

Marketing Authorisations for Pandemic Influenza vaccines in Europe

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3 November 2005

Overview

- **Marketing authorisations for pandemic influenza vaccines: guidance documents**
- **Core dossier and ‘mock-up’ vaccine approach**
- **Composition of Pandemic Influenza vaccines**
- **EMA experience with ‘mock-up’ vaccines**
- **Concluding remarks**
- **EMA Pandemic influenza crisis plan**

EMA Guidance Documents for Pandemic influenza vaccines

Two guidance documents published on EMA

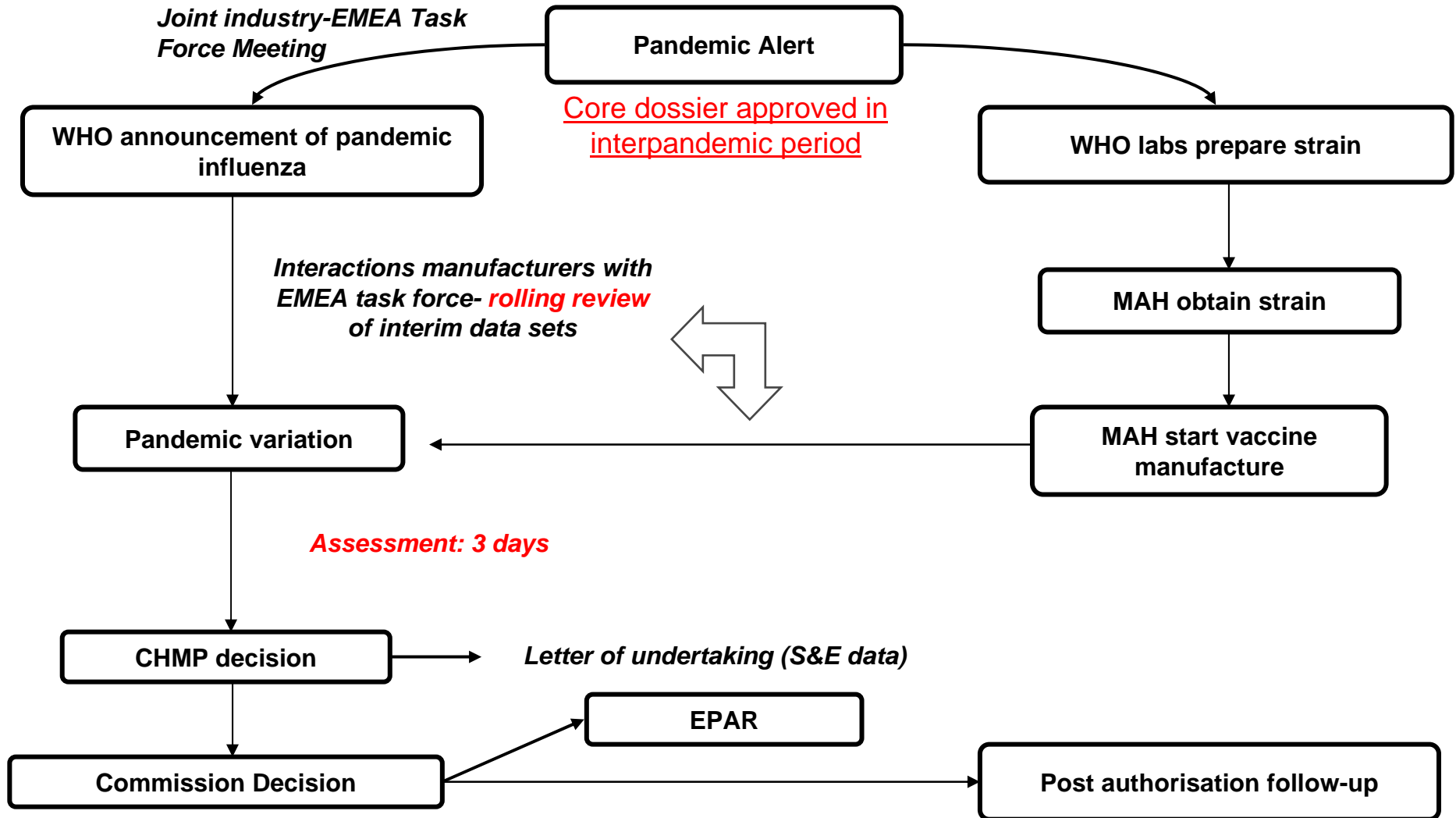
Website: <http://www.ema.eu.int>

- **Note for guidance on dossier structure and content of marketing authorisation for pandemic influenza vaccines**
 - = Scientific guidance
 - = Introducing the **principle of 'core' dossiers**
- **Guideline on submission of marketing authorisation applications for pandemic influenza vaccines via the centralised procedure**
 - = Procedural guidance

