South African Health Products
Regulatory Authority
Building A
Loftus Park
Arcadia
Pretoria

18 September 2022

GUIDELINE POST IMPORTATION TESTING

The objective of this procedure is to define the process to be followed and to provide instruction to the Holder of the Certificate of Registration (HCR) when submitting application for Post-Importation Testing Exemption of imported products.

To ensure that the integrity of imported products is not compromised during transit.

To confirm the imported product's integrity prior to release for sale in South Africa.

Document History

Final Version	Reason for Amendment	Effective Date
1	First issue and published for implementation	December2003
2	Second revision and published for implementation	March 2017
3	Third revision and published for implementation	January 2021
4	General update to include Biological/ Biosimilar Products, finalised and published for implementation	April 2022
5	− Content structured on the latest SAHPRA Guideline Template − Old guideline number 2.04 changed to SAHPGL-INSP-01	September 2022

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CHIEF EXECUTIVE OFFICER

Contents

Glossary

Abbreviation/ Term	Meaning
ALCOA	A commonly used acronym for “attributable, legible, contemporaneous, original and accurate”
ALCOA +	A commonly used acronym for “attributable, legible, contemporaneous, original and accurate”, which puts additional emphasis on the attributes of being complete, consistent, enduring and available
AMT	Analytical Method Transfer
AMV	Analytical Method Verification
APQR	Annual Product Quality Review
CEO	Chief Executive Officer
CTD	Common Technical Document
COA	Certificate of Analysis
CRO	Chief Regulatory Officer
FPRC	Finished Product Release Control
GMP	Good Manufacturing Practice
GRN	Goods Received Note
HCR	Holder of Certificate of Registration also referred to as the “Applicant”
MOA	Memorandum of Agreement
MOU	Memorandum of Understanding
MRA	Mutual Recognition Agreement
MRD	Master Release Document
MBR1	Medisyne Beheer Raad
MRF1	Medicines Registration Form
PI	Professional Information
PIC/S	Pharmaceutical Inspection Convention Pharmaceutical Inspection Co-Operation Scheme
PIL	Patient Information Leaflet

PIT	Post Importation Testing
PITE	Post Importation Testing Exemption
PQP	Product Quality Portfolio
RH	Relative Humidity
RP	Responsible Pharmacist
RP-HPLC	Reverse Phase High-performance liquid chromatography
RRA	Recognized Regulatory Authority
SAHPRA	South African Health Products Regulatory Authority
UV/VIS	Ultraviolet–visible spectroscopy

1. INTRODUCTION

Meeting SAHPRA mandate on assuring Public health, the various processes that are implemented, demand that pharmaceutical products should not be treated in the same way as ordinary commodities. Their manufacturing and subsequent handling within the supply chain, both nationally and internationally, must conform to prescribed standards and be rigorously controlled. These precautions serve to assure that patients receive high standard quality of medicines and to prevent the infiltration of substandard and suspected falsified medicine into the supply system. The integrity of imported pharmaceutical products could be compromised at various stages during the life cycle. The market infiltration by substandard and suspected falsified medicines poses different hazards for public health and processes to ensure SAHPRA's mandate is deemed crucial to ensure high-quality medicines to patients. Counterfeit and substandard medicines are a risk to public health as they are often not effective and so do not benefit patients and can also actively harm patients, even causing death. Serialisation in the pharmaceutical industry is one of the best tools companies could use to combat counterfeit medicines. It is therefore the responsibility of the Applicant to confirm the imported pharmaceutical products integrity prior to release for sale in South Africa.

The guideline also includes a departure from the traditional reactive control system to a risk-based and pro-active approach under validated control and surveillance systems. The risk-based surveillance system which could include routine pre-release checks performed by applicants, routine post importation testing and market signals could identify risks and define the controls that will protect patients from substandard, falsified and unregulated medicines. This when added together, will assure not only the quality, but also the safety and efficacy of pharmaceutical products manufactured and distributed. Applicants and manufacturers must have robust quality management systems in place to ensure that the products that they place onto the market are safe, of good quality and efficacious.

