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GOVERNMENT NOTICES • GOEWERMENTSKENNISGEWINGS

DEPARTMENT OF HEALTH

NO. 5856 **12 February 2025**

MEDICINES AND RELATED SUBSTANCES ACT, 1965 (ACT No. 101 of 1965)

REGULATIONS REGARDING FEES PAYABLE IN TERMS OF THE PROVISIONS OF THE MEDICINES AND RELATED SUBSTANCES ACT, 1965 (ACT No. 101 of 1965)

The Minister of Health, in consultation with the Minister of Finance and the South African Health Products Regulatory Authority, in terms of Section 35(1)(xxxi) and (xxxii) read together with Section 35(4) of the Medicines and Related Substances, 1965 (Act No. 101 of 1965), makes the Regulations in the Schedule.

DR PAKISHE AARON MOTSOALEDI, MP
MINISTER OF HEALTH
DATE: 28/1/2025

SCHEDULE

Definitions

1. In these Regulations, any word or expression to which a meaning has been assigned in the Act shall bear such meaning and, unless the context otherwise indicates:

"the Act" means the Medicines and Related Substances Act, 1965, as amended (Act No. 1 of 1965).

API – Active Pharmaceutical Ingredient

BE – Bio Equivalence

CEP – Certificate of Suitability to the Monographs of the European Pharmacopoeia

CPQ – Confirmation of WHO API Prequalification

IVD – In vitro diagnostics

Pre-IND – Pre-Investigational New Drug

WHO – World Health Organization

Fees payable to the Chief Executive Officer or Director-General

2. The following fees shall be payable to the Chief Executive Officer or the Director General as the case may be:

(a) Application for all requests for priority review status considerations: Fee charged for a priority review status request: R11 500,
(b) For approved priority pre-registration evaluations:

(i) Priority Generic products (pharmaceutical, analytical and bioavailability evaluated) including generic dental, radio-pharmaceutical products (first strength and dosage form), including two API's and a BE study. Additional fees will be charged for in line with sub paragraph 3(a)viii and paragraph 3(g): R192 000,

(ii) Priority Generic products (pharmaceutical and analytical evaluated) including generic dental, radio-pharmaceutical products (first strength and dosage form) including two API's. Additional fees will be charged for in line with sub paragraph 3(a)viii and paragraph 3(g): R132 400,

(iii) Priority Generic products with clinical data (first strength and dosage form). Additional fees will be charged for in line with sub paragraph

3(a)x and paragraph 3(g): R188 000,

(iv) Priority New Chemical Entities, new biotherapeutics other than vaccines (first strength and dosage form), including two API's and a Final Finished Product. Additional fees will be charged for in line with sub paragraph 3(a)ii and paragraph 3(g): R300 000 and

(v) Priority Biological Medicinal Products e.g. vaccines and biosimilars (excluding new biotherapeutics). Additional fees will be charged for in line with sub paragraph 3(a)v and paragraph 3(g): R282 300.

(c) For approved priority post-registration evaluations relating to quality, including biologicals:

(i) Priority Quality Type II, major amendment: R23 000 per amendment.

(d) For approved priority post-registration evaluations relating to clinical variations, including biologicals:

(i) Priority Type II safety amendment: R29 500,

(ii) Priority Type II safety and efficacy amendment: R44 900 and

(e) Request for a borderline product status review: R15 000.

Category A medicines (Human Medicines)

3. The fees payable for human medicines, including Biologicals, for which an application for registration is submitted as contemplated in Section 15 of the Act, are:

(a) In respect of the submission of an application for registration of:

(i) New Chemical Entities, new biotherapeutics other than vaccines (first strength and dosage form), including two API's and a Final Finished Product. Additional API's and BE studies will be charged for in line with sub-paragraph (g): R217 200 per application,

(ii) Strengths and dosage forms other than those referred to in sub-paragraph (i): R85 400 per application,

(iii) Biological products (first strength and dosage form) i.e., vaccines (excluding new biotherapeutics): R184 400 per application,

(iv) Biological products (first strength and dosage form) i.e., biosimilars (excluding new biotherapeutics): R180 300 per application,

(v) Strengths and dosage forms other than those referred to in sub-paragraph (iii and iv): R57 300 per application,

(vi) Generic products (pharmaceutical and analytical evaluated) including generic dental and radio-pharmaceutical products (first strength and dosage form) including two API's. Additional API's will be charged for in line with sub-paragraph (g): R87 600 per application,

(vii) Generic products (pharmaceutical, analytical and bioavailability evaluated) including generic dental and radio-pharmaceutical products (first strength and dosage form) including two API's and a BE study. Additional API's and BE studies will charged for in line with sub-paragraph (g): R120 000 per application,

(viii) Strengths and dosage forms other than those referred to in sub-paragraph (vi and vii): R28 100 and BE studies will be charged for in line with sub-paragraph (g),

(ix) Generic products with clinical data (first strength and dosage form): R87 600 per application,

(x) Strengths and dosage forms other than those referred to in sub-paragraph (viii): R28 100 per application,

(xi) Evaluation of additional submitted clinical data (pre-registration): R5 300, per application and

(xii) An application in terms of Section 15C of the Act (supply of affordable medicines): R39 400.

