Innovative Regulatory Review Practices for Better Efficiencies - The Singapore Experience

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Overview

- Mission
- Background
- Regulatory Principles
- Evaluation Routes
- Data Requirements
- Regulatory Process
- Application Statistics
Mission

- Wisely regulate health products
- Safeguard public health
- Serve the administration of justice
- Secure the nation’s blood supply

Risk-based evaluation based on international regulatory practice and scientific standards

Ensure medicinal products marketed in Singapore meet the quality, safety and efficacy standards
Background

Licensing of medicinal products for sale & supply in Singapore

Legal requirements under the Medicines Act

Drug registration first implemented in 1987

Establish high standard regulatory framework for health products

85% applications meet target turnaround time
Regulatory Principles

Risk-based approach

- International Standards
- Reference agencies
- Local consideration
- Scientific knowledge
- Evidence based risk-benefit
Pre-market Evaluation

- Depth of evaluation varies following a risk- & confidence-based approach
- Three evaluation routes allowing flexibility yet ensuring robustness in the registration system
- In-house capabilities complemented by external experts and advisory committee
Application Type

Pre-market approval
- New drug application (NDA)
- Generic drug application (GDA)

Post-market variation
- Major variation application (MAV-1)
- Major variation application (MAV-2)
- Minor variation application (MIV-1)

Post-market variation via notification
- Minor variation application (MIV-2)
Innovation – HSA’s 3-route System

Pre-submission consultation

Product yet to be approved by any regulatory agency
  - Full Evaluation
    - Full evaluation & Regulatory Decision

Product approved by one drug regulatory agency
  - Abridged Evaluation
    - Abridged evaluation & Regulatory Decision

Product approved by reference regulatory agencies*
  - Verification
    - Evaluation & Regulatory Decision based on assessment report by benchmark regulatory agency

Risk-Based Approach

* Reference regulatory agencies refer to US FDA, Health Canada, UK MHRA, Australian TGA, EMEA
Evaluation Routes (NDA & MAV-1)

**Full**
- No prior approval by any drug regulatory agency
- Full quality, non-clinical, & clinical internal & external evaluation
- Evaluation: 210 WD
- Reg Decision: 60 WD
- Total: 270 WD

**Abridged**
- Approved by one drug regulatory agency
- Full quality & abridged clinical internal & external evaluation
- Evaluation: 120 WD
- Reg Decision: 60 WD
- Total: 180 WD

**Verification**
- Approved by two reference agencies
- Reference agency assessment report internal evaluation only
- Evaluation: 40 WD
- Reg Decision: 20 WD
- Total: 60 WD
Data Requirements (NDA/MAV-1)

**Full**
- Chemistry, manufacturing & control data
- Biopharmaceutic study reports
- PK study reports
- PD study reports
- Toxicology reports
- Clinical study reports (Phase I, II, III)
- Post-marketing reports (if applicable)

**Abridged**
- Chemistry, manufacturing & control data
- Summaries (biopharmaceutics, PK, PD, toxicology, efficacy, safety)
- Clinical study reports (Phase II & III)
- Post-marketing reports or study report (Phase IV, if applicable)

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- Assessment report from 2 reference agencies
Evaluation Routes (GDA)

Abridged
- Approved by one drug regulatory agency
- Full quality & BE (POMs in oral dosage form)
  Internal evaluation.
- Total: 240 WD

Verification
- Approved by one reference agency
- Reference agency assessment report
  Internal evaluation.
- Total: 120 WD
Data Requirements (GDA)

- Chemistry, manufacturing & control data
- Bioequivalence studies (for POMs in solid oral dosage forms)

 Verification

- Chemistry, manufacturing & control data
- Bioequivalence studies (for POMs in solid oral dosage forms)
- Assessment report from reference agency
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*WD: working days
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verification

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- Bioequivalence studies (for POMs in solid oral dosage forms)
- Assessment report from reference agency
Regulatory Process (NDA/MAV)

- Pre-submission Consultation
- Submission of application
- Screening
- Acceptance of application
- Queries
- Clinical Peer Review
- Quality Peer Review
- Evaluation
- Triage
- Advisory Committee
- Regulatory Outcome
- Final Regulatory Decision
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- Final Regulatory Decision
- Regulatory Outcome
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  - Queries
  - Evaluation
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  - Regulatory Outcome
  - Quality Peer Review
Regulatory Decision

- Approvable subject to conditions
- Non-approvable due to major deficiencies
- Application withdrawal
- Applicant’s response
- Satisfactory
- Unsatisfactory

Approval

Product Licence

Rejection

To be the LEADING INNOVATIVE AUTHORITY protecting and advancing NATIONAL HEALTH and SAFETY
NDA Approval Timelines

N.B. Approval timelines in working days (excluding stop-clock time)
Conclusion

Resources are always limited in most regulatory agencies

- Adopting a risk based approach to triage drug applications
- Titrate the evaluation workload by leveraging on reference agencies assessment reports
- Managing Access to important medicines without prolonging timelines
- For small markets like Singapore, this unique system of drug evaluation, ensures that market entry of drug products is vetted in an efficient manner without compromising on stringent standards for safety and efficacy.
Thank you