1.2 Purpose

To ensure that the integrity of imported products are not compromised during transit from source site to the patient. It is therefore important that the HCR confirms the imported product's integrity prior to release for sale in South Africa. In terms of Regulation 53 (1) of Act 101 of 1965, this is done by:

- Identification and assay, and/or other applicable tests performed locally on the final product. Or
- Return of samples to overseas testing laboratories or the manufacturers that supplies the product, for identification and assay and/or other applicable testing.

1.3 Scope

This guideline applies to the following pharmaceutical products:

a) Category A = Medicines which are intended for use in humans and which are, without manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine;

b) Category B = Medicines intended for use in humans and animals which cannot normally be administered without further manipulation;

c) Category C = Medicines intended for veterinary use which are, without further manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine; and

d) Category D = Complementary medicines intended for use in humans and animals which are, without further manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine.

2. LEGAL PROVISION

This guideline provides the framework of where SAHPRA systems are at this point. The default position of SAHPRA remains Post Importation testing and the guideline features that process as well as the process for exemption from this if the requirements are met. SAHPRA acknowledges that the system outlined herein is not static and we will be moving to a scenario where the Post Market surveillance processes will be strengthened and that SAHPRA endeavors to strengthen the partnership with other recognized Regulatory Authorities through a process of Memorandums of Agreements. This will enable us to leverage these systems to constantly review this guideline and move towards a system based on elimination of post importation controls as we have them at moment.

This guideline is intended to provide recommendations to applicants wishing to submit, have submitted or is the current Holder of the Certificate of Registration applications for the registration of medicines. The integrity of imported products could be compromised during the life cycle of the product including during transit both from source site and to patient. According to Regulation 53 of Act 101 of 1965 Subregulation (1) Every medicine must continue to comply with the standards and specifications which were furnished to the Authority and which have been accepted by the Authority regarding such medicine. (2) Any proposed deviation from accepted standards and specifications referred to in subregulation (3) must be submitted to the Authority for prior approval as determined by the Authority and such deviation must not be introduced before the said approval has been granted. Therefore, as has been the accepted standard to comply with Regulation 53, the applicant confirms the imported product's integrity prior to release for sale in South Africa, by testing conducted post importation. This is performed by: Qualitative (Identification) and quantitative (assay), and other performed locally on the final product or Returning of the samples to overseas testing laboratories or the manufacturer that supplied the product, for identification and assay and other relevant testing. This occurs under the environmental conditions

described and registered for the product.

It represents the SAHPRA's position on medicines meeting the requirements for the safety, quality and efficacy of medicines. SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. If an importer/exporter of medicines cannot meet the requirement of post importation testing, this guideline is also intended to provide recommendations to applicants wishing to submit applications for waiver of Post-importation testing after the registration of medicines. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications. SAHPRA is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. Guidelines and application forms are available from the office of the CRO/CEO and the SAHPRA website (www.sahpra.org.za).

3. POST IMPORTATION EXEMPTIONS (PITE's)

3.1 As stipulated prior, the default position of SAHPRA to ensure the quality safety, and efficacy of imported medicinal products, the Applicant ensures the following tests:

- Identification and assay, and/or other applicable tests as approved in the registered dossier performed locally on the final product. Or
- Return of samples to overseas testing laboratories or the manufacturers that supplies the product, for identification and assay and/or other applicable testing.

Exemptions from post-importation testing will be considered in the following circumstances:

3.2 The applicant must in all instances provide full motivation for exemption from post-importation testing.

3.3 Required Documentation: The Company should submit a Product Quality Portfolio, which will provide evidence that the manufacturing and subsequent handling of the product within the distribution chain, both nationally and internationally, which conforms to prescribed standards and which are rigorously controlled.

3.4 This Product Quality Portfolio will serve as evidence to assure that patients receive high standard of quality medicines and to prevent the infiltration of substandard and suspected falsified medicine into the supply system.

