South African Health Products
Regulatory Authority
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GUIDELINE FOR FEE DETERMINATION AND PAYMENTS OF GXP AND PRODUCT RELATED INSPECTIONS

This document has been prepared to serve as a guidance document on the fees structure employed to calculate the fees for GxP and product-related inspections.

Document History

Final Version	Reason for Amendment	Effective Date
1	First issue and published for implementation	March 2021
2	– Content structured on the latest SAHPRA Guideline Template – Old guideline number 4.13 changed to SAHPGL-INSP-06	September 2022

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Contents

Glossary

Abbreviation/ Term	Meaning
Active pharmaceutical ingredient (API)	Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when so used, becomes an active ingredient of that pharmaceutical dosage form. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.
Certificate of registration	A certificate of registration issued under section 15, 15A or 15B of the Act.
Compensatory calculated fee	A compensatory calculated fee is fee calculated to compensate for services rendered by the Authority in line with Section 33A of the Act.
Distributor	Holder of Certificate of Registration (HCR) or proposed Holder of Certificate of Registration (PHCR) of pharmaceutical product.
Holder of Certificate of Registration	A person in whose name a registration certificate has been granted and who is responsible for all aspects of the medicines, including quality and safety and compliance with conditions of registration.
Manufacturer	A person manufacturing a medicine and includes a manufacturing pharmacy.
Multicentre Site	A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.
Person	Means a natural or juristic person
Pharmaceutical Quality Control Laboratory	Carries out the required tests and assays to verify that APIs, excipients and pharmaceutical products meet the prescribed specifications.
Protocol	A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline the term protocol refers to protocol and protocol amendments.
Service rendered	Service rendered includes, but is not limited to, conducting the inspection on-site and/or virtually, and the completing (writing and review) of the inspection report in order take an administrative action while effecting

	the objects and functions of the Authority as per the Act.
Sponsor	An individual, company, institution, or organization, which takes responsibility for the initiation, management, and/or financing of a clinical trial.
Sponsor-Investigator	An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.
Trial Site	The location(s) where trial-related activities are actually conducted.
Wholesaler	A person who holds, stores, delivers or purchases medicines or Scheduled substances from a manufacturer and sells them in terms of Section 22H of the Act.

1. INTRODUCTION

The South African Health Products Regulatory Authority (SAHPRA) (hereinafter referred to as the Authority) is a statutory body, established to provide for the monitoring, evaluation, regulation, investigation, inspection, registration and control of medicines, Scheduled substances, clinical trials and medical devices, IVDs and related matters in the public interest according to section 2A of the Medicines and Related Substances Act, Act 101 of 1965, as amended (hereafter, "the Act"). The Authority must ensure medicines registered by the Authority, during its entire life cycle, comply with the information that has been evaluated and approved by the Authority through section 2B(1)(c) of the Act.

Regular inspections are performed at the applicant, manufacturing, quality control, wholesalers, distributors and clinical trial sites, of medicines, in order to ensure compliance with quality control, good manufacturing, wholesaling, distribution and clinical practices (GxP) as well as compliance with the relevant registration dossier and approved clinical trial protocols according to section 2B(1)(e)-(f) of the Act. Such inspections can be initiated on request by the applicant and/or SAHPRA may initiate an inspection.

1.1 Purpose

This guideline is intended to assist applicants in identifying the correct category of fees to accompany GxP and product related inspections.

1.2 Scope

This guideline is applicable to GxP and product-related inspections, however, this does not cover inspections for medical device establishments.

2. LEGAL PROVISION

Section 35 (xxxii) of the Act 101 0f 1965

3. EXPLANATORY NOTES

3.1 The fees are calculated to raise funds for the Authority as provided by Section 33A(1)(b) of the Act in order for the Authority to defray expenses incurred as per Section 33A(3), taking into consideration the objects and functions of SAHPRA determined by the Act.

3.2 Fees are determined per hour for service rendered. In order to be transparent, fair and objective in its determination of the fees to be charged, the Authority will charge a compensatory calculated fee after completion of the inspection in the form of hours service rendered during on-site inspection, desktop inspection and/or remote virtual inspection.

For example:	
Total number of billable hours involved in sterile facility/site services rendered:	
Service	**Duration/Time**

Inspection (On-site / per inspector) (two (2) Inspectors) 40 hours (5 days) x 2	80 hours (Maximum)
Total Duration	**80 hours**
Previous billed hours for 2 inspectors	
Inspection	40 hours

3.3 Accommodation and subsistence for inspections occurring within South Africa will not be charged to the applicant.

3.4 Travel time within South Africa will be charged per hour per inspector to the applicant. This will be included as a separate line in the invoice.

