



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

## **Biologicals/Vaccines/ Advanced Therapies/Biosimilars**

---

Instrument for Pre-accession Assistance Programme (IPA)  
1 – 2 February 2010, London, European Medicines Agency

Mrs. Glenda Silvester  
European Medicines Agency

An agency of the European Union



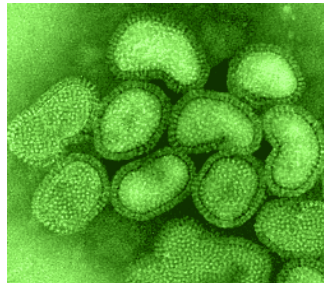
## **Content**

---

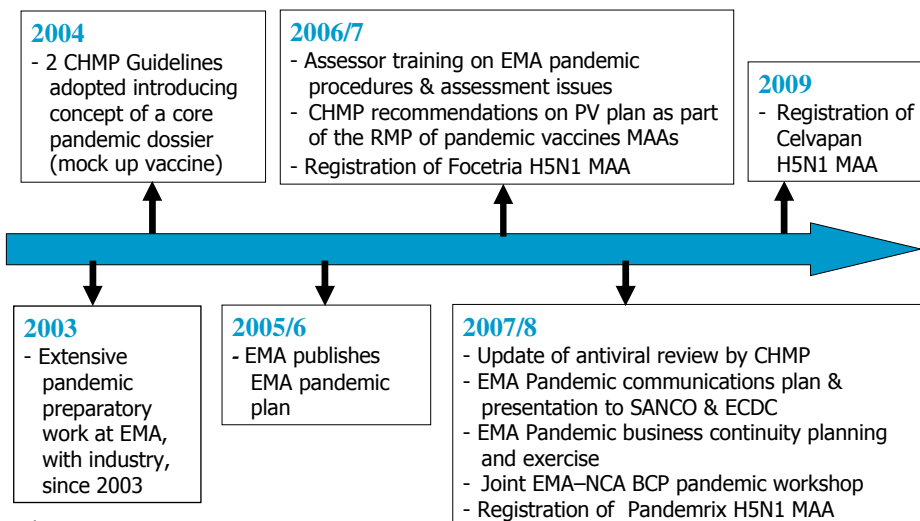
- Pandemic influenza
- Advanced therapies
- Biosimilars
- Investigational Medicinal Products

## Pandemic Influenza

The role of the European Medicines Agency in pandemic influenza preparedness planning



## Highlights of the preparedness activities since 2003

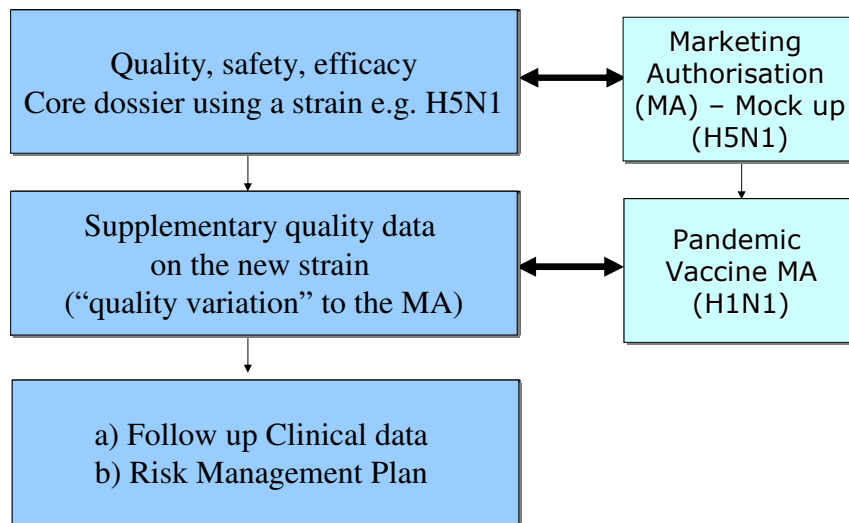


## What is a Mock-Up Pandemic Vaccine?

- Mock-up vaccine is a vaccine containing viral antigen(s) to which humans are immunologically naïve, e.g. H9N2/H5N1.
- Specific data with a mock-up vaccine are relevant for the pandemic vaccine:
  - Manufacturing and quality data
  - Clinical experience in naïve population
  - Evaluation of novel concepts prior to a pandemic e.g. use of adjuvants with the objective of increasing available doses, establishment of dosing schedule

