Trade in Pharmaceuticals and Medical Devices between the EU and Singapore - Opportunities under the EUSFTA and Beyond
Webinar

Pharma & MedTech in the EU: Regulation, Strategy, Recent Developments - Brief Overview

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Introduction

- Network of regulatory authorities from the 30 EEA countries (27 EU MS plus Iceland, Liechtenstein and Norway), the European Commission and EMA.
- EMA and Member States
  - Cooperate and share expertise in assessment of new medicines & new safety information
  - Exchange information on the regulation (reporting of side effects of medicines, oversight of clinical trials, conduct of inspections of medicines' manufacturers, compliance with good clinical practice (GCP), good manufacturing practice (GMP), good distribution practice (GDP), and good pharmacovigilance practice (GVP))
- EU Member States operate under same rules and requirements re: authorisation and monitoring of medicines

Marketing Authorisation

- **Centralised procedure**
  - allows the marketing of a medicine on the basis of a single EU-wide assessment and MA
  - pharma companies submit a single application to EMA
  - Committee for Medicinal Products for Human Use (CHMP) or Committee for Medicinal Products for Veterinary Use (CVMP) carries out a scientific assessment → recommendation to the European Commission
  - European Commission grants centralised MA, valid in all EU Member States.
  - Centrally authorised procedure compulsory for most innovative medicines, incl. medicines for rare diseases.
- **Decentralised procedure**
  - application for simultaneous authorisation of a medicine in more than one EU Member State
  - if not yet authorised in any EU country and not within the scope of the centralised procedure
- **Mutual-recognition procedure**
  - medicine already authorised in one EU Member States
  - application for authorisation to be recognised in other EU countries (allows Member States to rely on each other's scientific assessments).

Pricing and reimbursement

- Pricing and reimbursement regulated at Member State level, not harmonized – national health systems
- Member States required to comply with the EU Transparency Directive (Directive 89/105/EEC)
  - decisions on pricing or reimbursement of medicines to be taken within 90 days after each dossier submission (or within 180 days for joint pricing and reimbursement)
  - competent authorities to follow transparent processes in pricing and reimbursement decisions based on objective and verifiable criteria, published
  - possibility of appeal to an independent body against
- Price regulation
  - Most MS have price controls for reimbursable medicines (wholly or partially covered by a public payer)
  - Some countries (incl. Belgium and Lithuania) for all medicines, including non-reimbursable medicines
  - Others (incl. Bulgaria and Romania) for prescription-only medicines.
  - Price regulation covers ex factory price; remuneration of wholesalers, pharmacists and further distributors and dispensers; taxes (such as value-added tax), duties and other mark-ups.

Role of EMA and National Competent Authorities

- EMA
  - responsible for the scientific evaluation, primarily of innovative and high-technology medicines
  - prepares scientific guidelines in cooperation with experts from its scientific committees and working groups
  - gives product-specific scientific advice to companies for the development of medicines
  - manages centralized MA procedure
- National competent authorities (NCAs)
  - responsible for the regulation of human and veterinary medicines in the EU
  - responsible for decentralized and mutual recognition procedures
  - coordinate their work in forum “Heads of Medicines Agencies (HMA)”
  - NCAs work closely with EMA and the European Commission

Role of the European Commission

- Important direct role in the regulation of medicines in the EU
  - On the basis of scientific assessments carried out by EMA:
    - grants or refuses, changes or suspends marketing authorisations for medicines submitted via centralised procedure
    - may take EU-wide action when a safety issue has been identified for a nationally authorised product and when harmonised regulatory measures in all MSs are considered necessary following assessment by EMA's PRAC
- Can also take action re other aspects of medicine regulation
  - Right of initiative: proposes new or amended legislation for the pharmaceutical sector
  - Implementation: adopts implementing measures, oversees correct application of EU law on pharmaceuticals
  - Global outreach: ensures appropriate collaboration with relevant international partners and promotes the EU regulatory system globally

Authorisation and Supervision of Manufacturers

- Manufacturers, importers and distributors of medicines in the EU must be licensed
- Regulatory authorities of each Member State are responsible for granting licences for activities in their territory
- All manufacturing and importing licenses are entered into EudraGMDP, public database operated by EMA
- Manufacturers listed in the application of a medicine to be marketed in the EU are inspected by an EU competent authority; includes manufacturers located outside the EU unless an MRA is in place
- Inspection outcomes can be accessed by all MS, publicly available across the EU through EudraGMDP
- Equivalence between Member States' inspectorates is ensured and maintained in a variety of ways, including common legislation, common good manufacturing practice (GMP), common procedures for inspectorates, technical support, meetings, trainings, and internal and external audits
- Imported API needs to be accompanied by a written confirmation issued by the competent authority of the country of production, confirming that the GMP applied is at least equivalent to the recognised EU GMP standards
- Waiver for countries which had their regulatory systems for the supervision of manufacturers of active pharmaceutical ingredients assessed by the EU
- Mandatory batch release by EU QP for imported pharmaceuticals, in addition to GMP, except where MRA covers
- (Post-market: Pharmacovigilance etc.)