Province	Hours per inspector	
	Travel Time one way per inspection	Travel Time Round Trip per inspection
Gauteng	0.5 hour	1 hour
Northwest Limpopo Mpumalanga KwaZulu-Natal Free State	1 hour	2 hours
Western Cape Eastern Cape Northern Cape	2 hours	4 hours

3.5 Travel time outside of South Africa will be charged per hour per inspector to the applicant.

	Hours per inspector	
	Travel Time one way per inspection	Travel Time Round Trip per inspection
Neighbouring Countries	4 hours	8 hours
Rest of Africa	8 Hours	16 Hours
International	16 Hours	32 Hours

See section 12 for further details of charges for international inspections.

4. GOOD MANUFACTURING PRACTICE (GMP) INSPECTIONS

4.1 GMP Local Inspections [QC Laboratory, Holder of Certificate of Registration and Manufacturer]:

The scope of local site inspections will be based on the (proposed) licensed activities of each facility/site.

Local site inspections will attract a fee on the activities performed at the facility/site.

Hourly Rate	Rationale

R 1600 / h per inspector	Application of compensatory calculation for the hours involved in inspection and travel. Travel time and Inspection time to be charged separately.

4.2 GMP International Inspections:

The scope of international site inspections will be based on dosage forms and will be limited to the activities and areas associated with the production of the specified dosage form. For International Inspections, SAHPRA may perform desktop review / evaluate the valid GMP certificates issued by PIC/s aligned Regulatory Authority(ies) for GMP compliance evaluation. However, SAHPRA reserves the right to inspect international sites inspected by PIC/s aligned Regulatory Authorities.

Hourly Rate	Rationale
R 1600 / h per inspector	Application of compensatory calculation for the hours involved in inspection and travel. Travel time and Inspection time to be charged separately.

5. REMOTE INSPECTIONS

Remote virtual inspection for facility/site.

Hourly Rate	Rationale
R 1600 / h per inspector for inspections	Application of compensatory calculation for the hours involved in inspection

6. GOOD CLINICAL PRACTICE (GCP) INSPECTIONS

GCP inspections at clinical trial sites will be payable per protocol and/or per activity.

6.1 GCP Local Inspections

Local site inspections will attract a fee based on the activities performed at the site.

Hourly Rate	Rationale
R 1600 / h per inspector	Application of compensatory calculation for the hours involved in inspection and travel. Travel time and Inspection time to be charged separately.

6.2 GCP International Inspections

International sites performing BE studies will be inspected following a risk-based approach. Inspection fees for international GCP inspections at sites will be payable per protocol and/or per activity. International site inspections will attract a fee on the activities / protocol inspected at the site.

Hourly Rate	Rationale
R 1600 / h per inspector	Application of compensatory calculation for the hours involved in inspection and travel. Travel time and Inspection time to be charged separately.

7. GOOD WHOLESALING PRACTICE (GWP) INSPECTIONS

Site inspections will attract a fee based on the activities performed at the site.

Hourly Rate	Rationale
R 1600 / h per inspector	Application of compensatory calculation for the hours involved in inspection and travel. Travel time and Inspection time to be charged separately.

8. CANNABIS CULTIVATION INSPECTIONS

Site inspections will attract a fee based on the activities performed at the site.

Hourly Rate	Rationale
R 1600 / h per inspector	Application of compensatory calculation for the hours involved in inspection and travel. Travel time and Inspection time to be charged separately.

9. PHARMACOVIGILANCE INSPECTIONS

Inspections will attract a fee based on the activities performed at the site.

Hourly Rate	Rationale
R 1600 / h per inspector	Application of compensatory calculation for the hours involved in inspection and travel. Travel time and Inspection time to be charged separately.

10. INTERNATIONAL TRAVEL AND ACCOMODATION

10.1 Travel and accommodation required for an international inspection shall be in line with SAHPRA travel policy requirements.

10.2 The Applicant shall be responsible for travel (including transfers) and accommodation costs.

SAHPRA shall be responsible for costs associated with visas and travel insurances.

