Accelerated approvals
MCC position

3rd Annual Regulatory Workshop
New Developments in Drug Regulation

9 September 2015

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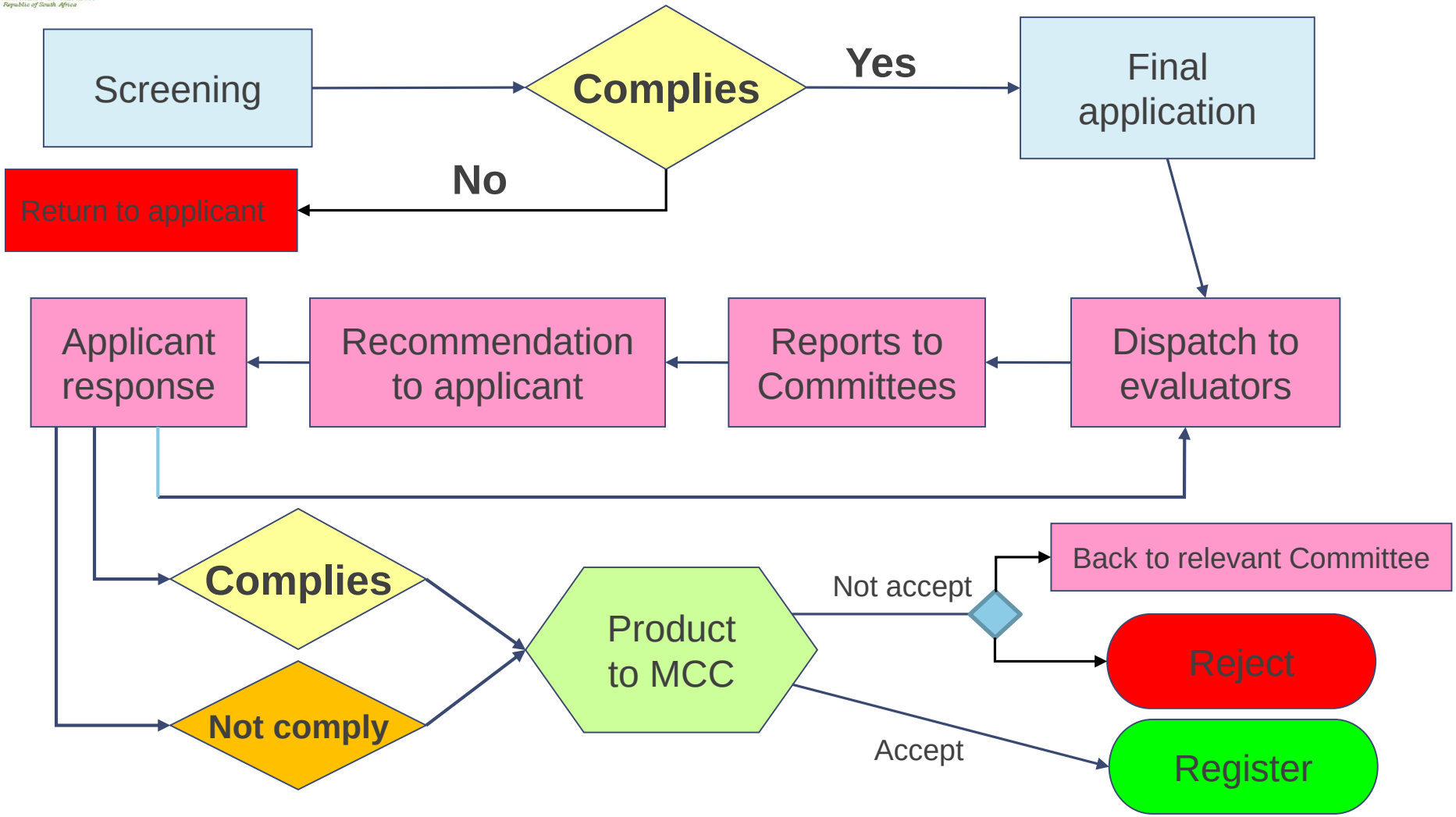
Overview

- Registration process
- Fast track in the Act, regulations and guidelines
- Experience to date
- Multiple submissions
- The way forward

Registration process



Fast tracks

Fast track
Act 101 section 15

15 Registration of medicines

(2) The registrar shall

(b) ensure that such an application in respect of medicine which appears on the latest Essential Drug List or medicine which does not appear thereon but which, in the opinion of the Minister, is essential for national health is subject to such procedures as may be prescribed in order to expedite the registration.

(12) For the purposes of this section, 'Essential Drug List' means the list of essential drugs included in the latest edition of the official publication relating to guidelines for standard treatment which is compiled by the Department of Health.

