse would **not** be allowed.

## Air quality for sunscreen manufacture

The use of closed systems of processing and transfer in order to protect liquid, cream or ointment product from contamination are recommended (Annex 9). Production areas where the products, or open clean containers, are exposed should normally be effectively ventilated with filtered air.

The PIC/S Guide to GMP (PE009-13) does not reference a specific standard for air quality, or filtration, for non-sterile manufacturing areas and there are no Australian or ISO standards for air quality specific to sunscreen manufacture.

As a general guide, those areas used for manufacturing and packaging microbiologically sensitive sunscreen products should be supplied with air filtered to remove 85% of particles above 1 micron, or EU 7 standard. These areas should be at a positive pressure relative to the rest of the facility to ensure that the correct standard of air quality is maintained.

If you can demonstrate that closed systems are used, filtered air requirements can be reduced to only those areas where the product is exposed.

In all cases, it is your responsibility to ensure that adequate and appropriate qualification and monitoring processes are in place to justify the heating, ventilation and air conditioning (HVAC) design and to demonstrate that areas are effectively ventilated with adequately filtered air where sunscreen products, or open clean containers are exposed.



Give special attention to manufacturing environments that include the manufacture of products other than sunscreens.

## Minimum air quality for microbiologically sensitive products

As a minimum expectation for areas where microbiologically sensitive products or open clean containers are exposed:

- air quality requirements (physical and microbiological) should be defined during system design and compliance demonstrated through qualification and on-going monitoring
- air filters used in manufacturing areas where product is exposed should be at least EU7 grade or equivalent
  - air filters with a greater filter efficiency than EU7 may be required where adjacent products or processes, other than sunscreen manufacture, present a potential contamination risk
- room pressures and air flows must be defined and appropriate

## Additional guidance

For additional guidance in relation to recommended levels of air filtration, consult:

- WHO heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms ([Annex5, TRS 961](#))

## Cleaning and sanitisation

The PIC/S Guide to GMP (PE009-13) contains limited detail on requirements for cleaning and sanitisation.

Cleaning of equipment with potable water is generally acceptable where equipment is:

- subjected to a final rinse with process ([potable water that is appropriately treated to meet a designated specification for use](#)) or purified water

OR

- sanitised with an alcohol-based solution or similar

Annex 15 contains information about the [validation of cleaning](#).

## Premises and equipment definitions

### Campaign manufacture

Campaign manufacture is defined as being a separation in time of production (clause 5.19). That is, manufacturing a series of batches of the same product in sequence in a given period of time and/or maximum number of batches followed by an appropriate (validated) cleaning procedure.

A system should be in operation which ensures that cleaning and, where necessary, sanitisation has occurred after use and before re-use of equipment. However, where equipment is dedicated to one formulation only, or used for a run of batches of the same formulation, a partial clean would be acceptable, involving removal of as much as practicable of each batch before proceeding to the next batch. For example, manufacturing tanks and other product contact equipment are visibly clean but transfer pipes and pumps are not required to be stripped down for a complete clean between campaign batches.

In such cases, the maximum period of time or maximum number of batches that are permitted to elapse before complete cleaning is carried out, as well as detailed instructions for inter-batch campaign cleaning, should be specified in a standard procedure. Campaign lengths should be supported by cleaning and process validation data.

## Warehouses and distribution centres

By definition, 'manufacture' includes all steps in bringing the product to its final form with 'release for supply' considered to be the last step in this process.

From a GMP point of view, warehousing and distribution after release for supply and after the product has left the manufacturer's control, is not currently regulated by the TGA. Hence, a facility that is used only for warehousing and distribution of fully finished and released products does not require a TGA manufacturing licence and is not required to comply with the PIC/S guide to GMP for medicinal products.

However, for an effective recall, cooperation from wholesalers and distributors is often essential. Wholesalers should have a procedure for conducting a recall at a sponsor's request. For more information, refer to:

- [Uniform recall procedure for therapeutic goods](#)

There may be state or territory regulatory licensing requirements that are applicable, which should be checked with the relevant state or territory authority. The provisions of the [Code of](#)

[Good Wholesaling Practice for Medicines in Schedules 2, 3, 4 and 8](#) are applied through applicable state and territory therapeutic goods legislation or drugs and poisons legislation, and/or state or territory wholesaler licensing arrangements.