In a Nutshell: Regulation of Medical Devices

- New Regulation (EU) 2017/745 on Medical Devices
  - Applies since 26 May 2021, covers all medical devices, widely defined
  - Tiered system of classification
    - Classes I, IIa, IIb, III
    - Classification rules: duration of contact; degree of invasiveness; anatomy affected; active/non-active
  - Most med devices require third party Conformity assessments → involvement of Notified Bodies
  - Variety of conformity assessment routes (*some* choice for manufacturers)
    - Quality system assessments – QMS ; production quality assurance
    - Product assessments – technical documentation; type examination; product verification
  - Clinical evaluations usually required to establish safety and performance
  - Obligations of manufacturers; authorized representatives; importers; distributors
  - For exports: Certificates of Free Sale
  - Transparency through a comprehensive EU database on medical devices (EUDAMED)
- Special cases: Medical devices combined with medicinal substances → EMA involvement

In a Nutshell: New IVD Regulation

- New Regulation (EU) 2017/746 on in vitro diagnostic medical devices to apply fully from 26 May 2022
- Goal: to (further) establish a well-regulated and smoothly functioning market for IVD medical devices within the EU that is better aligned with international guidelines
- Main features:
  - clear **obligations for economic operators** (manufacturers, importers, distributors), such as traceability of devices, registration of devices and as economic operator (for manufacturers and importers), verification of labelling
  - introduction of a **risk-based classification system with 4 risk classes** of in vitro diagnostic medical devices
  - **stricter control for high-risk in vitro diagnostic devices** via a new pre-market scrutiny mechanism with a pool of experts at EU level
  - reinforcement of the criteria for the designation and **oversight of notified bodies**
  - **improved transparency** through a comprehensive EU database on medical devices (EUDAMED)
  - a **traceability system** based on a unique device identifier (UDI)
  - **reinforced rules on clinical evidence and performance evaluation**
  - **strengthened post-market surveillance** requirements for manufacturers

The New EU HTA Regulation

- Health Technology Assessment (HTA)
  - has been applied by EU Member States for the past 2 decades
  - multidisciplinary process
  - examines relative effectiveness of new or existing health technologies
  - evaluates the medical, social, economic and ethical issues related to the use of a health technology
  - Basis *inter alia* for pricing and reimbursement
- New HTA Regulation
  - based on Art. 114 (Common Market) and Art. 168 (Health) TFEU
  - support framework and procedures for cooperation of MS on health technologies at EU level
  - mechanism stipulating that any information, data, analyses and other evidence required for the Joint Clinical Assessment (JCA) is submitted by the HT developer only once at EU level
  - common rules and methodologies for the JCA of health technologies
  - MS retain competence to draw conclusions on the relative effectiveness of health technologies and to take decisions on the use of a health technology in their specific national health context

Cornerstone of the EU HTA Regulation

Cooperation of MS on Joint Clinical Assessments (JCA)

- MS agree to cooperate and develop JCAs
- JCAs create a sound scientific foundation for pricing and reimbursement decisions for all MS
- MS remain responsible for drawing conclusions at national level on the clinical added value of a health technology, but also shall “give due consideration” to the JCAs
- Assurance of a high quality and a fixed time frame for JCAs
- Ensurance of the highest possible level of transparency regarding the submitted data
- **Exclusive competence of MS for pricing and reimbursement remains unaffected (Art. 168 (7) TFEU)**

The Pharmaceutical Strategy for Europe (2020)

» On 25 November 2020, the European Commission published a proposal for a new **Pharmaceutical Strategy for Europe** ("the Strategy"). 4 main objectives:

- Foster patient access to innovative and affordable medicinal products
- Support the **competitiveness and innovative capacity of the EU's pharmaceutical industry**
- Develop **strategic autonomy** and ensure **robust supply chains**, including in times of crisis
- Ensure a strong **EU voice on the global stage**

Action Plan

1) FOSTER PATIENT ACCESS TO INNOVATIVE AND AFFORDBALE MEDICINAL PRODUCTS

- modify the system of incentives to stimulate innovation in areas of unmet medical needs
- revise legislation on medicinal products for children and rare diseases

2) SUPPORT THE COMPETITITVENESS & INNOVATIVE CAPACITY OF THE EU PHARMA INDUSTRY

- revise current pharma legislation to adapt to innovative products & scientific developments (e.g. genomics, personalised medicinal products).
- set up European Health Data Space (2022) to facilitate secure cross-border analysis of health data (by 2025)
- modify pharma legislation to provide more flexibility re interplay of medicinal products and medical devices.

Action Plan

3) DEVELOP STRATEGIC AUTONOMY & ENSURE ROBUST SUPPLY CHAIN, INCL. IN TIMES OF CRISIS

- revise pharma legislation to enhance security of supply and better respond to shortages of medical products (incl. stronger obligations for supply and transparency, earlier notification of shortages and withdrawals, enhanced transparency of stocks, stronger EU coordination mechanisms to monitor, manage, and avoid shortages of medicinal products)
- establish an EU Health Emergency Response Authority ("HERA") to
  - strengthen the coordination of operations across the whole value chain in health emergencies
  - monitor production capacity, raw material requirements, and availability of medicinal products.

4) ENSURE A STRONG EU VOICE ON THE GLOBAL STAGE

- promote international regulatory convergence to ensure access to safe, effective, high-quality, and affordable medicinal products globally
- support WHO to strengthen regulatory capacity globally