Fast track
Regulation 5

EXPEDITED REGISTRATION PROCESS FOR MEDICINES FOR HUMAN USE

5 (1) Expedited registration process for medicines for human use shall be as follows:

a. an application for medicines that appear on the Essential Drugs List shall be accompanied by declaration by the applicant that such a medicine appears on such a list; and

b. for any medicines containing new chemical entities that are considered essential for national health but do not appear on the Essential Drugs List, written notification to that effect from the Minister must be submitted with the application.

Fast track - Regulation 5 *cont.*

(4) The Council may subject certain applications in respect of medicines containing new chemical entities to an **abbreviated medicine review process** as determined by the Council, where registration has been granted by other medicines regulatory authorities recognised by the Council for the purpose applied for.

(7) The Council shall, within nine months from the date of receipt of the application by the registrar, make a decision with regard to the application and inform the applicant of such decision.

(8) Notwithstanding the above subregulations, an application for an expedited registration process must still comply with regulation 22.

Regulation 22

APPLICATION FOR THE REGISTRATION OF A MEDICINE

22 (6) A medicine in respect of which an application for registration is made must comply with the technical requirements as determined by the Council.

General Information guideline

6 EXPEDITED REVIEW PROCESS (FAST-TRACK)

The Medicines Control Council may, under certain circumstances, (as in most other national drug regulatory authorities) speed up the registration process for specific medicines that have important therapeutic benefit and which are required urgently to deal with key health problems. In such cases, an accelerated review system is applied. For further information refer to **Regulation 5** of the Act.

The applicant should submit an expedited review request **to the Minister of Health for the attention of the Registrar of Medicines**, before submitting the full application for screening. ***A copy of the approval letter must be submitted with the application.*** Products that will be considered for expedited review are:

- Medicines on the Essential Drugs List (EDL) *now EML*
- New Chemical Entities that are considered essential for national health but do not appear on the Essential Drugs List.

6.1 MEDICINES ON THE EDL

A declaration from the applicant that such a medicine appears on the EDL is required.

6.2 NEW CHEMICAL ENTITIES

The following should be submitted with the application:

- A written notification from the Minister to the effect that the medicine is considered essential to national health;
- an expert report (which is not more than 2 (two) years old;
- a package insert (where the product has been approved) and
- a summary basis for the registration (SBRA) (refer to Clinical guideline for details of an SBRA).

The Registrar shall notify the applicant within 30 days of the date of receipt of the application whether or not the application is to be subjected to the expedited registration process as stipulated in Regulation 5 of the Act.

The Council may request any information with respect to an application under consideration and the information should be submitted by the applicant within a period indicated by Council, failing which the Council may reject an application.

The Council shall, within 9 months from the date of receipt of the application by the Registrar, make a decision with regard to the application and inform the applicant of such decision.

General Information guideline *cont.*

7 ABBREVIATED MEDICINE REVIEW PROCESS (AMRP)

The AMRP is a system initiated by Council to limit the evaluation time of pharmaceutical products that are registered in countries with which the Council aligns itself, ***if the evaluation report is readily available***.

The abbreviated medicine review process is based mainly on the ***expert reports*** of the pharmaco-toxicological and clinical data. It should be noted that the AMRP is an abbreviated **evaluation** process and not an abbreviated **application**.

7.1 Only ***new chemical entities*** registered with one or more of the authorities with which the Council aligns itself will qualify for AMRP. (Refer to section 3.1.4 of this guideline).

7.2 The applicant should obtain the Expert Reviewers' reports on safety, quality and efficacy from the relevant medicines regulatory authority.

7.3 The certificate of approval of registration of the new chemical entity by one of the recognised registering authorities should be included. (Refer to section 3.1.4 of this guideline).

7.4 Written confirmation that the proposed package insert is based on the package insert and the complete dossier of the licensing country is required.

Apart from the approved package insert on which the submission is based, the package insert of the other countries where registration has been approved, should also be submitted.

7.5 Written confirmation that the **data** submitted to the MCC are **identical** to that submitted to the authority which has granted approval should be given. Raw data of experimental and clinical studies should be excluded. A letter authorising the MCC to contact the relevant MRA for an evaluator's report or assessor's report should be included.

7.6 **Expert reports** on chemical-pharmaceutical, pharmaco-toxicological and clinical documentation should be included.

7.7 Relevant correspondence between the applicant and the registering authority including the negative (e.g. queries, non-acceptance of certain claims/statements) as well as the positive correspondence should be included.

7.8 Written confirmation that the **formulation** applied for is **identical** to that approved by the registering authority should be given.

7.9 Applications for AMRP can only be accepted if the product has been approved by the said authorities within the **last three years** of the licence in the licensing country.