## Documentation (Chapter 4)

### Retention of batch documents

Batch documents must be kept for at least one year after the expiry date or at least 5 years after release for supply by the authorised person, whichever is the longest. Other times of retention of batch documents may be required based on specific legislative requirements.

Investigational product batch documentation must be kept for at least 5 years following completion or formal discontinuation of the last clinical trial.

### Authorised person access to records

As the authorised person for release for supply takes responsibility for releasing and placing batches of product on the market, it is important that they have appropriate access to any documents that facilitate or influence their decisions. Accordingly, systems should be implemented to facilitate an authorised person's access to all documentation relevant to a specific batch, including, but not limited to, validation documents, stability data, test results, batch records, etc.

Guidance as to the minimum documentation requirements required to be held by authorised persons performing release for supply of products manufactured under contract may be found in the [Release for supply of medicines](#) guidance.

### Batch numbers in distribution records

Distribution records require batch numbers (clause 4.28). According to Clause 8.13 the recording of batch numbers in distribution records is mandatory.

### Signature list

You need to maintain a signature list. These should include the names, signatures and initials used by individuals who complete GMP documentation. The signature list is the key reference when providing traceability between manual signatures used on documents and the individuals who completed them.

## Production (Chapter 5)

### Water used in the manufacture of sunscreen products

Water used in the cleaning and formulation of sunscreens should be of an appropriate quality such that the finished product meets all chemical and microbiological quality attributes at release and throughout its shelf-life.

## Using purified water

Purified Water is preferable for use in the manufacture of sunscreens, as per the [default standards](#) i.e. the [British Pharmacopoeia](#) (BP), European Pharmacopoeia (EP) or [United States Pharmacopoeia – National Formulary](#) (USP).



If the ingredient list on the ARTG for a sunscreen product includes 'purified water' as a persistent ingredient, then the water used in the sunscreen product must meet the requirements of Purified Water EP, BP or USP.

## Using potable water

Where authorised by the specific marketing authorisation, it may be acceptable to use potable water in the manufacture of sunscreens. Potable water can be reasonably pure; however, it is always variable and, in some regions, of very poor quality.

When using potable water it may be necessary to substantially remove impurities and to control microbial levels to prevent product contamination. For an aqueous-based formulation water should be considered as a critical input.

## Specification for process water

Where potable water is used in the manufacturer of sunscreen products, a specification for 'process water' should be developed based on sound physical, chemical and microbiological principles taking into consideration relevant items such as:

- risk of chemicals commonly added to city water supplies and what effect these additives may have on product quality or stability.
- possible effect seasonal variations may have on source water quality.
- effect of manufacturing process on water quality, such as where water is heated to assist in emulsification, and how these processes will be controlled, recorded and validated.
- 'target', 'warning' and 'action' levels for microbiological load should be set based on risk and with consideration to the specification for in-process and final product, for example compliance with TGO 77, or the TGO that replaces this Order. The 'action' limit should not generally exceed  $10^2$  cfu/mL at point of use but may be set at a figure orders of magnitude lower.

## Microbial testing affected by municipal supplier water treatments

Where potable water is to be used for product formulation additional consideration must be given to the water treatment processes used by the municipal supplier that might affect microbiological testing.

The addition and presence of chlorine for example, in potable water may prevent detection of viable microorganisms rendering test results unreliable. In these cases, the addition to the sampling vessel of a suitable and sufficient neutralising agent, for example sodium thiosulphate, may be required.

## Additional monitoring of water quality when using potable water

Additional monitoring may be required to assess the quality of water following extensive sanitation of the water system by the municipal supplier. For example, it is common for additional sanitation of the water supply system to occur after a breach of the potable water

catchment area or purification system, which may result in sloughing biofilm from the potable water distribution system that might not be detected by the sunscreen manufacturer prior to use of the water for product manufacturer.

### **Additional verification of microbiological testing method when using potable water**

The sample size selected for microbiological testing of process water should be enough to give a countable number of colonies using the test method employed. A recommended test method is the relevant British Pharmacopeia/European Pharmacopoeia monograph for microbiological monitoring of purified water; however, further verification of the method may be required when analysing potable water.

### **Higher frequency of sampling when using potable water**

High frequency sampling of potable water systems would be expected due to their inherent variability and lack of user control. Samples should be tested for microbial load and indicator organisms.

