Regulatory Experiences on Plasma Quality and Plasma-derived Medicinal Products in Singapore

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Outline

• Introduction

• Regulation of plasma-derived medicinal products

• Plasma Quality

• Product quality
HSA Functions & Roles

- Blood Services
- Health Products Regulation
- Applied Sciences
- Corporate HQ
Product Regulation

Product Life Cycle Approach in Licensing

Pre-market activities

Drug/ Product devt

Investigational Testing/ Clinical Trial

Product approval for sale

Product manufacture

Pdt available for sale/ supply

Product purchase/ use

Post-market activities

GMP Inspection

Clinical Trial Application

Application for market authorisation

• Post-approval variations
• Alerts

Risk-based and Confidence-based Assessment

Review
Product Registration

Medicinal Product Application

Evaluation by HPRG staff & External Experts

Clinical  Quality  Non-Clinical

Deliberation by Expert Panel  Deliberation by Medicines Advisory Comm

Regulatory Decision
Plasma Quality

Quality

Compliance

Potential Risk

WHO Recommendations
European Pharmacopeia
US FDA Guidelines
Plasma Master File (PMF)

PMF is a compilation of scientific data on the quality and safety of human plasma

Courtesy: Dr Glenda Silvester, European Medicines Agency
PMFs and plasma Source

Global Source
18 PMFs

Plasma Sources
18 countries
USA, Austria, Belgium, Germany,
Netherlands, Hungary,
Switzerland, Czech Republic,
Sweden, Norway, Poland, Estonia,
Finland, Luxembourg, Slovakia,
Slovenia, Canada, Singapore.

Singapore Plasma
1 PMF

3 Products
Immunoglobulin
Albumin
Factor VII & VWF
Review of Plasma Quality

- Plasma source & collection
- Characteristics of donations
- Epidemiological data
- Selection / exclusion criteria
- Plasma quality and safety
- Storage & transport
- Specification
- Plasma pool batch analysis data

Risk-based & Confidence-based Assessment
Traceability of Plasma

PRISM
Pharmaceutical Regulatory Information system

Declaration of Information

Type of product
Use
Source
Challenges with Submission (1)

- PMF not available
- Incomplete information
- Unable to confirm source
- Lack of traceability
Challenges with submission (2)

- PMF holders are maintaining PMFs which cater for different markets
- PMFs different from the PMF approved by EU
- PMF is claimed to be “International PMF” or “PMF for non-EU region”
- Not approved by EMA or any HSA reference agencies

HSA Reference Agencies: TGA, FDA, EMA, Health Canada, MHRA
How was the challenges handled?

- Confirmation & clarification on differences between PMFs
- Clarification on blood collection & testing centres
- Approval status of blood collection centres by local authority.
How was the challenges handled?

- Testing centres are audited
- Virus testing methods are validated
- Assess epidemiological data
- Data and information conform to international requirements

Submission Issues has Impact:
Delay or unable to register products
Product Quality

Plasma-derived products registered
(February 2016)

- Chemical Products: 92%
- Biological Products: 448 (8.0%)
- Vaccines: 79 (18%)
- Other Biologics: 256 (57%)
- Plasma-derived Products: 113 (25%)
Risk-Benefit Assessment

- Quality (CMC)
- Non-clinical safety
- Clinical benefit
- Safety, disease profile & prognosis
- Alternative therapies
- Scientific, clinical & regulatory perspectives

Ensure quality, safety & efficacy of products and to Safeguard Public Health
Rigorous attention to safety

Hepatitis A, B & C
Parvovirus B19
Inactivation/removal
Emerging Infection
HIV
Selection of starting materials
Variant CJD
Testing

Defence against Infection
Courtesy: Dr Glenda Silvester, European Medicines Agency
Holistic Approach

Viral Testing

Viral Inactivation

Viral Clearance

Risk Assessment

Viral Surveillance
Post-approval Condition

Licensing Condition

The import of the product must be accompanied by a batch certification.

The batch certification and product movement records shall be maintained for 10 years from the date of importation and be made available upon request.
Challenges

- Grandfathered products not meeting current requirements e.g., viral clearance & Clinical data
- Inadvertent contamination during manufacture
- Difficult regulatory action:
  - non-approval
  - recall, quarantine
  - conditional release
  - lack of alternatives
  - supply issues

Addressing the challenges by co-operation by industry and collaboration with international regulators
### Conclusion

**Quality of plasma and plasma-derived products are the underpinning of safety and efficacy**

- The overall goal of regulation is to ensure that only products of demonstrated quality, safety and efficacy are used.

- Plasma and plasma-derived products are well controlled and safe due to high level of compliance by the industry stakeholders and robust regulatory oversight.
A regulator's job is never done!