(b) For the second response review of the evaluation outcome of New Chemical Entities, New Generic Medicines and New Biological Products other than vaccines (first strength and dosage form), per evaluation outcome:

(i) Response review of major queries: R45 000,

(ii) Response review of moderate queries: R22 500 and

(iii) Response review of minor queries: R9 000.

(c) For the second response review of Clinical evaluations with clinical data: R24 700 per evaluation outcome.

(d) For the second response review of the evaluation outcome of quality variations per application number per variation queried:

(i) Response review of Type II and multiple submissions (Type IA and IB): R6 800.

(e) For the second response review of the evaluation outcome of clinical

variations per application number:

(i) Response review for the evaluation outcome of Type IB, clinical variation application substantiated with data: R7 200,

(ii) Response review of Type IB: R3 000 and

(iii) Response review of Type IA: R1 900.

(f) Pre- Registration Consultation Meeting for Biological Medicines Under Development and with the intention to submit for registration (Pre-IND), per application:

(i) Type A - meetings conducted before finalisation of non-clinical tests: R43 200,

(ii) Type B - meetings conducted when non-clinical development is complete and Phase 1 trials are ready for submission: R32 400 and

(iii) Type C - meetings conducted during the clinical development phase and prior to final registration application: R21 600.

(g) Fees for additional API sources (excluding CEP's and CPQ's) and additional BE studies:

(i) New Chemical Entity and new Generic Medicine applications with more than two API's, for each additional API and API source: R18 600 and

(ii) New Chemical Entity and new Generic Medicine applications with more than one BE study, for each additional BE study: R26 200.

(h) Any medicine, the registration of which has been approved by the Authority in terms of Section 15(3) of the Act:

(i) In the case of medicines in minute-dose form; the fee encompasses different dilutions and different volumes, when submitted simultaneously for the same indication or intended use and in respect of which an application fee has been paid: R2 100 for each registration,

(ii) Evaluation of request for rescheduling of a product: R16 600,

(iii) Evaluation of request to amend Professional Information and Patient Information Leaflets in respect of which data relating to safety must be evaluated (post registration) per application: R16 200,

(iv) Evaluation of request to amend Professional Information and

Patient Information Leaflets in respect of which clinical data relating to safety and efficacy must be evaluated (post registration): R32 800,

(v) Evaluation of request to amend the Innovator or Generic medicine Professional and Patient Information Leaflet where clinical data is not required (post registration): R3 300,

(vi) Evaluation of request for approval of once-off deviation from registered requirements per product, including Section 36 exemptions: R5 500,

(vii) Evaluation of requests for exemption from registered post-importation testing requirements per product per year the exemption is valid for: R5 500,

(viii) Annually, in respect of the retention of the registration of a medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R5 200: Provided that this provision shall come into effect one year after the date on which the registration of the said medicine was approved by the Authority in terms of Section 15(3); Provided further that the said fees payable during a particular calendar year shall be payable on or before the last working day of June that year, failing which the registration may be cancelled in terms of Section 16(4),

(ix) Every five years, in respect of the renewal of a New Chemical Entity Health Product/Medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R34 000 per Master application and R13 500 per Line Extension up to a maximum of two line extensions,

(x) Every five years, in respect of the renewal of a Generic Health Product/Medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R31 600 per Master application and R9 600 per Line Extension up to a maximum of two line extensions,

(xi) Evaluation of medicine proprietary name changes (post registration) per application: R3 400 and

(xii) Authorised Prescribers Amendment per application: R35 800.