### **Water testing frequency**

All water used in the manufacture of sunscreen products should be tested sufficiently frequently to demonstrate that it meets the requirements for Purified Water (BP/EP/USP), or the manufacturer's specification for process water, whichever is appropriate.

The frequency of water testing should be based on risk considering the data collected from qualification and historical monitoring of the water system, potential levels of contaminants (including microbial) and risk to product quality.

## **Process validation for sunscreen manufacturers**

A separate guidance document is available for [Process validation for listed and complementary medicines](#), which can also be applied to sunscreens.

## **Supplier qualification for sunscreens**

A separate guidance document is available for [Supplier assessment, approval and qualification for listed and complementary medicines](#), which applies to sunscreens.

## **Labelling and packaging**

### **Label counting and verification**

Roll labels must be counted either on receipt or at issue. Supplier counts are not acceptable unless the supplier is specifically qualified and the supplier certifies the exact count for each roll. Supplier sequential numbering on the backing web of labels is an acceptable alternative.



You, the manufacturer, must count and effectively verify cut labels, because of the risk of mix-ups.

## Unique batch numbering

The system that you adopt for batch numbering may include numerals, letters or symbols (or any combination of these) and must effectively serve to identify uniquely a batch of product, and from which it is possible to trace that batch through all stages of manufacture and distribution. You should be able to demonstrate that the system for batch numbering meets these requirements and is effective.

Unpacked bulk products, should have a batch number that is unique to both product and batch, to minimise the potential for mix-ups during manufacturing. For finished products that are easily distinguished, a batch numbering system that only designates batches from that product may be acceptable.

The topic of batch numbering is dealt with in [Medicines labels: Guidance on TGO 91 and 92](#).

## Quality control (Chapter 6)

### Sampling and testing of starting materials used in sunscreen manufacture

Quality Control is concerned with sampling and testing of all materials used throughout the manufacturing process to established specifications, including starting materials, intermediates, excipients, preservatives, sunscreen agents and final bulks or products, to ensure quality before release for further processing or supply.

### Standards applicable to starting materials used in sunscreen manufacture

You must demonstrate an active ingredient or an excipient meets the requirements of the default standard, if an applicable monograph exists (Part 3-1: standards, Therapeutic Goods Act 1989), [unless we have given the sponsor consent](#) for the goods not to comply with that standard.

See the tables below for guidance on current TGA expectations for minimum sampling and testing of sunscreen agents, excipients and preservatives.

For more detail on supplier qualification see [Supplier assessment, approval and qualification for listed and complementary medicines](#), which applies to sunscreens.

**Sunscreen agents: minimum sampling and testing**

Criteria – Pre Qualification		Criteria – Post Qualification
<b>Sampling</b>	All containers to be sampled.	$\sqrt{n} + 1$ , or reduced sampling plan based on risk assessment. Manufacturer to justify.
<b>Testing</b>	<p>As per EP/BP/USP monograph, or to an established specification if no monograph is applicable.</p> <ul style="list-style-type: none"> <li>• Identity testing performed individually on all sampled containers.</li> <li>• Composite of all samples for other tests.</li> <li>• Full testing required to demonstrate compliance to EP/BP/USP monograph, or established specification if no monograph is applicable.</li> <li>• A minimum of 3 different batches of material should be fully tested to qualify the supplier.</li> </ul>	<p>Established specification</p> <ul style="list-style-type: none"> <li>• Identity testing performed individually on all sampled containers.</li> <li>• Composite of all samples for other tests.</li> <li>• Critical tests on composite samples on all deliveries. Assay considered critical if part of release specification.</li> <li>• All other tests may be rotated across subsequent deliveries. It is expected that all test be included in the rotation schedule and none are excluded without adequate justification.</li> <li>• Documented Certificate of Analysis review against agreed specification for all quality attributes not tested.</li> </ul>

**Excipient and preservatives: minimum sampling & testing**

Criteria – Pre Qualification		Criteria – Post Qualification
<b>Sampling</b>	$\sqrt{n} + 1$ (where n = number of containers received)	1 sample per delivery
<b>Testing</b>	<p>As per EP/BP/USP monograph, or to an established specification if no monograph is applicable.</p> <ul style="list-style-type: none"> <li>• Identity testing performed individually on all sampled containers.</li> <li>• Composite of all samples for other tests.</li> <li>• Full testing required to demonstrate compliance to EP/BP/USP monograph, or established specification if no monograph is applicable.</li> <li>• A minimum of 2 different batches of material should be fully tested to qualify the supplier.</li> </ul>	<p>Established specification.</p> <ul style="list-style-type: none"> <li>• Identification test, and other tests identified as critical for the manufacturing process and/or product stability.</li> <li>• Documented Certificate of Analysis review against established specification.</li> </ul>

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## Sampling and testing of finished sunscreen product

### Bulk & finished product: minimum sampling

We expect:

- sampling plans to be documented
- consideration to be given to sampling of bulk product from formulation tanks prior to packaging
- where testing occurs on the finished pack for release purposes, samples to be taken throughout the packaging run and be representative of the entire batch.