The experience to date

- Fast tracks are clogging the system
  - Capacity constraints
  - No limit on number
- Application for fast track approved
  - Not only 1 application submitted, but multiples
  - Committee advising Minister unaware
- Administrative burden
- Applicant expects registration in 9 months, *despite*
  - Regulation 22 (6)
  - Registration process
- Fast track approval applied for after submission of application
  - Administrative, logistical, audit issue

The experience to date *cont.*

The experience to date *cont.*

3 Applications

1 recommendation	1 recommendation	3 recommendations
1 response	3 responses	3 responses
1 product registered	3 products registered	3 products registered
2 products in backlog		

The experience to date *cont.*

- Business focus on fast tracks
- Lawyers letters

The experience to date *cont.*

Post-registration

- 1 dossier maintained, others not marketed
- Outdated dossier sold to new applicant
- Duplicate no longer the same as marketed product
- Burden on new applicant and on regulator (post-reg unit)

The way forward

- Change in policy on approval of fast tracks required
  - e.g. sunset clause, number accepted
- Policy on submission of multiple applications required
- Change in process re work flow and control required

Multiple submissions

Proposed policy published for comment

MULTIPLE SUBMISSIONS OF THE SAME APPLICATION WITH DIFFERENT PROPRIETARY NAMES

For the purpose of this process the following definitions apply:

- **Multiple** or duplicate applications are defined as **duplicates** of an application submitted by the **same** applicant or a subsidiary company of the same applicant, which are **identical** in every respect except for the proposed proprietary name(s) (includes duplicate applications of innovator and generic products).
- A **clone** is defined as a duplicate application submitted by the **innovator** of its own product under a different proprietary name at any stage during the product life cycle.

NCEs (submitted without duplicates) and Biological medicines are excluded from this process.

Multiple submissions *cont.*

2 Process

2.1 A single “master” dossier for registration application is submitted with a module 1.2.1 for each proprietary name, together with *a single* sample and *a single PI/PIL* including a list of all the proposed proprietary names, and the relevant application fees for each duplicate applied for.

2.2 The applicant indicates which proprietary name should be regarded as the “master”; if not indicated the invented name will usually be regarded as the master.

Multiple submissions *cont.*

2.3 For **more than three** of the same applications the applicant has to submit a **motivation** as to why the further applications are required. Council reserves the right not to accept the additional applications.

2.4 Additional product applications (same API, same indications) not linked to the master will not be handled as duplicates.

The applicant has to submit a motivation as to why these products are required. In this case, each application will stand on its own, and be evaluated on its own, and a committee recommendation on one product may not be applied and responded to for the other applications.

2.5 An application number is allocated to the master dossier, and a linking application number to the master for the additional proprietary names, e.g. 500010 for the master and the additional proprietary names 500013.10, 5090016.10 – the ".10" indicates the link to the master application.

Multiple submissions *cont.*

2.6 Duplicates are *not accepted* as such if they are not submitted at the same time as the master application, e.g. if an application is submitted two months or two years after the master, it is regarded as not being linked to a master and would follow the normal process. A motivation for Council to accept this application has to be submitted – see 2.4 above.

2.7 The single master dossier is fully evaluated by all the relevant Committees and all the proposed proprietary names are reviewed by the Names and Scheduling Committee.

2.8 When approved by all Committees the master product and all the duplicates are registered.

2.9 A registration certificate is issued for each approved proprietary name linked to the master dossier, (including the application number indicating the link) e.g. 50/2.5/0013.10

Multiple submissions *cont.*

2.10 Post-registration changes are effected to and reviewed only for the single master dossier.

2.10.1 The declaration provided with submission of amendments has to include a clause in which the Responsible Pharmacist confirms that the change will be made unilaterally across the range of linked dossiers.

2.10.2 If an amendment is applied for which is ***not intended*** to be implemented unilaterally across the range of linked dossiers, then the dossier will be automatically delinked and will be considered to be a stand-alone dossier.
If the dossier has not been updated within the past two years, a full update has to be submitted with the amendment applied for. If the dossier is up-to-date, a full update has to be submitted within one year of the delinking.
The registration certificate will also be amended and the relevant amendment fee be submitted because of the change in registration number.

Multiple submissions *cont.*

2.10.3 In cases where the amendment affects the registration certificate (e.g. a transfer of applicant), the relevant dossier will be delinked from the master application and the new certificate will not be issued until a full update in current regulatory format and complying with current regulatory standards is submitted, evaluated and approved.

2.11 Upon approval of a stand-alone dossier the linking number is removed (500013.10 becomes 500013) and this application then stands on its own.

Phased approach for submissions already in the system

Conclusion

A team effort is required

Coming together is a
BEGINNING
Keeping together is
PROGRESS
Working together is
SUCCESS
Henry Ford