DEPARTMENT OF HEALTH

NO. 3759 **4 August 2023**

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 intends, 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, to make the Regulations in the Schedule.

Interested persons are invited to submit any substantiated comments or representations on the proposed regulations to the Director-General of Health, Private Bag X828, Pretoria, 0001 (for attention of the Director: Public Entities Governance; mihloti.mushwana@health.gov.za and paul.tsebe@health.gov.za), within three months of the date of publication of this notice.

DR JOE PHAAHLA, MP
MINISTER OF HEALTH
DATE: 20/07/2023

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. 101 of 1965).

Fees payable to CEO 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 priority review assessment: Fee charged for a declined priority review application: R11 500;

(b) For approved priority pre-registration evaluations:-

(i) Generic Medicine application, including 2 API's, 2 BE studies and response review per. Additional API's and BE studies will be charged for in line with the Fee Regulation: R475 000,

(ii) New Chemical Entity application, including 2 API's, Final Finished Product, and response reviews. Additional API's and BE studies will be charged for in line with the revised fee regulation: R300 000 and

(iii) Biological Medicine application, including response reviews: R322 000.

(c) For approved priority post-registration evaluations relating to quality variations, including biologicals:
(i) Priority Quality Type II, minor amendment: R6 500, and

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

(d) For approved priority post-registration evaluations relating to quality variations, including biologicals:
(i) Priority Type II safety amendment: R29 500,

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

(iii) Priority Clinical responses with clinical data per application: R24 700.

(e) Request for an application number: R2 000 per number and

(f) 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, first dosage form): 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 i.e., vaccines (excluding new biotherapeutics): R184 400 per application,

(iv) Biological products i.e., biosimilars (excluding new biotherapeutics): R180 300 per application,

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

(vi) Generic products (pharmaceutical and analytical evaluated) including generic dental and radio-pharmaceutical products (first strength, first dosage form): R87 600 per application,

(vii) Generic products (pharmaceutical, analytical and bioavailability evaluated) including generic dental and radio-pharmaceutical products (first strength, first dosage form): R120 000 per application,

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

(ix) Generic products with clinical data: R87 600,

(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), per application: R5 300 and

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

(b) For the response review of the evaluation outcome of New Chemical Entities, New Biological Products other than vaccines (first strength, first 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) Response review of the evaluation outcome of all types of Variations per application number per variation queried:

(i) Response review of Type II: R6 800,

(ii) Response review of Type IB: R2 400 and

(iii) Response review of Type IA: R1 300.

(d) Pre- Registration Consultation Meeting for Biological Medicines Under Developments 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 Ph-I 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.

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

(i) Generic application with more than 2 APIs, for each additional API and API source: R18 600 and

(ii) Generic application with more than 1 BE study, for each additional BE study: R26 200.

(f) 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 (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 or reclassification 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 to amend the innovator or Generic medicine professional information and Patient Information Leaflet where clinical data is not required (post registration): Type IB R6 000 and

(vii) Response to clinical variation application substantiated with data: R7 200.

(g) For quality variations, 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,

(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,

(vi) Evaluation of requests for approval of once-off deviations from registered requirements per product: R5 500,

(vii) Evaluation of requests for exemption from registered post-importation testing requirements per product 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 5 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): R50 000 per Master application and R20 000 per Line Extension up to a maximum of three lines including the Master,

(x) Every 5 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): R40 000 per Master application and R12 000 per Line Extension up to a maximum of three lines including the Master,

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

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

(h) 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 for the first 12 months of this

Gazette and R146 500 thereafter and

(ii) Re-release per batch (previously tested): R35 000 for the first 12 months of this Gazette and R75 500 thereafter.