### Bulk & finished product: testing

Sufficient testing, including active ingredient assay, should be conducted to verify the quality of the product. For multi active products, reduced and/or rotational testing may be implemented where justified.

Chemical testing can occur on either the bulk or packed product provided studies are available to demonstrate the bulk product remains homogeneous across the bulk product's storage period, and throughout the filling process. Special consideration for additional sampling and testing may need to be given to products that do not remain in a homogenous state e.g. suspension products.

There is normally no need for repeat chemical testing of the packed product if it is already performed on the bulk product.

Microbiological testing on the finished packed product should normally be conducted prior to release. Sunscreen products must comply, throughout the shelf life, with the microbiological requirements outlined in [Therapeutic Goods Order No. 100 Microbiological Standards for Medicines](#). The frequency of microbiological testing should be justified based on the following:

- the normal expected microbial quality of starting materials, including water quality
- the manufacturing processes employed, and their ability to control/reduce microbial contamination
- product formulation including the water content of the product and the effectiveness of any preservative system
- historical microbiological test results for the product
- risk to patient safety

### Validation of test methods

Validate and/or verify all microbiological methods used in the testing of starting materials and finished products for the material under test. Evidence of these studies should be recorded.

### Using analytical methods included in BP, EP or USP

Analytical methods for starting materials do **not** require additional validation where the pharmacopoeial method is employed.



Analytical pharmacopoeial methods for finished formulations **do need** validation to determine any effects from the formulation process. All analytical method validations should be recorded.

## Using analytical methods not included in BP, EP or USP

All methods not listed in a relevant pharmacopeia should be validated for testing of starting materials or product formulations.

For guidance on the characteristics for consideration during the validation of analytical procedures, see:

- [CPMP/ICH/381/95](#): ICH Topic Q 2(R1) – Note for Guidance on Validation of Analytical Procedures: Text and Methodology

## Conducting ongoing stability studies

### Responsibility for the ongoing stability program

Stability testing for sunscreens is mandatory. All responsibilities related to ongoing stability testing should be defined in a GMP agreement (unless the sponsor, manufacturer and authorised person conducting release for supply are all from the same entity).

The sponsor needs to:

- ensure that there is stability data to support the shelf life of the product
- have access to the laboratory results

The individuals conducting release for supply need to:

- have adequate information to support the shelf life of the product being released
- have adequate information to confirm that the batch meets the requirements for marketing authorisation

The stability testing program can be contracted out to third parties. This can include physical storage under the specified controlled conditions and undertaking the testing at the specified time points.

### Development of stability protocol

Conduct the initial stability study in accordance with a predetermined protocol, which should be in line with the ICH Guideline time points for stability testing outlined in [CPMP/ICH/2736/99: ICH guideline is ICH Topic Q 1 A \(R2\)](#) - Note for Guidance on Stability Testing: Stability Testing of New Drug Substances and Products. Ongoing stability studies may use different time points as the data is used to confirm that the product remains stable over its shelf life when the initial studies have already been confirmed as acceptable.

Include in the protocol relevant physical, chemical and microbiological testing to support the marketed shelf life of the product. The protocol for an ongoing stability program should extend to at least the end of the shelf life period.

## Stability conditions

Stability testing for sunscreens should be conducted in real time at the storage conditions specified on the product label. For example:

- 30 °C ± 2 °C when the label storage conditions are 'store below 30 °C' or 'store at room temperature'
- 25 °C ± 2 °C when the label storage conditions are 'store below 25 °C'

Humidity control is not required for on-going stability studies of sunscreen products.

## Accelerated stability studies in the ongoing stability program

Accelerated stability studies are **not** required for post market ongoing stability studies.