3.5 The Applicant completes the application letter and Product Quality Portfolio for post-importation testing exemption, and submits the requirements to SAHPRA, accompanied by the relevant fees. At this stage, the Applications will be uploaded to the FTP folder and proof of submission should be submitted

to inspectorate@sahpra.org.za

3.6 Included conditions are that the medicinal products must be transported via a qualified shipping solution.

3.7 Ensure use of Calibrated monitoring devices (recording both minimum and maximum temperatures and where applicable RH) must be inside the container to record the conditions (temperature and relative humidity where applicable) whilst the product is in transit. Pre-existing global shipping validation data from other shipping routes to be used in lieu of transport validation of the specific route used for shipping of the product from the Principal to South Africa would require scientific justification and would be subject to approval from SAHPRA

3.8 Products which are exempted from post-importation testing are not exempt from meeting regulatory release parameters, including, but not limited to, product release specifications and the absence of environmental condition excursions i.e., temperature and humidity as applicable.

3.9 Requirements: submission of PITE requests refer to (Attachment 1)

3.10 Evidence to Support Product Quality Portfolio: (Attachment 2)

3.11 Continuous monitoring and control of transport conditions. Refer to (Attachment 3) transportation of products for monitoring and control of transport conditions.

3.12 Final Product Release (Attachment 4)

4. GUIDELINES FOR MONITORING OF TRANSPORT

4.1 The parameters that the Applicant should comply with are specified in the Product Quality Portfolio and one of the aspects is the monitoring of transport.

4.2 This section provides guidance monitoring and control of transport, that is, evidence that the conditions during transport are continuously monitored and controlled, including relevant parameters, such as temperature, humidity, and freeze conditions.

4.3 The transport monitoring and control conditions of each shipment are recorded by a suitable device which provides a printout or data in a GMP compliant, validated data base that will form a permanent record of the specific shipment and is filed with the batch release documents as applicable. Should the printout relate to different products of the same shipment, a QA verified transportation data should be reviewed and filed and/or be available electronically in relation to the batch release documentation.

4.4 An SOP, specifying the details of inclusion of the recorders, should be available for inspection. The procedure should include amongst others, the number of recorders, position of placement, date of activation and inactivation (on leaving the place of dispatch i.e., factory, and on receipt by the applicant i.e., warehouse) and evaluation of the printout with the reference to the stability data and/or product distribution stability data

4.5 The monitoring and control mechanism should be qualified and/or calibrated as applicable and relevant records should be available for inspection. Thermo logger locations must be scientifically justified.

4.6 If the data obtained through accelerated and long-term stability studies does not support that the excursion has no impact on the long-term stability, then this data would not be considered as justification for release of products which have been exposed to environmental excursions observed during product transportation. This would include products sensitive to vibrations and lower temperatures. Note that monitoring as well as control of these parameters must be assured throughout transportation. The Applicant is to provide assurance that short term excursions do not have any impact on the long-term stability of the product. Appropriate thermal cycling studies can be used to support excursions above or below the approved storage conditions, provided there is no impact on the long-term stability and in these studies data for assay and other relevant tests for batches would be evaluated after exposure to short periods (cycles) of storage at each of two temperature extremes with ambient temperature used between the cycles. The cycle periods and extreme temperatures would be selected with consideration of the type of product (formulation, packaging, dosage form) and approved storage conditions.

4.7 Please note that exemption is applicable only for shipments monitored and controlled, and shipments not in compliance should therefore be identified and assayed and other relevant tests performed as stated in 3.1 if not otherwise justified.

4.8 Post-importation testing exemptions are only applicable for product packed in the final container.

4.9 The transport monitoring and control method, and parameters must be specified in the Master Release Document.

4.10 A tabulated summary indicating the method of transport, the conditions during transport and the method of controlling the respective conditions should be submitted.

4.11 Outcome of the evaluation of the transport conditions and relevant action, i.e., further testing to be

performed.

4.12 The type of recorder used in transit and confirm temperature of transport vs temperature range of loggers.

4.13 A specification that the received certificate of analysis is valid, is complete (reflects the actual results of the tests performed) and reflects compliance with the registration requirements.

4.14 Visual identification of the product and dosage form.

4.15 Confirmation of the integrity of the containers, seals, and labels. Each aspect should be specified and controlled to ensure that no damaged articles are accepted.