(i) For quality variations of any medicine, the registration of which has been approved by the Authority in terms of Section 15(3) of the Act, the fees are applicable per application: number:

(i) Type II Level 1 (post registration) - Evaluation of request for major technical amendments in respect of which data relating to quality must be evaluated for the first two variations in the same application: R29 700 per variation and for the third and

subsequent variation of the same application: R4 600,

(ii) Type II Level 2 (post registration) - Evaluation of request for major technical amendments in respect of which data relating to quality must be evaluated for the first two variations in the same application: R13 800 per variation and for the third and subsequent variation of the same application: R4 600,

(iii) Type II Level 3 (post registration) - Evaluation of request for major technical amendments in respect of which data relating to quality must be evaluated for the third and every subsequent Type II Level 1 and Level 2 variations in the same application: R4 600,

(iv) Type IA (post registration) - Evaluation of request for minor technical amendments (per grouping of a maximum of three variations per application) in respect of which data relating to quality must be evaluated: R3 500 and

(v) Type IB (post registration) - Evaluation of request for minor technical amendments (per grouping of a maximum of two variations per application) in respect of which data relating to quality must be evaluated: R5 600.

(j) In respect of the testing of a human vaccine for purposes of batch release by the National Control Laboratory:

(i) New applications per batch: R70 000 and

(ii) Re-release per batch (previously tested): R35 000.

Category C medicines (Veterinary Medicines)

4. Veterinary medicines, including veterinary Biologicals, for which Authority has determined by resolution that they are registerable:

(a) In respect of the submission of an application for registration of:

(i) New Chemical Entities not previously included in a veterinary medicine for non-food producing animals, including two API's and two species per application. Additional fees will apply in line with sub-paragraph (b): R40 000,

(ii) New Chemical Entities previously included in a veterinary medicine for non-food producing animals including two API's and two species per application. Additional fees will apply in line with sub-paragraph (b): R35 000,

(iii) New Chemical Entities not previously included in a veterinary medicine for food producing animals including two APIs and two

species per application. Additional fees will apply in line with sub-paragraph (b): R45 000,

(iv) New Chemical Entities previously included in a veterinary medicine for food producing animals including two API's and two species per application. Additional fees will apply in line with sub-paragraph (b): R30 000,

(v) Line extensions with additional indications for food producing animals including two API's and two species per application: R27 000,

(vi) Line extensions with additional indications for non-food producing animals including two API's and two species: R20 000,

(vii) Generic products (bioavailability evaluated) including two API's and two non-food producing species per application: R25 000,

(viii) Generics for food producing animals, including two species and two API's per application. Additional fees will apply in line with sub-paragraph (b): R30 000,

(ix) For Biowaivers (Generics) for food producing animals, including two species with AMR evaluation and two API's per application. Additional fees will apply in line with sub-paragraph (b): R21 900,

(x) For Biowaivers (Generics) for non-food producing animals, including two species and two API's per application. Additional fees will apply in line with sub-paragraph (b): R15 100 and

(xi) Evaluation of additional submitted clinical data (pre-registration) per application: R2 900.

(b) Fees for additional API sources and BE studies:

(i) New Chemical Entity and Generic application with more than two API's and two species, for each additional API and API source and species: R18 600 and

(ii) Generic application with more than two BE/Biowaiver studies, for each additional BE/Biowaiver study and species: R15 100.

(c) Any medicine, the registration of which has been approved by the Authority in terms of Section 15(3):

(i) In the case of medicines in minute-dose forms; the fee encompasses different dilutions and different volumes, when submitted simultaneously for the same indication or intended use and in respect of which an application fee has been paid: R1 900 for each registration,

(ii) Every five years, in respect of the renewal of a New Chemical Entity Health Product/Medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R34 000 per Master application and R13 500 per Line Extension up to a maximum of two line extensions,

(iii) Every five years, in respect of the renewal of a Generic Health Product/Medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R31 600 per Master application and R9 600 per Line Extension up to a maximum of two line extension,

(iv) Evaluation of request for rescheduling of products per application: R6 400,

(v) Request to amend Professional Information in respect of which data relating to safety must be evaluated (post registration) per application: R9 400,

(vi) Request to amend Professional Information in respect of which clinical data relating to safety and efficacy must be evaluated (post registration): R16 200,

(vii) Request to amend the Innovator or Generic medicine Professional Information and where clinical data is not required (post registration): R3 300,

(viii) Annually, in respect of the retention of the registration of a medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R2 400: Provided that this provision shall come into effect one year after the date on which the registration of the said medicine was approved by the Authority in terms of Section 15(3): Provided further that the said fees payable during a particular calendar year shall be payable on or before the last working day of June that year, failing which the registration may be cancelled in terms of Section 16(4),

(ix) Evaluation of request for approval of once-off deviation from registered requirements per product, including Section 36 exemptions: R5 500,

(x) Evaluation of requests for exemption from registered post-importation testing requirements per product per year the exemption is valid for: R5 500 and

(xi) Evaluation of medicine proprietary name changes (post registration) per application: R3 400.

