

GHSI

Public Health Emergency Medical Countermeasures  
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# EU: Regulatory Procedures for the Authorisation of Vaccines against Influenza A (H1N1)

Sabine Atzor

[sabine.atzor@ec.europa.eu](mailto:sabine.atzor@ec.europa.eu)



**European Commission**  
Enterprise and Industry

# Two types of authorisation in the EU

## 1) Central marketing authorisation

- Allows market access in all Member States (MS)
- Mandatory for certain products and processes, e.g. biotechnological process
- **Scientific Assessment:** European Medicines Agency (EMA)
- **(Management) Decision:** European Commission

## 2) National marketing authorisation

- Only applicable in MS for which applied
- > 1 MS (ex ante): **Decentralised Procedure - DCP**
- > 1 MS (ex post): **Mutual Recognition Procedure - MRP**
- Coordination mechanisms
- **Scientific assessment and management decision** by national authorities

# Types of central authorisations

## Regulation 726/2004

### 1. „Regular“ authorisation

- Full data for **quality, safety, efficacy**
- Data assessment: **210 days**, can be reduced to 150 days

### 2. Conditional Marketing Authorisation

- **Emergency situation** recognised by WHO or Community
- **Unmet medical needs**
- Full **quality data**
- Less comprehensive clinical data (**safety and efficacy**)
- Sufficient proof of **positive risk-benefit balance**
- Specific obligations: additional data, pharmacovigilance
- Validity of 1 year, can be renewed

### 3. Exceptional Circumstances

- Objective, verifiable reasons of public health
- Limited data
- Specific obligations concerning safety
- Annual reassessment

- No need for placing on the market within 3 years



# „Mock-up“ Concept for Pandemic Influenza Vaccines

- **Mock-up** mimics future of pandemic vaccine
  - re. composition (antigen, excipient, adjuvant)
  - re. manufacturing process and control
  - Needs to be varied for adjustment of pandemic virus strain
- **Core pandemic dossier**
  - Subtype of Influenza A (here: H5N1)
  - Quality data, safety and immunogenicity data
- **„Proof of principle“**
  - **Immune responses** expected to predict responses to same vaccine construct\* in comparable population
  - **Safety data** in clinical studies expected to predict safety profile with same vaccine construct\* in comparable population
- Specific **guidance** developed by EMEA
  - CPMP/VEG/4986/03, CPMP/VEG/4717/03

# Specific Legal Provisions for Variation of Pandemic Vaccines\*

- In case of **declared pandemic** by WHO or Community
- Commission may **exceptionally** and **temporarily accept variation** after receipt of application and before completion of full procedure
- **Provisions:**
  - full quality data
  - positive benefit risk assessment on given data
- **Obligations:** MAH must submit complete clinical safety and efficacy data

# Practical Implementation

- **EMA Task Force (ETF)**  
involving experts from EU network
- „**Rolling review**“ assessment  
on data upon availability (2 week cycles)
  - Quality
  - Non-clinical
  - Clinical
  - Pharmacovigilance
  - Labelling
- Subsequent formal **submission of application** by company, within few days:
  - **Scientific opinion** by EMA\*
  - Subsequent formal **Commission decision**

# Centrally authorised Pandemic Vaccines

Authorisation of Mock-up dossier Influenza (H5N1)	Characteristics	Variation of Influenza (H1N1) Strain
2007 <b>Focetria®</b> (Novartis) 7,5 µg	Egg based Surface antigen Adjuvant MF 59C.1	29 Sept 2009
2008 <b>Pandemrix®</b> (GSK)* 3,75 µg	Egg based Split virion Adjuvant AS03	29 Sept 2009
2009 <b>Celvapan®</b> (Baxter) 7,5 µg	Cell based Whole virion	6 Oct 2009


\*For Daronix® (GSK): no strain update to date

# Summary of Product Characteristics

- Prophylaxis of influenza in **officially declared pandemic situation**
- Vaccine to be used in **accordance with Official Guidelines**
- **Posology** for all age groups > 6 months
- Use during **pregnancy** if considered necessary
- Recommendation for **2 doses**

# Conditions & Obligations for Marketing Authorisation Holders (MAH)

- **Traceability** of vaccine administration to patient
- Continuous access to **updated information**
- **Targeted communication on**
  - Preparation of vaccines
  - Priorisation and ways for adverse event reporting
- **Official batch release** by OMCL



# Conditions & Obligations for MAH Clinical

- **Clinical studies** on
  - safety
  - immunogenicity (also on 1 vs 2 doses)
- **Clinical studies in children**
- **Benefit-risk surveillance/  
Safety and effectiveness studies**  
in accordance with strategy developed  
between EMEA and ECDC\*

# Conditions & Obligations for MAH Pharmacovigilance

- Simplified **monthly** Periodic Safety Update Reports (**S-PSUR**)
- Studies following Pharmacovigilance Plan:
  - Epidemiological **cohort studies in > 9000 patients** covering different age groups, including immunocompromised subjects
  - Additional **pharmacovigilance studies** on emerging risk-benefit balance
- Study with reference to Member States' **pregnancy registries**



# Vaccination campaigns

- **Commission coordinates common approaches\***
  - **Objectives**
    - Maintaining essential services
    - Protecting the vulnerable
    - Limiting the spread of the disease
  - **Target groups**
    - Healthcare workers & workers in other essential services
    - All children >6 to 24 months
    - All persons >24 months to 64 years with underlying chronic conditions
    - Pregnant women
    - Persons > 65 years
  - **Priority groups**
- **Ultimate responsibility of Member States!**

# References on the Web:

- European Commission, Directorate Enterprise and Industry (**DG ENTR**):  
[http://ec.europa.eu/enterprise/pharmaceuticals/index\\_en.htm](http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm)
- European Commission, Directorate General Health and Consumer Protection (**DG SANCO**):  
[http://ec.europa.eu/health/ph\\_threats/com/Influenza/novelflu\\_en.htm](http://ec.europa.eu/health/ph_threats/com/Influenza/novelflu_en.htm)
- European Centre of Disease Prevention and Control (**ECDC**):  
[http://ecdc.europa.eu/en/healthtopics/Pages/Influenza\\_A\(H1N1\)\\_Outbreak.aspx](http://ecdc.europa.eu/en/healthtopics/Pages/Influenza_A(H1N1)_Outbreak.aspx)
- European Medicines Agency (**EMA**):  
<http://www.emea.europa.eu/influenza/vaccines/home.htm>

# Thank you