5. PRODUCT QUALITY PORTOFOLIO

The Product Quality Portfolio will include the following:

5.1 Medicine Registration Certificate.

5.2 A summary of historical number of shipments over the last three years as applicable, and shipment details including quantity of product imported and the yearly projection for future per annum. New products won't have this historical data, and this will be considered when determining the period of PITE validity granted.

5.3 Product Dossier status including in terms of format e.g., MBR1, MRF1, CTD, amendment history and evidence of effective dossier management e.g., Procedure on Dossier management and Dossier Amendment History.

5.4 Container closure systems of the product and stability profile.

5.5 Current GMP certification of source site in terms of SAHPRA RRA and laboratories including contract laboratories, as this is applicable to the HCR. Standalone local laboratories are authorised by SAHPRA. For overseas contract laboratories, evidence that GMP status are verified as part of the Contract testing and vendor approval is required to be provided.

5.6 The previous year data including at period before time of application for Market Surveillance Evidence including complaints, recalls, suspensions and withdrawals of the product this could have a material impact on the validity of the PITE granted.

5.7 The pharmacovigilance system is there to assess the safety profile of the medicine. If an ADR happens in another country in relation to a product that is marketed in South Africa, this could ultimately

influence the PIL or PI in SA and thus there must be an awareness and review of this data. The PV SOP and relevant data will be evaluated by Inspectorate and as part of Quality Portfolio and where additional expertise required the information will be channelled to the relevant specialists If there are market signals in terms of Post Market Surveillance and the product may be required to be tested. There may be a requirement to either send the product to local laboratory to be tested or return to source site. Thus, the Validation/Verification status of Analytical Methods and/or the Analytical Method Transfer will be required when products are required to be tested should exemption be withdrawn.

5.8 The GMP certificate from an RRA does not necessarily reflect the HCR product/s and a declaration is required to clearly show that the product/s complies to the Validation requirements. Confirmation of the Validation status of the product the Applicant is applying for exemption, both in terms of process validation, cleaning validation continuous cleaning and process validation related at the source site.

5.9 Historical Post- importation testing data assessment including trend analysis. The data may not be available for new products but may be available for established products and the time requirement would be the previous year and that information could be retrieved from APQR.

5.10 Product transportation studies/principles and risk assessment profile which may be obtained from historic monitoring data which maybe specific to the mode of transport and route.

5.11 The continuous monitoring process that is defined for controls during transport for each shipment of pharmaceutical product including relevant parameters, such as temperature, humidity, and freeze conditions utilizing a qualified process with calibrated instruments.

5.12 Provide evidence that the latest APQR has been performed and that a summary of this, including the pertinent products were provided.

5.13 Serialisation means the application of a unique pharmaceutical products to the countries those who have implemented serialisation regulations. Evidence of serialisation or /tamper evident seals/ devices/ unique product identifiers etc should be submitted where applicable. As the Reliance Model relies on a RRA reports and Certificates, some of those authorities are expecting a serialisation process. SAHPRA has not implemented this process yet although is aligned with PICS, thus evidence of Counterfeit combating system but not limited to serialization/tamper evident seals/ devices/ unique product identifiers etc.

5.14 Nitrosamine Content declaration. Nitrosamine Content is a measure of the Quality Assurance of the

Product that throughout the supply chain of the product no Nitrosamine inducing substances or processes are introduced. New guidance documents recommend steps manufacturers of APIs and drug products should take to detect and prevent unacceptable levels of nitrosamine impurities in pharmaceutical products. The guidance also describes conditions that may introduce nitrosamine impurities. The recent unexpected finding of nitrosamine impurities, which are probable human carcinogens, in drugs such as angiotensin II receptor blockers (ARBs), ranitidine, nizatidine, and metformin, has made clear the need for a risk assessment strategy for potential nitrosamines in any pharmaceutical product at risk for their presence. Based on the current understanding, the guidance discusses potential root causes of nitrosamine formation and advises API and drug product manufacturers that they should conduct risk assessments of their approved or marketed products and products with pending applications and take appropriate actions to reduce or prevent the presence of nitrosamines in APIs and drug products

5.15 As part of Post Marketing Surveillance, SAHPRA may draw samples to be tested by SAHPRA at selected Laboratory. SAHPRA will provide the applicant with the full details of the surveillance testing, including the laboratory chosen which may be the source site. The methods will be provided by the applicant and the Applicant will provide details of the AMT/AMV.

