Regulatory Assessment of Biosimilar Products in Hong Kong

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Registration of Pharmaceutical Products

- According to the Pharmacy and Poisons Ordinance (Cap.138) and its subsidiary legislation
  - '... no person shall sell, offer for sale or distribute or possess for the purposes of sale, distribute or other use any pharmaceutical product unless it is registered with the Board.'
- Pharmaceutical products include chemical or "***biological***" materials as active ingredients

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Criteria for Registration under the Pharmacy and Poisons Ordinance and its Subsidiary Legislation

- Safety
- Quality
- Efficacy

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Biological Products

- Biological products are derived from living organisms and have complex molecular structures
- They require special quality consideration, including the starting materials; the manufacturing processes, and/or the test methods needed to characterize batches of the products

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Biological Product

Filgrastim

Formula: $C_{845}H_{1343}N_{223}O_{243}S_9$

Molar mass: 18802.8 g/mol

Chemical Product

Aspirin

Formula: $C_9H_8O_4$

Molar mass: 180.157 g/mol

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Biosimilar Products

- The expirations of patent and/or data protection of the originator biological products have led, or will lead, to the development of copy versions of the originator products (commonly referred as biosimilar products
- They are merely "***similar***" to the originator products because of the differences in molecular structures and quality attributes arising from their different manufacturing processes.

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International Practice

- The World Health Organization (WHO) "Guidelines on Evaluation of Similar Biotherapeutic Products"
- Registration requirements of biosimilar products by the drug regulatory authorities of the EU, US, Canada, Australia, Japan and Singapore.

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Scientific Consensus

- The registration of biosimilar products cannot use the same approach of generics for chemical products, i.e. cannot rely on bioequivalence and quality data only.
- Safety and efficacy data in comparison with the originator products are also necessary (comparability studies)

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Registration of Biosimilar Products in Hong Kong

- The Department of Health (DH) adopts the principles set out in the WHO guidelines and has taken reference of the registration requirements by the drug regulatory authorities of the EU, US, Canada, Australia, Japan and Singapore
- Draft version of "Guidance Notes for Registration of Biosimilar Products" was prepared in 2014 (biosimilar guidelines)

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Registration of Biosimilar Products in Hong Kong

- The guidelines entails the special considerations for registration of biosimilar products
- The biosimilar guidelines are supplementary to the main "Guidance Notes on Registration of Pharmaceutical Products/Substances"

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Consultation with Stakeholders (1)

- Consultation with different stakeholder groups, including
  - Pharmaceutical trade associations and companies
    - the Hong Kong Association of the Pharmaceutical Industry
    - the Hong Kong Pharmaceutical Manufacturers Association
    - the Pharmaceutical Distributors Association of Hong Kong

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Consultation with Stakeholders (2)

- Consultation with different stakeholder groups, including
  - Professional associations of doctors and pharmacists
    - The Pharmaceutical Society of Hong Kong
    - The Society of Hospital Pharmacists of Hong Kong
    - The Practising Pharmacists Association of Hong Kong
    - The Hong Kong Pharmacists Union
    - The Hong Kong Doctors Union
    - The Hong Kong Medical Association

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Consultation with Stakeholders (3)

- Consultation with different stakeholder groups, including
  - Patient group
  - Overseas expert

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Comments received after Consultation

- Comments on the following issues were received:
  - Clinical/immunogenicity studies in comparability exercise
  - Extrapolation of data from one indication to other indications
  - Penalty for non-compliance of the biosimilar guidelines
  - Registration status in 2 instead of 1 reference health authority

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Responses to the Comments (1)

- Clinical/immunogenicity studies in comparability exercise
- Extrapolation of data from one indication to other indication
  - The biosimilar guidelines have been updated in accordance with the latest EU guidelines on clinical/immunogenicity studies, and extrapolation of data

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Responses to the Comments (2)

- Penalty for non-compliance of the biosimilar guidelines
  - For non-compliance of the biosimilar guidelines, the applicant must provide complete registration dossiers with clinical and non-clinical documentations to support the safety, quality and efficacy of the product

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Responses to the Comments (3)

- Registration status in 2 instead of 1 reference health authority
- DH has taken reference of the registration requirements in overseas situations to decide the requirement on registration status of the product in one reference health authority