(d) For veterinary quality variations, the fees are applicable per application number:

(i) Type II veterinary medicine variation (post registration) - Evaluation of request for major technical amendments relating to quality for the first two variations in the same application: R13 800 per application and R4 600 for the third and subsequent variation of the same application,

(ii) Type IA veterinary medicine variation (post registration)– Evaluation of request for minor technical amendments (per grouping of a maximum of three variations per application) in respect of which data relating to quality must be evaluated: R3 500 and

(iii) Type IB (veterinary medicine variation (post registration)– Evaluation of request for technical amendments (per grouping of a maximum of three variations per application) in respect of which data relating to quality must be evaluated: R5 600.

Category D medicines (Human medicines)

5. Human medicines for which an application for registration has been submitted as contemplated in Section 15 of the Act,

(a) In respect of the submission of an application for registration of:

(i) Products submitted, with clinical and or toxicological data (first strength and dosage form) per application: R16 700,

(ii) Strengths and dosage forms other than those referred to in sub-paragraph (i) per application: R6 500,

(iii) Products submitted with no clinical or toxicology data (first strength and dosage form) per application: R8 500 per application,

(iv) Strength and dosage forms other than those referred to in sub-paragraph (iii) per application: R4 000,

(v) Evaluation of additional submitted clinical data (pre-registration) per application:R3 000 and

(vi) An application in terms of Section 15C of the: R36 100.

(b) Any medicine, the registration of which has been approved by the Authority in terms of Section 15(3) of the Act:

(i) In respect of registration of any medicine, the registration of which has been approved by the Authority in terms of Section 15(3) of the Act and in respect of which an application fee has been paid

per registration: R1 900,

(ii) Evaluation of request for rescheduling of products per product registered: R6 000,

(iii) Evaluation of request to amend Professional Information in respect of which clinical data relating to safety and efficacy must be evaluated (post- registration) per application: R3 600,

(iv) Annually, in respect of the retention of the registration of a medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R1 900: Provided that this provision shall come into effect one year after the date on which the registration of the said medicine was approved by the Authority in terms of Section 15(3); Provided further that the said fees payable during a particular calendar year shall be payable on or before the last working day of June that year, failing which the registration may be cancelled in terms of Section 16(4),

(v) Evaluation of request for approval of once-off deviation from registered requirements per product, including Section 36 exemptions: R5 500,

(vi) Evaluation of requests for exemption from registered post-importation testing requirements per product per year the exemption is valid for: R5 500 and

(vii) Evaluation of medicine proprietary name changes (post registration) per application: R3 400.

Category D medicines (Veterinary medicine)

6. Veterinary medicines for which Authority has determined by resolution that they are registerable:

(a) In respect of the submission of an application for registration of:

(i) Products submitted with clinical and or toxicological data, (first strength and dosage form) per application: R5 900,

(ii) Products submitted with no clinical or toxicology data (first strength and dosage form) per application: R4 800,

(iii) Strengths and dosage forms other than those referred to in sub-paragraphs (i), (ii) per application: R3 500 and

(iv) Evaluation of additional submitted clinical data (pre-registration) per application: R1 600.

(b) Any medicine, the registration of which has been approved by the Authority in terms of Section 15(3):

(i) In respect of the registration of any medicine, the registration of which has been approved by the Authority in terms of Section 15(3) and in respect of which an application fee has been paid: R1 900 for each registration,

(ii) Evaluation of request for rescheduling of products per product registered: R6 000,

(iii) Evaluation of request to amend Professional Information in respect of which clinical data relating to safety and efficacy must be evaluated per application: R3 600,

(iv) Annually, in respect of the retention of the registration of a medicine, the registration of which has been approved by the Authority in terms of Section 15(3): R1 400: Provided that this provision shall come into effect one year after the date on which the registration of the said medicine was approved by the Authority in terms of Section 15(3): Provided further that the said fees payable during a particular calendar year shall be payable on or before the last working day of June that year, failing which the registration may be cancelled in terms of Section 16(4) and

(v) Evaluation of medicine proprietary name changes (post registration) per application: R3 400.

Fees for clinical trials (Human and Veterinary)

7. Fees payable:

(a) In respect of the submission of an application for the authorisation of the use of an unregistered medicine, medical devices and IVD's for clinical trials:

(i) Clinical trial application (Safety and efficacy): R33 700,

(ii) Clinical trial application (Bioequivalence study): R31 700,

(iii) Clinical trial application (Postgraduate study) with pharmaceutical company involvement: R11 200 and

(iv) Phase 4 Clinical Trial Application and any other clinical trial application, including university involved postgraduate qualification and/or pre consultation of clinical trials (i and ii above): R5 100.