6. FEES

6.1 The set fees will apply to submission of the Product Quality Portfolio.

6.2 The fee required is the fee for evaluation of requests for exemption from registered post importation testing requirements per product as per the gazetted fees

7. SUBMISSION

7.1 The data pack comprising of the Product Quality Portfolio will be submitted to SAHPRA for assessment and review as per 5.0, and based on the supporting evidence assessed, SAHPRA will potentially exempt that pharmaceutical products from post- importation testing for the period determined by the evaluator of the application

7.2 Following the submission SAHPRA will provide an approval/non-approval within an envisaged 30-day timeframe.

7.3 Exemption, if approved, will be valid for a period of one to up to three years provided that after the full or partial requirements detailed in 4.0 above are complied with and this will be decided on the review of the Product Portfolio submission.

7.4 Following this exemption, there could be a periodic review of the Product Quality Portfolio based on variations/amendments and further exemptions could then be granted based on the updated review and submission of applicable fees.

8. POST IMPORTATION EXEMPTION GRANTED

Once SAHPRA has reviewed and approved the Product Quality Portfolio to support the exemption request, the process followed by the Applicant will include the following (This will be the responsibility of the RP of the HCR and the systems will be evaluated at time of audit but primarily the RP will inform SAHPRA as required).

8.1 Ensure that inbound and outbound logistics meet the storage conditions based on the validated routes and temperature and humidity.

8.2 Evaluate excursions outside of registered storage conditions in terms of root cause and product impact.

8.3 It is the Applicants responsibility to perform root cause analysis when there is an excursion as well as determine impact that the excursion could have on the long-term stability of pharmaceutical product.

8.4 Check visual container integrity, noting any tampering, potential contamination and potential for falsified products.

8.5 Serialisation and track and trace process in terms of counterfeit prevention, where implemented.

8.6 Data loggers within the consignment, based on the transport validation, are removed on arrival, the validated software is available to read the data and the data is used as part of the release to market.

8.7 If data loggers are faulty (no download or data) there will be requirement by default to test the product and thus it be required that HCR have a laboratory registered as FPRC. The HCR will need to provide a rationale on a case-by-case basis if there is a probability to release product to market.

8.8 Transfer product within a defined timeframe to assure compliance to registered storage conditions especially thermolabile pharmaceutical products.

8.9 Ensure other conditions e.g. protect from light, humidity, etc. are complied with.

8.10 Where applicable, remove the retention/release samples and transfer to the HCR for evaluation for release. Ensure the storage conditions of the retention /release samples where applicable are maintained as these samples could be utilized for testing post marketing.

8.11 The data gathered from temperature monitoring devices must be recorded and analysed on a regular basis to demonstrate that biological medicines are being stored and transported at the correct

temperatures.

8.12 Should there be a need to amend and address specific issues for Biological Medicines, this will be assessed. Some elements are issues that are specific to different Biological Products (e.g., The use of the identity and purity testing (RP-HPLC method) and the protein content (UV/VIS method) for post importation of biologicals in place of the cell-based bioassay test).

9. CONDITIONS OF EXEMPTION

9.1 Post-importation testing exemption does not negate the need for the Applicant to assume full responsibility for product quality and for the release of products which are safe, effective and of high quality.

9.2 SAHPRA reserves the right to withdraw the exemption should the Applicant give cause based on e.g., deviations from the approved Product Quality Portfolio or Any changes to the Product Quality Portfolio including the transport monitoring and control equipment, commitments and data previously submitted, invalidate the post-importation testing exemption granted. The Applicant has the responsibility of post market surveillance including all serious adverse drug reactions reported in South Africa, in relation to the imported medicine, in accordance with the SAHPRA vigilance guideline Post-Marketing Reporting of Adverse Drug Reactions to Human Medicines in South Africa, as well as notification and market signals e.g., Complaints, Withdrawals and Recalls in accordance with the relevant SAHPRA guidelines.

