The Regulatory Hurdles and Challenges for Post Approval Changes of Legacy (Existing) Products

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About Me

• 22 years experience in Pharmaceuticals and Medical Devices
• 15 years in Regulatory Affairs
• Manufacturing, planning, quality and management
• TGA Prescription Medicines IWG
• PDA AUS committee member 2004-2008
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Overview

• What are Legacy Products?
• Causes for Change – Quality
• Hurdles and Challenges
• Regulatory – Keys to Success
• Regulator Plan
• Opportunity and Benefits
What are Legacy Products?

• Originally developed in the past (as early as 1930’s).
• Dossier were developed when there was a lack of framework and regulation.
• Old Registered Products > 15 years
• Minimal Documentation regarding the Pharmaceutical Development or Validation
What are Legacy Products?

• Legacy Products are refer to "grandfathered“ products.

• Grandfathered products are products that were in the market before the commencement of the current legislation.
  
  – Australia: Therapeutic Goods Act 1989 (i.e. in 1991)
## Causes for Change - Quality

<table>
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<tr>
<th>Category</th>
<th>Items</th>
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</table>
| Manufacturing Site Transfers  | - Drug Product  
- Drug Substance  
- Testing sites               |
| Change to Manufacturing Process | - Equipment  
- Use of new technology  
- Method of manufacture  
- Increase in batch size    |
| Formulation                   | - Reformulation  
- Excipient  
- Stability  
- Container closure          |
| New Products                  | - New fill  
- Pack sizes  
- Extension of existing products into new markets |
Hurdles and Challenges

• Lack of Baseline Information
  – Regulatory dossier
  – Site documentation

• Project Scope
  – Poorly defined
  – Project creep

• Communication
  – Project management
  – Cross functional team
Hurdles and Challenges

• Regulator engagement
  – Pre-submission Scientific/Strategy meeting
  – Audit
• Changes are based on Good Science not just cost or this is how we always did it.
• Non Quality consequential changes
• Hidden Markets
• Supply Strategy
• Cost
Regulatory- Key to Success

- Involve RA during the scoping of your changes
- Project Plan
- Management commitment to the project
- Communicate changes of scope, regulation and delays
- Regulator engagement
- Realistic timeframes
- Good Data Package
- Document a Regulatory Plan/Strategy and keep it updated.
Regulatory Strategy

• Regulatory Strategy Plan documents the regulatory strategy for the implementation of a post approval change event or series of events.
• Initiated at any point of the post approval change cycle and is a living document intended to be updated as the project changes.
• Used to communicate to “in country” sales and marketing
• Not a change control but can be added as an addendum to a change control
• Dynamic – Electronic Document
• Version controlled - not a formal controlled document.
Regulatory Strategy

Scope and Background

Submission Strategy & LCM

Regulatory Strategy Document

Cost and Timelines

Version Control (Unique Identifier)

Risk Management

Regulatory Documentation Requirements
Opportunities and Benefits

- Harmonising process and products
- Regulatory compliance
- Regulator confidence
- Robust, reliable, product and processes
- Opportunities to extend products into new markets.
- Safer and consistent products
- Better Patient outcomes