## Method development and validation

Analytical methods are researched, developed and validated for a product or group of products. The methods used for the stability testing of products need to be **stability-indicating**.

As a minimum, validate methods for specificity and robustness in accordance with the TGA's [Finished product \(medicine\) analytical procedure validation for complementary medicines](#).

It is unnecessary to monitor the level of impurities for sunscreen products.

## GMP certified laboratory or facility for on-going stability studies

Storage of ongoing stability samples and the associated testing do not need to be conducted in a GMP certified laboratory or facility, because ongoing stability testing is not considered to be a step in manufacture, as defined by the *Therapeutic Goods Act 1989*.

However, the results from these studies are required to be reliable and meaningful. It is the responsibility of the contract giver to ensure that any facilities or laboratories used for ongoing stability testing is appropriate. For that reason, other certification may be used in lieu of GMP certification, such as a licence issued by a regulatory authority acceptable to TGA or a current ISO 17025 accreditation certificate.

The results from the on-going stability monitoring studies must be considered as part of release for supply, which is the final step in manufacturing.

## Types of product

Ongoing stability testing is of the finished packed product.

Consider whether bulk product should also be part of the ongoing stability program, particularly where bulk product is stored prior to being packaged or transported from a manufacturing site to a packaging site. To determine whether further studies are necessary, use a risk assessment process to evaluate the impact of storage of bulk products on the stability of the packaged product.

In general, further studies may be appropriate if storage is more than one month for bulk sunscreen products.

## **Types of testing**

### **Physical testing parameters**

Include physical testing parameters specific to the sunscreen product, including pack integrity.

### **Microbiological testing**

Consider microbiological testing throughout the study to support compliance with the expiry specifications. At a minimum, conduct microbiological testing at the initial and the end time points of the study.

### **Sunscreen agents**

Test the active ingredients that are claimed on the label throughout the study using validated stability-indicating methods.

Reduced ongoing stability testing may be acceptable, with a documented risk assessment and justification, if full stability data for the support of the product listing shelf life is available for all active ingredients as per the label claim.

### **Grouping for the purposes of stability testing**

A grouping approach can be undertaken with stability studies in recognition of the similarity of many sunscreen products. Scientific justification of the rationale to establish product groupings should be documented.

Justifications should be based on groupings for products having similar formulations and with a similar method of manufacture. The groupings used for the preparation of PQRs would generally be acceptable for sunscreen products. The packaging of the product should also be taken into consideration.

An on-going stability program commences when a batch of product within a group is placed on stability, provided that the justification is documented for this particular product being representative of the grouping. Rotating of products within a group would also be acceptable.

At least one batch of product from each group each year should be placed on the ongoing stability program under the predetermined study protocol.

### **Release for supply and ongoing stability program results**

The results of the ongoing stability program are expected to be available to the authorised person who should consider the results before releasing a batch for supply.

### **Ongoing stability study reports**

Ongoing stability study reports should be available to:

- the authorised person responsible for release for supply
- the sponsor
- the TGA for review when requested

Ongoing stability reports should be summarised and authorised by a suitably experienced and qualified individual with a quality and/or technical and/or regulatory background for inclusion in the Product Quality Review.

The operation of an appropriate ongoing stability program including the results of ongoing stability studies, are normally reviewed during GMP inspections. If there are any concerns, the inspector can refer the evaluation to the area of TGA responsible for regulating the product ARTG entry.

## **Notifying TGA of ongoing stability issues**

All significant departures from established stability profiles must be notified to the TGA. It is acknowledged that some normal variability in the results of ongoing stability studies can be expected.

In general, if an assessment of stability data highlights that there is a likelihood that new batches may not stay within their label claim for the duration of a sunscreen product's shelf life, then the manufacturer or sponsor should notify TGA.

A departure from physical quality attributes, such as phase separation, is also significant and should be reported to TGA.

# **Outsourced activities (Chapter 7)**

## **Change in scope of chapter 7**

The title of chapter 7 has changed to 'Outsourced activities' from 'Contract manufacturer and analysis' in recognition of the fact that there are a number of outsourced (contracted) activities that may have a direct effect on the quality of medicinal product manufactured by a site. The previous title of the chapter did not allow appropriate management of the risk associated with all outsourced activities as it restricted the extent of GMP controls to only outsourced manufacturing and testing services.

