

REGISTRATION AND LICENSING REQUIREMENTS FOR THE MANUFACTURE AND SALE OF PHARMACEUTICALS

All medicines sold in South Africa must be registered by the Medicines Control Council, [MCC], the Medicines Regulatory Authority set up under the Medicines and Related Substances Control Act [Act 101 of 1965] as amended, to control all aspects of the manufacture and sale of medicines.

An application for registration must be compiled in a specified format by a pharmaceutical company registered and operating in South Africa. At present this company must be registered under the Company's Act and then with the South African Pharmacy Council, and must have an operating license from the Medicines Control Council. In addition, a "responsible pharmacist" must be appointed as the person legally responsible for compliance with all laws and regulations, codes of good practice and ethical obligations.

The applicant company must compile an Applicant Master File with details about the company, its physical address in South Africa, its organogram including the skills and experience of the staff responsible for the production, testing, storage and distribution of its medicinal products.

The product dossier compiled by the applicant company must be submitted to and approved by the MCC and is regarded as a legal contract. The Certificate of Registration of a medicine confirms this and is the license to sell the medicine. Any amendment made by the company after registration must be approved by the MCC.

The type of information that must appear in the application is specified in the above legislation and more details are given in a number of MCC Circulars which represent guidelines for both the registration and the control of medicines.

This includes:

1. The claims made for the medicine with regard to the indications for its use. These must appear on the package insert which must accompany each pack of a medicine.

Registration approval is based on these claims after MCC evaluation of the scientific and clinical data provided to support the claims. In addition, a Patient Information Leaflet to be made available to the patient taking the medicine, must also be compiled by the company and approved by the MCC.



2. Specifications and quality control procedures for all raw materials and packing materials, as well as the final dosage form in its final sales pack. These must be described in detail with exact specifications and control procedures described.
3. Manufacturing processes and in-process quality controls.
4. A validation program to ensure that all components and processes produce products of a consistent quality every time. This includes a stability testing program to ensure that the product retains all its quality parameters for the full shelf life of the product.
5. A Site Master File with specified details of the actual factory where the medicine is made.
6. For innovative medicines, details of the results of all pharmaceutical [laboratory], animal and human testing must be supplied. These include data generated throughout the product development from the initial tests done to determine the absorption, distribution, metabolism and excretion of the drug in animals and healthy human volunteers [pharmacodynamic data] to the results obtained in clinical trials in sick patients.

The time needed for the extensive testing required is usually 8 – 12 years while the average total cost to bring such new products to the market are in the region of US \$ 1,2 Billion. The studies may be done in South Africa or in other countries but the data must be evaluated and approved by the MCC for registration of the medicine to be granted.

7. For generic medicines the applicant must provide proof that the product has a comparable therapeutic effect to that of the originator's product. This can be done by conducting comparative clinical trials, or by providing proof of bioequivalence or in some cases by laboratory testing.
8. All advertising must be based on the approved claims for the medicine i.e., those which appear on the approved package insert. Advertising does not require prior approval by the MCC but the MCC Inspectorate does deal with any infringement as a contravention of the regulations.
9. Generally the industry controls infringement of advertising and promotional practices by self-regulation e.g. PIASA has a Code of Practice for the Marketing of Medicines to healthcare professionals. This is aligned with the IFPMA Code of Practice and the Perverse Incentives Policy applicable to South African Healthcare professionals.
10. The manufacturing facility where a medicine is made, tested and packed is subject to inspections and approval by the MCC which may also test specific products and audit the product dossiers to ensure that these have been kept updated.



MEDICINE APPROVAL PROCESS

Once the application for registration has been compiled, a specified number of copies together with the applicable application fee, and a sample of the product appropriately labeled, must be submitted to the MCC Secretariat in Pretoria with the required fee. MCC will not accept partial submissions with further data to follow at a later stage.

The MCC evaluates the submission and will usually respond with questions or requests for further data. Once this is submitted and accepted, registration of the product will be “approved” or “not approved”. The time taken for evaluation varies depending on the workload but should be approx. 24 months for innovative products and 12 months for generic medicines, although backlogs have frequently developed in practice so that approval can take much longer. During this time there can be several interchanges between the MCC and the applicant company.

The time taken for approval of variations to registered product dossiers depends on the nature of the changes required but would usually take from 2 – 4 months for pharmaceutical changes and 6 – 12 months for changes involving clinical data. Again backlogs frequently develop in practice so approval can take much longer.

PRICING AND REIMBURSEMENT

It is the expressed intention of the National Drug Policy of the ANC-led Government to ensure a more equitable and affordable health care system for all South Africans.

Pricing Regulations requiring a transparent pricing system with all medicines having a Single Exit Price [SEP] from the manufacturer were published in 2004. The Pricing Committee of the Department of Health is the statutory body responsible for monitoring and controlling the price of medicines and charges throughout the supply chain e.g., logistics and dispensing fees.

There are two main channels of medicine supply and distribution in South Africa.

1. The Public Sector:

This sector is funded by the State [at different levels]. It supplies approx. 70 - 80 % of all medicines by volume but this only represents approx. 30 – 40 % by value. These medicines are obtained from the private sector on a tender basis. Many of the medicines supplied are generics.



2. The Private Sector:

This sector is funded by medical schemes, medical insurers or other private sector health care funders. It supplies approx. 20 – 30 % of all medicines by volume but this represents approx. 60 – 70 % by value. Some of these organisations have introduced a Maximum Medical Aid Price [MMAP] for certain medicines. i.e., they will reimburse the patient at the cost of a generic medicine regardless of whether the patient received the original medicine or a generic substitute. Alternatively the patient may be required to make a co-payment of up to 25 % if they wish to receive the originally prescribed medicine. Recently medical schemes have also encouraged the practice of therapeutic substitution provided the medical practitioner agrees.

Further documents and guidelines can be accessed on the MCC's website at the bottom of the home page: www.mccza.com.