10.3 Travel authorisation: The Inspectorate Unit shall request authorisation for the international trip as per National Treasury's National Travel Policy Framework. Once authorisation is received, quotations for flights, accommodations and transfers (where required) shall be requested from the travel agent. Once quotations are approved by SAHPRA management in line with internal approval procedures, the itinerary and costs shall be provided to the Applicant. The quotations will be provided to the Applicant upon request.

10.4 Applicants who have a mutual benefit resulting from one inspection or whose site may be part of multiple inspections being undertaken in one trip by SAHPRA inspectors, may share costs.

10.5 Upon approval of the quotation for the travel and accommodation as per SAHPRA internal procedures, the travel agent itinerary and costs will be provided to the applicants. A full itinerary detailed per day will also be provided by Inspectorate, indicating flights (including internal flights), hotels, sites and transfers.

10.6 Upon inspection report completion, the inspection report cover letter will be provided to the applicants with the travel/accommodation costs and inspection costs. Applicants may opt to split the payment according to their own cost review, failing which SAHPRA will split the payment.

10.7 The cost-split must be communicated back to Inspectorate who will facilitate the issuing of invoices per applicant from SAHPRA Finance. Invoices will be provided with the respective inspection reports.

11. FEE PAYMENT

11.1 After the inspection, the inspection report and the invoice will be sent in PDF format via email to the HCR / Manufacturer / Laboratory / Sponsor / CRO / Principal Investigator. The inspection report shall contain the number of hours to be charged for the inspection and the number of hours spent on travel. The costs of accommodation and travel will be listed as separate line items in the invoice.

11.2 The invoice will contain the banking details of the Authority, the due date of the inspection fee payment, a unique reference number and the amount payable by the HCR / Manufacturer / Laboratory / Sponsor / CRO / Principal Investigator for the inspection.

11.3 The HCR / Manufacturer / Laboratory / Sponsor / CRO / Principal Investigator must ensure that the unique reference number is used as the reference number for payments made to the Authority. Proof of payment documentation must be submitted to inspectorate@sahpra.org.za and finance@sahpra.org.za and accompany inspection report response. The latest Guideline on the Payment of Fees to SAHPRA must be consulted for requirements related to payment to SAHPRA.

11.4 Fees are due within thirty (30) calendar days of receipt of invoice.

11.5 The fees are calculated based on the accurate time spent on site and will be rounded off to the nearest half-hour.

11.6 For the purpose of these guidelines, the applicant for GCP Inspection refers to the Sponsor or Principal Investigator.

11.7 It should be noted that the inspection fee will be reviewed as per SAHPRA requirements and timelines.

11.8 Note that for easy reference Applicants may use the addendums attached below.

12. REFERENCES

The following related documents are referenced:

12.1 Medicines and Related Substances Act. Act 101 0f 1965, as amended.

13. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the guide for Fee Determination and Payments of GxP and Product Related Inspections, old document number 4.13. It will be reviewed on this timeframe or as and when required.

14. ADDENDA

14.1 Addendum 1: Onsite Inspections

The following table below depicts the maximum number of hours to be levied per activity per type of inspection.

Inspection Type	Inspection Time (hours)	Number of inspectors	Total Time Spent (hours)
GMP Biologicals - Upstream	40	2	80
GMP Biologicals - Downstream	40	2	80
GMP sterile	40	2	80
GMP non- sterile	32	2	64
GMP non-sterile – QC Laboratories*	32	2	64
		1	32
GMP non-sterile – Cannabis Cultivation	32	2	64
HCR	16	1	16
GCP– Sponsor Driven*	32	2	64
		1	32
GCP– Investigator Driven*	24	2	48
		1	24
GWP	16	1	16
Pharmacovigilance*	32	2	64
		1	32

* = Number of inspectors dependent on complexity of site/trial

14.2 Addendum 2: Remote / Hybrid# Inspections

Inspection Type	Inspection Time (hours)	Number of inspectors	Total Time Spent (hours)
GMP Biologicals - Upstream	50	2	100
GMP Biologicals - Downstream	50	2	100
GMP sterile	50	2	100
GMP non- sterile	40	2	80
GMP non-sterile – QC Laboratories*	40	2	80
		1	40
GMP non-sterile – Cannabis Cultivation	40	2	64
HCR	20	1	20
GCP– Sponsor Driven*	40	2	80
		1	40
GCP– Investigator Driven*	30	2	60
		1	30
GWP	20	1	20
Pharmacovigilance*	40	2	80
		1	40

* = Number of inspectors dependent on complexity of site/trial

= Hybrid - Combination of remote and onsite inspection