Core-dossier approach: “Mock-Up” Vaccine (1)

- **Aim**
 - » Fast track authorisation of pandemic influenza vaccines
- **Two steps approval of pandemic influenza vaccines:**
 - » During **inter-pandemic period**: Core dossier (Quality, Non-clinical and Clinical data with a ‘**mock-up**’ vaccine).
 - Accelerated review
 - » During **pandemic**: Variation to introduce Pandemic strain
 - In order to further shorten approval time of pandemic variation: Rolling review

Core-dossier approach: “Mock-Up” Vaccine (2)



Core SPC for pandemic influenza vaccines

- **Aim: to facilitate the submission of core dossiers**
- **Product information will be approved as part of the core dossier authorisation**
- **Minimal changes needed as part of the pandemic variation approval (only information related to pandemic strain)**

Pandemic influenza vaccine: composition (1)

- **Formulation based on interpandemic influenza vaccines (no adjuvant, 15 µg Ag or more, split unit or surface Ag vaccine) can be used ...**
- **BUT: need for high Ag content to get adequate immune response in naïve population:**
 - e.g. H5N1-NIH trial: 2 x 90 µg needed
- ➔ **Not realistic for pandemic situation**

Pandemic influenza vaccine: composition (2)

- **Proposed composition for pandemic vaccine:**
 - » Adjuvated (Alum, other)
 - » Reduced antigen content ('Antigen sparing')
 - » Preservative containing for multidose vials
 - » Whole virus vaccine might be more immunogenic
 - » Ideally: single administration
 - » Egg or cell culture derived

EMA experience with 'mock-up' vaccines

- **Published data with H5N3 (A/Duck/Singapore/97) mock-up vaccines**
 - » Lancet 2001, 357, 1937-43 (Nicholson et al.)
 - » Vaccine 2003, 21, 1687-1693 (Stephenson et al.)
 - » JID 2005, 191, 1210-1215 (Stephenson et al.)
- **Published data with H2N2 (A/Singapore/1/57) and H9N2 (A/Hong Kong/1073/99) mock-up vaccines**
 - » Med. Microbiol. Immunol. 2002, 191, 203-208 (Hehme et al.)
 - » Vaccine Research 2004, 103, 163-171 (Hehme et al.)

EMEA experience with 'mock-up' vaccines

- **Yearly meetings of the Joint EMEA-Industry Task Force (JEIF)**
 - » EVM and manufactures associated with EVM present:
 - Progress in development of core dossier
 - Manufacturing, non-clinical studies, clinical experience & clinical development plans
 - Future developments (e.g. cell culture vaccines)
- **Scientific advice and presubmission meetings with companies planning to submit core dossiers**

Concluding remarks (1)

- **Europe considers Pandemic influenza vaccine different from interpandemic vaccines:**
 - » Full (new) authorisation instead of variation of the interpandemic vaccines
- **EMA has developed a fast-track approval procedure for pandemic influenza vaccines**
 - » Core dossier approach limits risk that non-effective/non-safe pandemic vaccines will be used during pandemic
 - » Manufacturers are convinced about the value of this approach and are preparing core dossiers

Concluding remarks (2)

- **EMA actively promotes the development of pandemic influenza vaccines:**
 - » 2004: Scientific and procedural guidelines published
 - » 2005: Core SPC for pandemic influenza vaccines
 - » 2005: 100 % fee waivers for pandemic influenza vaccines core dossiers
 - Core dossier authorisation
 - Scientific advice (related to core dossiers)
 - » 2005: CHMP agrees on fast track assessment of core dossiers & scientific advice

Concluding remarks (3)

- **Pandemic influenza vaccines with reverse genetics strains pose no regulatory hurdles**
 - » However GMO licenses, containment, IP issues etc. to be resolved by manufacturers
 - » EMEA actively encourages manufacturers to include RG strains in core dossier submission
- **EMEA is ready for business!**

Concluding remarks (3)