5

## Mock up strategy



6

## Mock-Up Pandemic Vaccines

Product name	Adjuvanted/ non-adjuvanted	MAH
FOCETRIA	Adjuvanted with MF59	Novartis Vaccines and Diagnostics S.r.l MAA approved on 2 <sup>nd</sup> May 2007
PANDEMRIX	Adjuvanted with AS03	GlaxoSmithKline Biologicals SA MAA approved on 20 <sup>th</sup> May 2008
CELVAPAN	Not Adjuvanted	Baxter AG MAA approved on 4 <sup>th</sup> March 2009

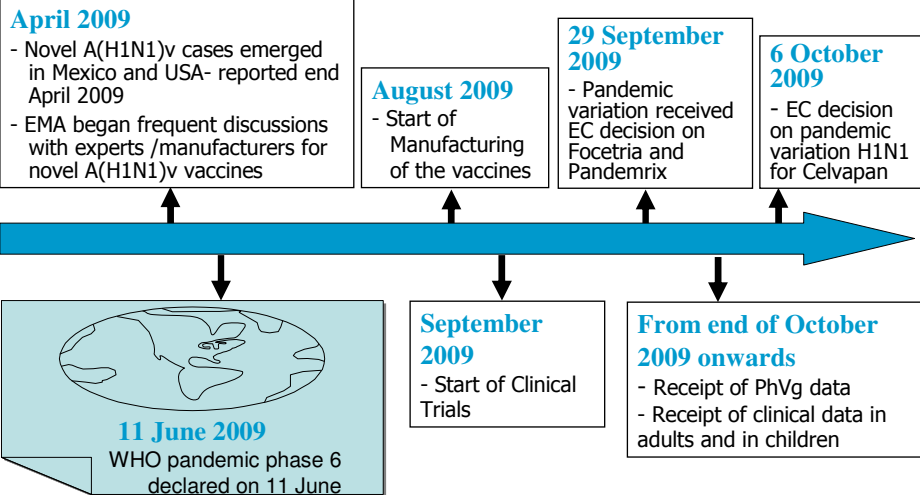
7

## What has been done by the Agency during the 2009 Pandemic?

- In order to get approval of pandemic vaccines as soon as possible after an outbreak of pandemic:
  - Strategy to update the 3 mock-up MAs (based on H5N1 data) with data on new virus strain (H1N1) A/California/07/2009
  - 3 vaccines: Focetria (Novartis), Pandemrix (GSK Biologicals) and Celvapan (Baxter)
- Follow-up of pandemic vaccines / antivirals approved
- Clear Communications on issues within remit of the Agency

8

## Highlights of pandemic activities since April 2009



9

## Pandemic vaccines activities are not over!

- The Agency publishes Pandemic pharmacovigilance update every week to monitor and inform about the safety of the vaccines.
- The B/R balance of the pandemic vaccines used for the current H1N1 influenza pandemic continues to be positive.
- At least 29.4 million persons and 218,000 pregnant women have been vaccinated to-date in Europe. No unexpected serious safety issues have been identified.
- Two emergency procedures are ongoing.

10

## Regulation on Advanced Therapies Key elements

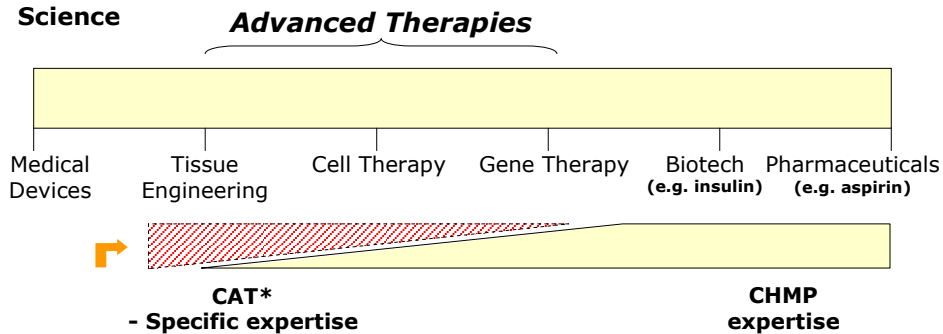
- Advanced Therapy medicinal products (ATMP)
  - Gene therapy products
  - Somatic Cell therapy products
  - Tissue engineered products
- Principles of existing legislation on medicines apply to advanced therapies
- New legislation provides incentives for companies developing ATMP
  - Fee reductions, certification procedure (SME)

## Advanced Therapies - Regulation EC (No) 1394/2007

### Legislation



### Science



## Evaluation of Advanced Therapy Medicinal Products

---

New Committee for Advanced Therapy products (CAT)

- Specific expertise required (e.g. surgery, medical devices)
- Prepares draft opinion for final CHMP approval

MAA procedures

- **ChondroCelect** (characterised viable autologous cartilage cells expanded ex vivo expressing specific marker proteins) – Authorised October 2009
- **Cerepro** – (sitimagene ceradenovec - adenoviral vector-mediated Herpes Simplex Virus-thymidine kinase gene used with subsequent administration of ganciclovir) - Negative opinion December 2009

ATMP classifications

- 9 Products have received CAT scientific recommendations on ATMPs classification (status 11 January 2010).