9.3 The re-submission of the PQP, if triggered, will require a new application with concomitant fees.

9.4 SAHPRA reserves the right to request for the applicant to supply samples of the imported medicinal product for testing and which will be for the Applicants cost

9.5 GMP status can change and an exemption can be withdrawn if, during an audit conducted by SAHPRA, deficiencies are found which could affect the validity of the PITE granted previously and can occur at any time regardless of the PITE period allowed.

9.6 Exemption, if approved, will be valid for a period of one to up to three years provided that after the full or partial requirements detailed in Section 4.0 above, are complied with and this will be determined on the review of the Product Portfolio submission and motivation.

10. PRODUCT RELEASE TO MARKET

10.1 Products which are exempted from post-importation testing are not exempt from meeting regulatory

release parameters.

10.2 As part of the release to market process, the Responsible Pharmacist or Deputy Responsible Pharmacist is required to review the following (not exhaustive list) based on a robust internal procedure:

10.2.1 Product storage conditions and product description as per current dossier

10.2.2 Confirmation of the integrity of the containers, seals and labels. Each aspect should be specified and controlled to ensure that no damaged pharmaceutical products are accepted.

10.2.3 Evidence to support that the product imported is not subject to conditions that may result in tampering / counterfeiting of the imported product.

10.2.4 Serialization and track and trace process in terms of counterfeit prevention.

10.2.5 The Batch Manufacturing and Packaging Record. The system that the Applicant uses needs to be defined in terms of ensuring that the relevant dossier documents and the current source documents at the manufacturing facility are the same. Any deviations from the source documents needs to be provided to the Applicant. The rationale for the system in use will be evaluated by SAHPRA as part of the

10.2.6 Out of Specifications and Out of Trend data summaries.

10.2.7 Deviations/Change Control.

10.2.8 Valid COA.

10.2.9 Data Logger Data: The product under discussion must be transported via a qualified shipping solution. Calibrated monitoring devices must be placed inside the container to record the conditions (temperature and relative humidity where applicable) whilst the product is in transit.

10.2.10 Outcome of the evaluation of the transport conditions and relevant action, i.e. further testing to be performed.

10.2.11 Artwork and Labelling (Is it clear that the company details are available if there was a complaint).

10.3 Release to be completed with the review of the Release Samples which are stored at approved storage conditions.

11. REFERENCES

The following related documents are referenced:

11.1 Medicines and Related Substances Act, as amended Act 101 of 1965

11.2 General Regulations to the Medicines and Related Substances act 101 of 1965, as amended

11.3 Regulation 53 of Act 101 of 1965 Sub-regulation (1)

12. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the Post Importing Testing guideline, old document number 2.04. It will be reviewed on this timeframe or as and when required.

13. ATTACHMENTS

13.1 Attachment 1: Application Template for PITE

The Chief Executive Officer South African Health Authority (SAHPRA)

SAHPRA Head Office

Building A Loftus Park 2nd Floor

402 Kirkness Road

Arcadia 0083

Reference Number:

ATTENTION: **Inspectorate and Regulatory Compliance**

Dear Sir / Madam

REQUEST FOR POST-IMPORTATION TESTING EXEMPTION

Product Propriety Name	**Application Number**	**Dosage Form**	**API**

First Time Exemption Request	**YES**	**NO**
Renewal of Existing Exemption		
Date first time exemption granted		

Motivation Summary for Exemption: *Summary of reasons why exemption should be considered*

13.2 **Attachment 2:** Evidence to support Product Quality Portfolio

Medicine Registration Certificate	
A summary of historical number of shipments, and shipment details including quantity of product imported and the yearly projection for future per annum as applicable	
Product Dossier status including in terms of format e.g. MBR1, MRF1, CTD, amendment history and evidence of effective dossier management.	
Container closure systems of the product and stability profile.	
Current GMP certification of source site and laboratories including contract laboratories as this is applicable to the HCR.	
Market Surveillance Evidence including complaints, recalls, suspensions and withdrawals of the product	
Pharmacovigilance system and listing of all serious adverse drug reactions reported in South Africa and internationally which may be pertinent to South Africa, in relation to the imported medicine.	
Validation status of Analytical Methods and the Analytical Method Transfer required when products are required to be tested should exemption be withdrawn, or post market surveillance testing is required	
Declaration that Data Integrity management at source site is complying to ALCOA+.	
Confirmation of the Validation status of the product the Applicant is applying for exemption, both in terms of process validation and cleaning validation at the source site	
Confirmation that the source site performs Continuous cleaning and process validation	

