IP is a pharmaceutical or biotech company’s most valuable resource and its protection is key to that company’s future success
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1. Legislative requirements for registration of medicinal products with South Africa
2. Documents submitted to the Medicines Control Council
3. Handling regulatory submissions in South Africa - practical points to consider.

PRODUCT DEVELOPMENT

Discovery
Pre-clinical Studies
Pharmaceutical Development
Clinical Studies
Registration
Launch

~ 7 Years (goal)
~ 10 years (current)
~ 12 Years (5 years ago)
Legislative requirements for registration of medicinal products with South Africa

- MEDICINES AND RELATED SUBSTANCES ACT 101 OF 1965
  - 15. Registration of medicines
  - 1. Every application for the registration of a medicine shall be submitted to the registrar in the prescribed form and shall be accompanied by the prescribed particulars and samples of the relevant medicine and by the prescribed registration fee.

**MEDICINE REGISTRATION FORM 1**

<table>
<thead>
<tr>
<th>Part</th>
<th>Title</th>
<th>Contents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Administrative Particulars</td>
<td>Particulars of Applicant, Pharmacist to communicate with MCC, manufacturer, packer, QC site, FPRR and basic particulars. Amendment history table.</td>
</tr>
<tr>
<td>1B</td>
<td>Table of content</td>
<td>Comprehensive TOC for all dossier Parts</td>
</tr>
<tr>
<td>1C a)</td>
<td>Package insert</td>
<td>Scientific Package Insert</td>
</tr>
<tr>
<td>1C b)</td>
<td>Patient Information Leaflet</td>
<td>PIL</td>
</tr>
<tr>
<td>1C c)</td>
<td>Label</td>
<td>e.g. Blister, vial, carton printing</td>
</tr>
<tr>
<td>1D</td>
<td>Foreign Registration</td>
<td>EU, Australia, UK, USA, Canada, Sweden, Japan details</td>
</tr>
</tbody>
</table>
### MEDICINE REGISTRATION FORM 1 ctd

<table>
<thead>
<tr>
<th>Part</th>
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</thead>
<tbody>
<tr>
<td><strong>2A</strong></td>
<td>Pharmaceutical and Biological Availability</td>
<td>In vivo and/or in vitro equivalence studies as proof of efficacy</td>
</tr>
<tr>
<td><strong>2B</strong></td>
<td>Summary Basis for Registration Application (SBRA)</td>
<td>Summary of clinical data</td>
</tr>
<tr>
<td><strong>2C</strong></td>
<td>Pharmaceutical Expert Report (PER)</td>
<td>Independent, objective and comprehensive discussion of the quality of the product</td>
</tr>
<tr>
<td><strong>2D</strong></td>
<td>Pre-clinical Expert Report (PCER)</td>
<td>Independent, objective and comprehensive discussion of the pre-clinical product development</td>
</tr>
<tr>
<td><strong>2E</strong></td>
<td>Clinical Expert Report (CER)</td>
<td>Independent, objective and comprehensive discussion of the clinical product development with reference to the clinical information in the PI</td>
</tr>
<tr>
<td><strong>3A</strong></td>
<td>Active ingredient(s)</td>
<td>Chemical details Source (name &amp; address) Drug Master File</td>
</tr>
<tr>
<td><strong>3B</strong></td>
<td>Formulation</td>
<td>Unit formula and purpose of ingredients</td>
</tr>
<tr>
<td><strong>3C</strong></td>
<td>Raw Materials</td>
<td>Specifications and limits Control methods Control Labs</td>
</tr>
<tr>
<td><strong>3D</strong></td>
<td>Container/packaging materials</td>
<td>Specifications and drawings of immediate container Control procedures Description of bulk container Indication of supplier tests</td>
</tr>
<tr>
<td><strong>3E</strong></td>
<td>Manufacturing procedure</td>
<td>Manufacturer and packer Manufacturing and packaging procedures Validation protocol</td>
</tr>
<tr>
<td><strong>3F</strong></td>
<td>Finished product</td>
<td>Specifications and limits Control methods Validation FPRC FPRR Certificate of Analysis</td>
</tr>
</tbody>
</table>
**MEDICINE REGISTRATION FORM 1 ctd**

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<thead>
<tr>
<th>Part</th>
<th>Title</th>
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<tbody>
<tr>
<td>3G</td>
<td>Stability data</td>
<td>Programme, Data, Shelf-life, Control procedures and validation if different to 3F</td>
</tr>
<tr>
<td>3H</td>
<td>Pharmaceutical development</td>
<td>Description of pharmaceutical development process</td>
</tr>
<tr>
<td>4</td>
<td>Pre-clinical studies</td>
<td>Toxicology, teratogenicity, carcinogenicity, animal pharmacokinetics and pharmacodynamics. PCER</td>
</tr>
<tr>
<td>5</td>
<td>Clinical studies</td>
<td>Efficacy, pharmacology, pharmacokinetics, safety. CER</td>
</tr>
</tbody>
</table>

**Documents submitted to the Medicines Control Council**

- **PRACTICAL AREAS OF CONCERN:**
  - **MRF1**
  - **MRF2**
  - **Additional Requirements**
    - SAMPLES
    - SITE MASTER FILES? CONFIDENTIALITY
    - MANUFACTURING SITE INSPECTION REPORTS etc
34. Preservation of secrecy

No person shall, except for the purpose of the exercise of his powers or the performance of his functions under this Act, or for the purpose of legal proceedings under this Act, or when required to do so by any competent court or under any law, or with the written authority of the Director-General, disclose to any other person any information acquired by him in the exercise of his powers or the performance of his functions under this Act and relating to the business or affairs of any person, or use such information for self-gain or for the benefit of his employer.