Examples of outsourced activities that this chapter would now apply to include, but are not limited to:

- contract manufacturing and analysis
- maintenance and calibration services
- providers of critical consumables, e.g. gowns, sterilised componentry
- provision of training and consulting services
- validation services associated with facilities, equipment, utilities, process and product design, qualification and validation
- provision of transport and logistical services for products
- contract cleaning and waste management services
- contract pest control services
- agencies that provide temporary or contract personnel

For raw materials, packaging materials and printed artwork used in the manufacture of medicinal sunscreen products, it is not required to establish a formal GMP or technical agreement with suppliers.

## Managing outsourced activities

Manufacturers (normally 'contract givers') are expected to manage all relationships with contract acceptors in accordance with existing principles of chapter 7. All outsourced GMP-related activities that may impact on product quality should be assessed, defined and covered by a written contract. Agreements should be maintained in accordance with the Pharmaceutical Quality System.

## Legality of outsourced activities

The term 'legality' in clause 7.4.1 means that contract givers are responsible for making sure that the entity undertaking the outsourced activities is appropriately authorised to undertake the activity. This may be achieved by many means including ensuring that the contract acceptor:

- holds the appropriate manufacturing authorisation (licence) to undertake the specific steps in manufacture
- is nominated as being authorised to undertake the specific activity in the specific marketing authorisation of the products
- holds any necessary licenses or permits applicable to the outsourced activities, e.g. wholesale authorisations, Schedule 8 drugs permits etc.
- holds the necessary accreditation related to the activities undertaken, e.g. a contract calibration company may hold NATA or ISO 17025 certification

## Monitoring the contract acceptor

The contract giver should have a system in place to measure and monitor the quality of products (or service) provided by the contract acceptor, in accordance with risk management principles. Where quality related issues are identified, it is expected that appropriate actions are taken to address and remediate the concerns. Records of actions taken should be recorded within the PQS.

## Responsibility for review of records and results

The contract giver is responsible for reviewing and assessing the records and the results related to the outsourced activities (clause 7.5).

It is expected that the responsibility for review of the records and results be specified by contract and should be based on the risk and nature of the service provided, for example:

- for contract manufacture and analysis it may be appropriate for the contract giver to rely fully on the contract acceptor where an authorised representative of the contract acceptor, e.g. quality manager, has authorised the data and records.
- for contract service providers (for example contract calibration services) it would be appropriate for the contract giver to review the available records and data to ensure that the results or work provided meet the requirements of the contract giver's quality system and procedures.

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## Complaints and product recall (Chapter 8)

### Counterfeit products

The procedures on complaints handling require an assessment for counterfeit products (clauses 8.7 and 8.8 of PE009-13). If counterfeiting is detected the TGA must be notified in accordance with the [Uniform Recall Procedure for Therapeutic Goods](#).

A recall procedure should be in place as per the requirements of uniform recall procedure for therapeutic goods.

### Sampling of starting and packaging materials (Annex 8)

TGA's interpretation and expectations for compliance with Annex 8 of the PIC/S Guide to Good Manufacturing Practice for Medicinal Products, PE009-13 have been incorporated into topics on [Supplier Qualification for Sunscreens](#) in Production (Chapter 5), and [Sampling and Testing of Starting Materials used in Sunscreen Manufacture](#) in Quality control (Chapter 6).

### Manufacture of liquids, creams and ointments (Annex 9)

TGA's interpretation and expectations for compliance with Annex 9 of the PIC/S Guide to Good Manufacturing Practice for Medicinal Products, PE009-13 have been incorporated into [Premises and Equipment](#) (Chapter 3) and [Production](#) (Chapter 5).

### Computerised systems (Annex 11)

#### Implications of changes to Annex 11

Annex 11 has been updated to provide clarification of existing requirements to ensure that computerised systems are managed appropriately, particularly in relation to data management and integrity. In some cases, the wording of the clauses has become less prescriptive to allow better use of quality risk management principles in the validation and control of computerised systems.

#### Data management and data integrity

Refer to [Data Management and Data Integrity \(DMDI\) Guidance](#).

#### Validation and control of computerised systems

All computerised systems (including commercial off the shelf systems) used by licensed manufacturers in the manufacture of medicines should be validated and controlled in accordance with Annex 11 requirements.

The level, extent and formality of system control should be commensurate with the criticality of the system. Manufacturers should have a good understanding of all the systems used, and the impact and criticality of each system.