related to the product that the Applicant is applying for exemption	
Historical Post- importation testing data assessment including trend analysis.	
Product transportation studies/principles and risk assessment profile.	
The continuous monitoring process that is defined for controls during transport for each shipment of pharmaceutical product including relevant parameters, such as temperature, humidity, and freeze conditions utilizing a qualified process with calibrated instruments.	
APQR profile and history.	
Evidence of a Robust Self - inspection program and how this was adapted to internal and external audits	
Evidence of Counterfeit combating serialization or applicable process to support track and trace system	
Nitrosamine Content declaration	

Application Fee and Proof of Payment attached:

I declare that

- the request for post-importation testing is in line with the relevant current guidelines and/or a motivation for any deviation has been submitted
- no amendments, other than those stated in the amendment's history, have been made.

Signature of RP/DRP:

Name	Title	Qualification	Designation	e-Mail	Tel number

13.3 **Attachment 3:** Summary of data: transportation of product

NAME OF PRODUCT:

REGISTRATION NUMBER:

DOSAGE FORM:

APPROVED STORAGE CONDITIONS:

ASSURANCE: TEMPERATURE RECORDED IN EACH SHIPMENT

Name of Product	Batch Number	Maximum and minimum temperature recorded	Applicable other transport sensitive conditions e.g. vibration measurements or RH	Duration of transport (Date commenced and date terminated)	Mode of Transport	Signature of Responsible pharmacist who verified the printouts

13.4 **Attachment 4:** An Example of Master Release Document (MRD)

COMPANY MASTER RELEASE DOCUMENT (MRD) PRODUCT NAME: Code:		Page x of y Date:	
Batch number			
Approved storage conditions			
Date of Manufacture			
Final product specification reference number			
Expiry Date of Product compared against ZA CTD			
Receiving notice number (GRN)			
Dates of dispatch and of receipt			
Transit period specification, actual and conformity		YES	NO
Quantity dispatched			
Number of containers received			
Test	Specifications	Result	Signature
Shipping containers' condition	Clean, undamaged	Number approved: Number rejected	
Shipping container label	Not tampered with		
Shipping container seal	Present, intact		

Temperature and humidity printout (storage and transport conditions) Data loggers within the consignment, based on the transport validation, are removed on arrival, the validated software is available to read the data and the data is used as part of the release to market.	Present, attached; conforms to product specific storage and handling requirements		
Data Logger Data: The product under discussion must be transported in a validated container. Calibrated monitoring devices must be placed inside the container to record the conditions (temperature and relative humidity) whilst the product is in transit	Location and Assessment of Loggers		
Ensure that inbound and outbound logistics meet the storage conditions based on the validated routes, temperature and humidity	Route Analysis and excursions		

If data loggers are faulty (no download or reading) there will be requirement by default to test the product and thus it be required that HCR have a local laboratory registered as FPRC for if testing has to be done or to return product back to	Determine functioning and assess PIT		
Outcome of the evaluation of the transport conditions and relevant action, i.e. further testing to be performed.	Assessment of excursions		
Certificate of Analysis Valid COA and Data Trend summary.	Present, valid (batch specific), all test conducted as conforms to ZA CTD, complete		
The Batch Manufacturing and Packaging Record or defined	Present		
Out of Specifications and Out of Trend data summaries.	Declaration and outcome		
Deviations/Change Control	Record and impact assessed		
Transfer product immediately to registered storage conditions especially thermolabile	Product transfer		
Ensure other conditions e.g. protect from light, humidity, etc.	Storage Conditions		

Release to be done in conjunction of the review of the data of the previous APQR		Previous APQR Review								
Conclusion: Conformance		YES	NO		Further testing required?		YES		NO	
Comments										
Position/Function										

Originator		Reviewer Approved		Authorised	
Designation		Designation		Designation	
Signature		Signature		Signature	
Date		Date		Date	