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Guidance Notes for Registration of Biosimilar Products

- In 2015, the final version of the biosimilar guidelines has been endorsed by the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee under the Pharmacy and Poisons Board
- On 1 January 2016, the biosimilar guidelines become effective

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Guidance Notes for Registration of Biosimilar Products

In October 2015, the Department of Health (DH) Drug Office has issued the following announcements on the registration requirements of biosimilar products:

- Letters to the stakeholders
- Announcement on the DH Drug Office website
- Updated the Guidance Notes on Registration of Pharmaceutical Products/Substances
- Supplementary Guidance Notes for Registration of Biosimilar Products

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Guidance Notes for Registration of Biosimilar Products (1)

- Introduction
- Purpose and Scope
- General Requirements (See later slides on Reference Health Authorities)
- Specific Requirements (Note on Quality, Non-clinical and Clinical Documents)

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Guidance Notes for Registration of Biosimilar Products (2)

- Pharmacovigilance Requirements (See later slides)
- Labelling Requirements (See later slides)
- Remarks (See later slides on Post-approval Changes)
- Disclaimer (See later slides on Substitution)

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Highlights of the Biosimilar Guidelines – General Requirements (1)

- The dose form, strength, and route of administration should be the same between the biosimilar and reference products.
- The proposed indication(s) of the biosimilar product must fall within the clinical indication(s) granted to the reference product in Hong Kong.

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Highlights of the Biosimilar Guidelines – General Requirements (2): Reference Agency

- The biosimilar product should have been granted marketing authorisation(s) by at least one of the following reference agencies, otherwise, the application cannot be accepted for registration as a biosimilar product:
  - the United States Food and Drug Administration
  - the European Medicines Agency
  - the Japan's Ministry of Health, Labour and Welfare
  - the Australia's Therapeutic Goods Administration
  - Health Canada

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Highlights of the Biosimilar Guidelines – General Requirements (3): Reference Product

- The reference product must have been registered in Hong Kong for over 8 years
- A registered biosimilar product cannot be chosen as the reference product in another new application for registration as a biosimilar product

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Highlights of the Biosimilar Guidelines – Pharmacovigilance Requirements (1)

- The applicant is required to:

1. Report local suspected serious or unexpected adverse drug reactions related to the biosimilar product as soon as possible and within 15 calendar days of receipt of information

2. Submit Periodic Safety Update Reports of the biosimilar product every 6 months for the first 2 years, and then annually for the following 3 years

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Highlights of the Biosimilar Guidelines – Pharmacovigilance Requirements (2)

3. Provide information on the Risk Management Plan and/or Risk Evaluation and Mitigation Strategy for the biosimilar product as required by the reference health authority if applicable, and any proposed local risk management plan

4. Prepare educational materials for healthcare professionals on the specific risks of the biosimilar product and measures to reduce the risks; and package inserts for patients

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Highlights of the Biosimilar Guidelines – Labelling Requirements (1)

General Principles:

- As biosimilar product is similar but is not identical to the reference product, claims for any bioequivalence or clinical equivalence between the biosimilar and reference products will not be allowed

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Highlights of the Biosimilar Guidelines – Labelling Requirements (2)

- The product should be labelled with the following information:

1. a statement on the nature as a biosimilar product

2. product name, manufacturer's name and invented, common or scientific name of the active ingredient*

3. registered indications; and clinical studies that have been performed with the biosimilar product; and

4. warning statement on the risk of substitution of the reference product with biosimilar product.

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Disclaimer

- The Department of Health does not endorse the substitution of reference product with biosimilar product
- Healthcare professionals should exercise their own judgement; and inform their patients if necessary regarding the risk of substitution of reference product with biosimilar product.

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Post-approval Changes of a Registered Pharmaceutical Product

- After the biosimilar product is approved for registration, the registration certificate holder is responsible for ensuring that the product imported for local sale and supply is identical in all aspects to the approved product.
- For any major variations (e.g. change of manufacturing site and change in manufacturing process), the registration certificate holder must obtain approval before implementation as stipulated in the *Guidance Notes on Change of Registered Particulars of Registered Pharmaceutical Products*.

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Thank you
Q / A