- **Other EMEA activities related to pandemic influenza:**

- » 2004-2005: EMEA contribution to European Commission's pandemic influenza preparedness activities:

- EU preparedness plan
- PPP proposal

http://europa.eu.int/comm/health/index_en.htm

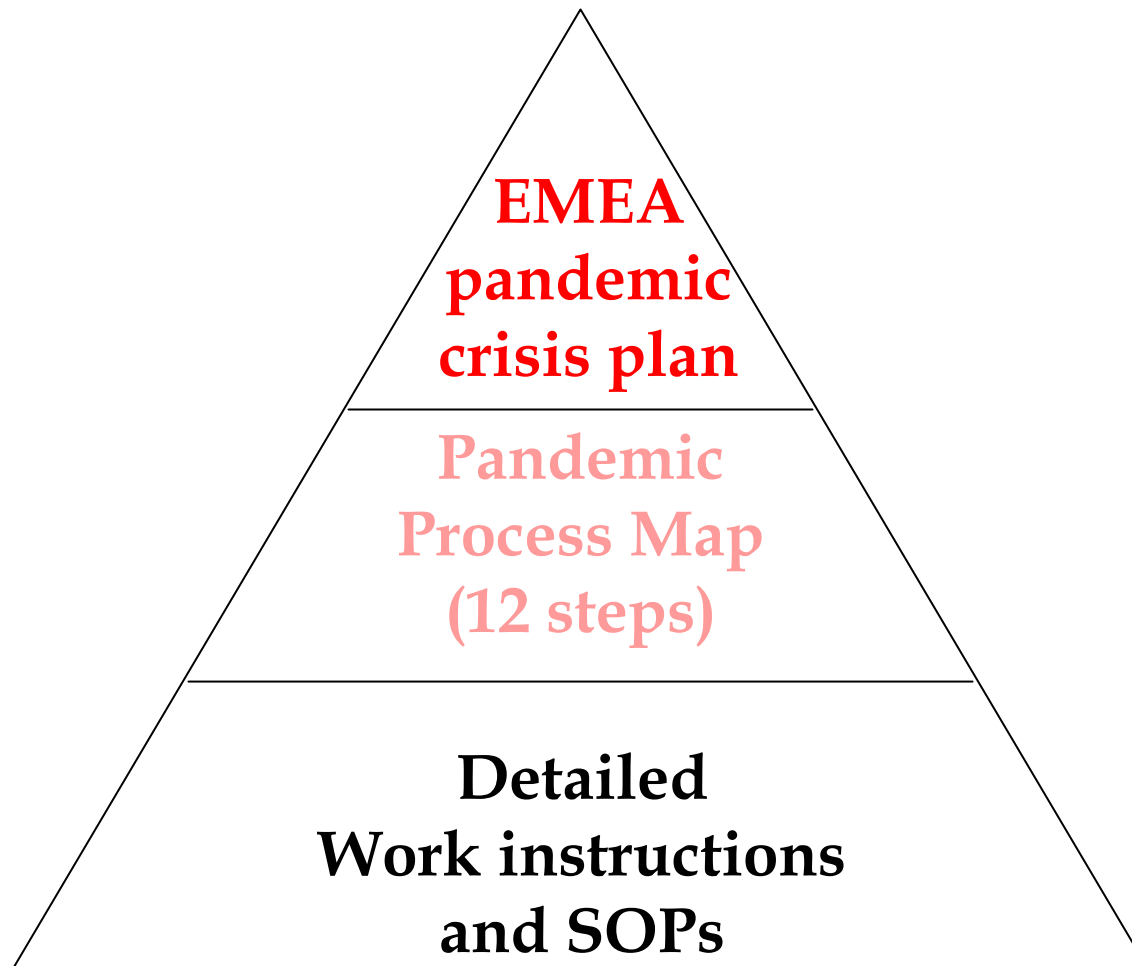
- » 2005: Review of antiviral medicinal products for potential use during pandemic (recently published on EMEA website)

- » 2005: Development of Pandemic influenza crisis plan

The EMEA Pandemic Crisis Plan

- **The pandemic plan outlines policy, strategy and procedures**
 - » for the fast track approval of pandemic influenza vaccines via the centralised procedure
 - »for the post-authorisation follow-up of centrally authorised vaccines and antivirals
 - »to react to safety signals from non-centrally authorised antivirals or from use of bulk active substance of (centrally authorised) antivirals

EMEA Pandemic Plan - 3-level approach



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