2.3 CONFIDENTIALITY/SECURITY

The confidentiality of information submitted to the MCC is governed by Section 34 of the Act. The MCC, committee members or staff of the Medicines Regulatory Affairs (MRA), may NOT disclose to any person, any information acquired in the exercise of powers or performance of functions under the Act and relating to the business affairs of any person, except for the purpose of exercising his/her powers, or for the performance of his/her functions under the Act, or when required to do so by any competent court or under any law, or with the written authority of the Director-General, or use such information for self-gain or for the benefit of his employer.

The MCC may insist on written confirmation of the identity and affiliation of an individual inquiring telephonically, or in person, about a medicine. No information shall be disclosed telephonically unless the Medicines Control Officer knows the enquirer is entitled to receive the information.
3.1 PART 3A ACTIVE PHARMACEUTICAL INGREDIENT (API)

3.1.4 The name and physical address of each manufacturer of the API being applied for should be stated. No API from any source, other than the approved source(s), may be used.

3.1.5 The Active Pharmaceutical Ingredient File (APIF), or the open part of the DMF, should be submitted in the dossier and should include the following information: (Neither the complete nor the open part of the DMF should be sent directly to the MCC.)

- The name and physical address of the manufacturer (including any intermediate manufacturer).
- The approved/INN name of the relevant API.
- The chemical name and chemical structure of the API.

PACKAGE INSERTS FOR HUMAN MEDICINES
Version 2 Date of Implementation1 August 2008

For a multisource medicine (MSM) the most recent approved innovator package insert and/or MCC approved standardised package insert (SPI) template, if available, should be used as reference for the compilation of MSM package inserts. The indications and the safety profile for a MSM should at least be in line with that of the innovator package insert. Any additional information as required by the applicant should be submitted with relevant clinical data.

Standardised package inserts (MCC approved) contain only the minimum information required. It is the applicant’s responsibility to add new safety information to a package insert which is based on an SPI as soon as such information becomes available and make any other necessary amendments, with supporting references (as it is for applicants of innovator products). The information is subject to approval by MCC.

Reference to the following standard references are generally acceptable if SPIs are not available:
- Pharmacological actions: Goodman & Gilman. The Pharmacological Basis of Therapeutics.
- Safety matters: Martindale, The Complete Drug Reference
- General: USP DI
GUIDELINE ON PROPRIETARY NAMES FOR MEDICINAL PRODUCTS

The issue of whether a particular proprietary name may constitute an infringement of another entity's intellectual property rights cannot be one of the Medicines Control Council’s concerns and is, therefore, not taken into account during consideration of the acceptability of a proposed proprietary name.

Handling regulatory submissions in South Africa—practical points to consider.

- TECHNICAL ASPECTS
PROCESS: REGULATORY AFFAIRS AND HANDLING OF IP

- MED REG DOSSIER TO ZA-CORPORATE
- DELIVERY COURIER SERVICE
- REG AFFAIRS PERSONNEL
- MCC PERSONNEL
- MCC IT (INTERNAL/EXTERNAL)
- IT (INTERNAL/EXTERNAL)
- MCC: DELIVERY OF RESPONSES
- MCC: FILING SYSTEMS
- MCC: PHOTOCOPY/SCANNING/SHREDDING
- DELIVERY COURIER SERVICE
- FILING SYSTEMS
- PHOTOCOPY/SCANNING/SHREDDING

INTELLECTUAL PROPERTY RIGHTS AND PHARMACEUTICAL PRODUCTS AND PROCEDURES

MAINTAINING CONFIDENTIALITY
  - CORRECT DELIVERY ADDRESS

COURIER BEEN INTERCEPTED-
  - MALICIOUS INDUSTRIAL ESPIONAGE
### REGULATORY AFFAIRS PERSONNEL

**IN-HOUSE/CONSULTANTS:**
- Training on handling information:
  - Intellectual property/confidentiality
- TEMP STAFF-copying etc
- Dealing with “outside world” – telephonically or other
- Potential resignation: consider info accessible to person

### I.T-( IN-HOUSE/EXTERNAL)

- ACCESS: INTER-DEPARTMENTAL IT limitations
- Back-up systems
# PHOTOCOPYING/SCANNING/ SHREDDING

- Outsourced copiers - internal hard drive — ??
- ACCESS TO COPING DOSSIERS
- FOOL PROOF SHREDDING SYSTEM

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# FILING SYSTEMS/OFF-SITE STORE

- ACCESS
- AUDIT
AUDITORS & OTHER

- IN-HOUSE/EXTERNAL
- ACCESS TO INFORMATION
- MARKETING/PROMOTIONAL INDIVIDUALS

IN CONCLUSION:

- PHARMACEUTICAL REGULATORY AFFAIRS PERSONNEL HAVE THE RESPONSIBILITY TO SECURE INTELLECTUAL PROPERTY!!