Category C medicines (Veterinary Medicines)

4. Veterinary medicines, including 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 x1 non-food producing species x1 API per application: R40 000,

(ii) New Chemical Entities previously included in a veterinary medicine for x1 non-food producing species x1 API per application: R35 000,

(iii) New Chemical Entities not previously included in a veterinary medicine for food producing species x1 API; more than one species; more than one indication and residue studies per application: R45 000,

(iv) New Chemical Entities previously included in a veterinary medicine for food producing species x1 API; more than one species; more than one indication and residue studies per application: R40 000

(v) Line extensions with additional indications for food producing animals per application: R27 000,

(vi) Line extensions with additional indications for non-food producing animals per application: R20 000

(vii) Generic products (bioavailability evaluated) for non-food producing species per application: R25 000,

(viii) Generics for food producing species, for more than one species, with safety clinical data; x1 API per application: R30 000,

(ix) For Biowaivers (Generics) for food producing species, for more than one species, with AMR evaluation; more than 1 API per application: R21 900,

(x) For Biowaivers (Generics) for non-food producing species, for more than one species, more than 1 API per application: 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) NCE/Generic application with more than 2 APIs, for each additional API and API source: R18 600 and

(ii) Generic application with more than 2 BE studies, for each additional BE study: additional R15 100

(c) 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) (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 5 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): R50 000 per Master application and R20 000 per Line Extension up to a maximum of three lines including the Master,

(iii) Every 5 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): R40 000 per Master application and R12 000 per Line Extension up to a maximum of three lines including the Master,

(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) and

(ix) 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, first 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, first dosage form) per application: R8 500per application,
(iv) Strengths 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) and
(v) 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, first dosage form) per application: R5 900,

(ii) Products submitted with no clinical or toxicology data (first strength, first 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 and medical devices 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.

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

(i) Fees in respect of an application for technical amendments: R7 200 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.

Medical devices fees (IVD'S and non IVD'S)

8. Medical devices fees payable for :

(a) Any Medical Device (IVD and non-IVD), for which an application for registration has been submitted as contemplated in Section 15 of the Act, per application for a device:
- (i) Reliance - Evaluation Class A (low risk medical device): R6 500
- (ii) Reliance - Evaluation Class B (low to moderate risk medical device): R14 700
- (iii) Reliance - Evaluation Class C (moderate to high-risk medical device): R17 400
- (iv) Reliance - Evaluation Class D (high risk medical device): R20 100
- (v) Full assessment - Evaluation Class A (low risk medical device): R28 900
- (vi) Full assessment - Evaluation Class B (low to moderate risk medical device): R62 800
- (vii) Full assessment - Evaluation Class C (moderate to high-risk medical device): R69 700
- (viii) Full assessment - Evaluation Class D (high risk medical device): R85 100
- (ix) Registration Approval Class A, B, C and D: R2 000
- (x) Notification Technical Amendment Class A, B, C and D: R800
- (xi) Prior-Approval Technical Amendment Class A, B, C and D: R6 100
- (xii) Administrative Amendment Class A, B, C and D: R3 000
- (xiii) Annually, in respect of the retention of the registration of a medical device, 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),
- (xiv) Transfer of certificate of registration or old medicine letter per product or the amendment of proprietary name, manufacturer, packer, or laboratory per product: R1 800,
- (xv) Evaluation of request for reclassification of a products: R16 600 and
- (xvi) Evaluation of request for approval of once off deviations from registered requirements: R5 500.

Fees for Licences (Including Medical Devices and Complementary Medicines)

9. Fees payable for licences are as follows:

(a) An application for a new licence in terms of Section 22C (1)(b) of the Act:
- (i) Manufacture: R26 200,
- (ii) Distribute: R15 600 (Holder of certificate of registration),
- (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 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 wholesaler of medical devices or IVDs; R15 600.

(c) An application for the renewal of a 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) Manufacture: R22 900

(ii) Distribute: R13 100 (Holder of certificate of registration),

(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 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; or
(ii) a distributor licence to import, export and distribute medical devices or IVDs: R13 100; or
(iii) a wholesale licence to act as 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 and

(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, scheduled substances and medical devices

10. 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

11. 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,
(v) Permits issued by the Director-General in terms of Section 22A of the Act, excluding government departments: R990 and
(vi) Review of port health and or border detainment products: R400

Amendment of information in the register

12. 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

13. Payable fee in respect of an application in terms of Section 158: R1 100 per application.

Appeal against the decision of the authority

14. Payable fee in respect of an application in terms of Section 24 (3): R52 500 per application.

Repeal of laws

15. Regulations published in Government Notice R1379 Government *Gazette* No 44026 are hereby repealed.

Short Title

16 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),2023.