In general, the following systems (list is not exhaustive) should be fully validated and controlled, such as those used:

- for the electronic acquisition of quality control data
- to control and monitor the operation of critical utilities, facilities and equipment
- to generate, store or access electronic GMP records
- to generate, process, calculate or monitor data that forms part of the batch processing record, or batch control testing records
- in the place of physical (hard-copy) records, e.g. electronic spreadsheets used to track records or perform calculations, electronic documents used to record data
- to control the status of materials, products, equipment or processes, e.g. Enterprise Resource Planning systems
- to perform the release of materials and release for supply of finished goods
- to track the distribution of products and/or control the reconciliation of products and materials in the case of quality defects or recalls

## ‘Regulated users’ definition

TGA regards ‘regulated users’ to be the licence or GMP certificate holder responsible for the application of Good Manufacturing Practice.

## ‘Life-cycle’ of a computerised system

The ‘life-cycle’ of a computerised system includes all stages from the initial concept, design, qualification, validation, and use through to the eventual retirement of the system and archival of all data.

You need to manage computerised systems effectively at all stages in the life-cycle to ensure that they function correctly. Therefore, validation not only applies at the initial introduction of the system, but throughout all stages of use. Further guidance regarding the life-cycle management of computerised systems may be found within the [Good practices for computerised systems in regulated GXP environments](#) on the PIC/S website.

## Qualification and validation (Annex 15)

For qualification and validation guidance, TGA encourage the use of [PIC/S recommendation publications](#), as these expand on various clauses within Annex 15 of the PIC/S Guide to GMP (PE009-13). However, these are for guidance only and may not fully reflect the current requirements of PIC/S PE009-13. For example:

- PI-006-3 Validation Master Plan, Installation and Operational Qualification, Non-Sterile Process Validation, Cleaning Validation (recommendations)

All equipment used in the manufacture of medicinal products must be appropriately qualified following the principles outlined in Annex 15 section 3. Acceptability of the approach taken will be assessed during inspections on a case-by-case basis.

The nature and extent of qualification should be determined based on risk management principles. Depending on the use, stage in the equipment lifecycle and nature of the equipment, some of the stages outlined in Annex 15 section 3 may be omitted where appropriately justified, based on risk. It is generally expected that all stages would be addressed in the qualification of new and/or complex equipment.

## **Retrospective process validation no longer permitted**

All products currently manufactured are expected to be validated. New products should undergo prospective or concurrent validation. Process validation is a critical step in assuring the quality of medicinal products. When Annex 15 was originally published in 2001 the provision for retrospective validation was given to provide a means by which existing products could be validated. As the process validation requirements of Annex 15 have been in place for over 15 years, the provision for retrospective validation is no longer applied.

Any existing validations based on retrospective validation will be accepted; however, any new products, processes, updates or changes to existing processes should undergo full concurrent or prospective process validation.

## **Application of concurrent process validation**

For sunscreen products concurrent process validation is permitted.

Concurrent process validations should be approved under the sites PQS and where used, the results and conclusion of any supporting data should be made available to the authorised person performing release for supply of the product.

## **Number of batches used in process validation**

The number of batches used for process validation should be determined and justified by the manufacturer based on risk management principles. TGA's general expectations are that:

- for a new process or product, 2 batches are to be conducted for process validation purposes
- for a process subject to technology transfer from one site to another a minimum of 2 batches are to be conducted for validation purposes
- for changes to existing (validated) processes (e.g. batch size increase), an evaluation should be conducted regarding the similarities and differences in manufacturing processes, equipment, methods and materials should be in place to justify the number of batches selected

## **Batch sizes for process validation**

The process must be validated for all batch sizes intended to be manufactured at industrial scale.

Process validation may not be required for all discrete batch sizes if it can be demonstrated, based on risk assessment, that equipment operational qualification demonstrates that mixing vessels operate consistently over a range of mixing volumes, and identifies the smallest and



largest batch sizes. Process validation should demonstrate that process consistency can be achieved for the representative batch size.

## Performance qualification and process validation

Performance qualification may be performed in conjunction with operational qualification and/or process validation.

A separate guidance document is available: [Process validation for listed and complementary medicines](#), which can also be applied to sunscreens.

## Critical Quality Attributes (CQA) and Critical Process Parameters (CPP)

A process validation protocol should be prepared which defines the critical process parameters (CPP), critical quality attributes (CQA) and the associated acceptance criteria which should be based on development data or documented process knowledge (Annex 15 clause 5.21).