(b) In respect of clinical trials amendments and other S21 applications:

(i) Fees in respect of an application for technical amendments: R7200 per amendment,

(ii) Fees in respect of an application for administrative amendment: R4 200 per amendment and

(iii) Any other application except for the purpose of performing a clinical trial: R400.

Fees for Licences (Including Medical Devices/IVD's and Complementary Medicines)

8. Fees payable for licences are as follows:

(a) An application for a new licence, including complementary medicines, in terms of Section 22C (1)(b) of the Act:

(i) Manufacture: R26 200,

(ii) Distribute: R15 600,

(iii) Wholesale: R15 600,

(iv) Import: R15 600 (Holder of certificate of registration) and

(v) Export: R15 600 (Holder of certificate of registration).

(b) An application for a new medical device and IVD establishment licence in terms of Section 22C (1) (b) of the Act.

(i) a manufacturer licence to manufacture, import or export medical devices or IVDs: R26 200; or

(ii) a distributor licence to import, export and distribute medical devices or IVDs: R15 600; or

(iii) a wholesale licence to act as a wholesaler of medical devices or IVDs; R15 600.

(c) An application for the renewal of a licence, including complementary medicines, in terms of Section 22D of the Act, the licensing of which has been approved by the Authority in terms of Section 22C(1)(b) of the Act:

(i) Manufacture: R22 900,

(ii) Distribute: R13 100,

(iii) Wholesale: R13 100,

(iv) Import: R9 600 (Holder of certificate of registration) and

(v) Export: R9 600 (Holder of certificate of registration).

(d) An application for the renewal of a medical device and IVD establishment licence in terms of Section 22D of the Act, the licensing of which has been approved by the Authority in terms of Section 22C(1)(b) of the Act:

(i) a manufacturer licence to manufacture, import or export medical devices or IVDs: R22 900,

(ii) a distributor licence to import, export and distribute medical devices or IVDs: R13 100 and

(iii) a wholesale licence to act as a wholesaler of medical devices or IVDs: R13 100.

(e) Annually, in respect of the retention of a licence issued in terms of Section 22C(1)(b) of the Act: R4 400, and this fee is payable on or before the last working day of June that year, failing which the license may be revoked.

(f) Licensing for any manufacturer, distributor, wholesale, import or export, the license of which has been approved by the Authority in terms of Section 22(1)(b) of the Act including medical devices: R3 500.

(g) Application for the amendment to an existing licence to manufacture, distribute, wholesale, import or export including medical devices: R5 500.

Fees for inspections to assess quality, safety and efficacy of medicines and scheduled substances.

9. Payable fees are:

(a) The charge out rate per inspector will amount to R1 660 per hour per inspector for all scheduled inspections conducted. Inspection hours and travel time will be charged for in accordance with the applicable guideline.

(b) Desktop inspection to assess quality, safety and efficacy of medicines or scheduled substances, review of GxP compliance status after license amendments and medical devices: R2 200 per day per inspector.

Fees for permits and certificates

10. Payable fees are as follows:

(a) In respect of the issuing of a permit or a certificate:

(i) Certificate [Certificate of a Pharmaceutical Product (WHO), Good

Manufacturing Practice (GMP) Certificate, Certificate of Free Sale]: R1 460,

(ii) Import permit (holder of certificate of registration): R990,

(iii) Export permit (holder of certificate of registration): R960,

(iv) Any other permit or certificate: R990 and

(v) Permits issued by the Director-General in terms of Section 22A of the Act, excluding government departments: R990.

Amendment of information in the register

11. In respect of all applications for amendments in terms of Section 15A, the name of the medicine approved by the Authority under Section 15(5), which shall be the proprietary name, the approved name of each active ingredient of the medicine and the quantity thereof contained in a dosage unit or per suitable mass or volume or unit of the medicine, the conditions of registration, the name of the applicant, the name and address of the manufacturer, packer, final product release control, final product release responsibility: R850 per application.

Transfer of certificates of registration

12. In respect of an application in terms of Section 158: R1 100 per application.

Appeal against the decision of the authority.

13. Fee payable in respect of an application in terms of Section 24 (3): R52 500 per application.

Repeal of laws

14. Regulations published in Government Notice R1379 Government *Gazette* No. 44026 of 22 December 2020 is hereby repealed.

Short Title

15. These Regulations are called Regulations regarding Fees Payable in terms of the provisions of the Medicines and related substances Act, 1965 (Act No. 101 of 1965), 2025.

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