- A CQA is a physical, chemical or microbiological property or characteristic of the final product that should be within an appropriate limit, range, or distribution to ensure the desired product quality. CQAs for sunscreens products would include assay, microbial limits, pH of formulation, viscosity, blend uniformity/homogeneity, etc.
- A CPP is a process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure the process produces the desired quality. CPPs for sunscreens manufacture could include processing temperature, heating and cooling rates, mixing methods and speeds, mixing times, etc.

CQAs and CPPs are important elements of product and process knowledge and should be utilised in the design, validation and control of manufacturing processes.

## Ongoing Process Verification (OPV)

Ongoing Process Verification (OPV) is used periodically to evaluate process parameters and trends and ensure that processes are consistent and remain in a validated state (clauses 5.28-5.32).

Manufacturers should develop a process to monitor product quality attributes such as in-process control points across production and packaging, and finished product test results; however, OPV need not be conducted under a formal protocol. Consideration should be given to recording CQA and CPP for each batch using control charts with upper and lower limits.

Manufacturers should investigate any adverse trends concerning product quality attributes to determine if processes are consistent and remain in a validated state.

OPV should be used to support the validated status of the product and documented in the Product Quality Review.

## Use of materials from approved suppliers for validation

When conducting validation exercises, it is expected that raw materials from approved suppliers are used. However, in some circumstances, materials from unqualified suppliers may be used where supported by a risk assessment. It is expected that this would only apply when

concurrent vendor approval is underway, such that the material under evaluation is part of the validation exercise.

There must however be an appropriate justification to use the unapproved material based on all of the following:

- the risk to the following manufacturing process, plant and other products
- assurance that the vendor has met the specifications required
- suitable controls regarding approval, analysis and release of the material
- adequate control regarding the starting material issuance and reconciliation
- relevant systems in place to prevent release of the validation batches prior to full qualification of the material

## Transport verification

The basic expectation is that all products (including bulk products, finished products and samples) are transported in full accordance with their labelled, authorised and appropriate storage conditions, and that the supply chain has been formally evaluated and confirmed as effective. This assessment should be conducted using sound quality risk management principles. It is not acceptable to store or transport medicines outside their labelled and approved storage conditions.

The responsibilities for the transportation, monitoring and storage of medicinal products should be clearly specified within quality or technical agreements.

TGA does not currently inspect the wholesale distribution of therapeutic goods that have been released for supply.

TGA inspections do include an evaluation of the transport conditions for starting materials, intermediates, bulk and packed medicines (prior to release for supply) between sites of manufacture and clause 1.8 (ix) would apply in these circumstances.

## Validation of cleaning processes

TGA generally expects cleaning processes to be validated and appropriately documented. The acceptance criteria of 'visibly clean' will be normally be accepted for sunscreens due to the low toxicity of permissible ingredients used in the manufacture of sunscreens. Cleaning validations can be grouped looking at worse case situations.

In addition to the acceptance criteria of 'visibly clean', cleaning validation studies should consider the following:

- microbiological bioburden of processed materials and cleaned equipment and their acceptable limits
- potential residues for chemical cleaning agents where used. In these cases, additional testing, for example pH, may be used where justified to demonstrate adequate cleanliness

## Reference and retention samples (Annex 19)

A reference sample is a sample for the purpose of future analysis, which could refer to starting materials, packaging materials or finished products.

A retention sample is a sample representing the batch of finished product as distributed.



Samples from a stability trial program cannot be used as retention samples.

## Quality risk management (Annex 20)

Annex 20 is a voluntary annex; however, the principles outlined in the annex are applicable to the manufacture of therapeutic sunscreens.

Annex 20 corresponds to ICH Q9 guideline on quality risk management. It provides guidance on a systematic approach to quality risk management facilitating compliance with GMP and other quality requirements. It includes principles to be used and options for processes, methods and tools which may be used when applying a formal quality risk management approach.

Chapter 1 (Quality Management of the PIC/S Guide to Good Manufacturing Practice for Medicinal Products, PE009-13), has been revised to include aspects of quality risk management within the quality system framework.

## Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Manufacturing Quality Branch Regulatory Guidance Team	October 2018
V2.0	Updates to reflect recent changes to TGA guidance material	Manufacturing Quality Branch Regulatory Guidance Team	June 2019

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