13

## Biosimilars (abridged biologicals)

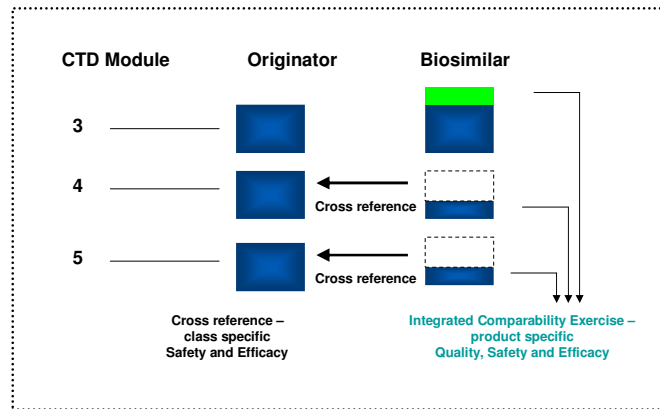
---

Legislation states:

- Where there are differences (particularly) in raw materials or manufacturing processes of biosimilar and reference product, then results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided.
- The results of other tests and trials from the reference medicinal product's dossier shall not be provided
- Article 10(4) of Directive 2001/83/EC, as amended (abridged but not generic)

14

## Dossier requirements for biosimilars



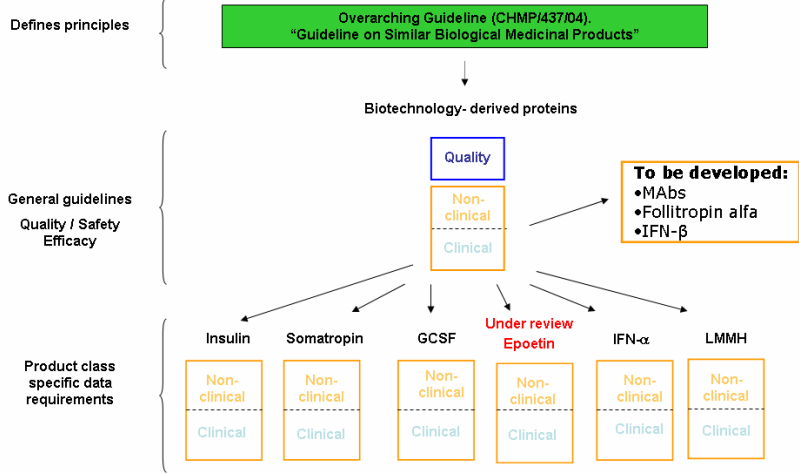
15

## Biosimilar MAA (status January 2010)

1 Omnitrope (somatropin)	Sandoz	Authorised
2 Valtropin (somatropin)	Biopartners	Authorised
3 Alpheon (interferon alfa)	Biopartners	Negative
4 Binocrit (epoetin alfa)	Sandoz	Authorised
5 Epoetin alfa Hexal (epoetin alfa)	Hexal	Authorised
6 Abseamed (epoetin alfa)	Medice	Authorised
7 Silapo (epoetin zeta)	Stada	Authorised
8 Retacrit (epoetin zeta)	Hospira	Authorised
9 Insulin Marvel Short (human insulin)	Marvel Life Sci'	Withdrawn
10 Insulin Marvel Intermediate (human insulin)	Marvel Life Sci'	Withdrawn
11 Insulin Marvel Long (human insulin)	Marvel Life Sci'	Withdrawn
12 Filgrastim Ratiopharm (filgrastim)	Ratiopharm	Authorised
13 Ratiograstim (filgrastim)	Ratiopharm	Authorised
14 Biograstim (filgrastim)	CT Arzneimittel	Authorised
15 Tevagrastim (filgrastim)	Teva	Authorised
16 Filgrastim Hexal (filgrastim)	Hexal	Authorised
17 Zarzio (filgrastim)	Sandoz	Authorised

16

## Biosimilar guidelines



17

## Biosimilar monoclonal antibodies

- Revised guideline on monoclonal antibodies (MAbs) and related products (CHMP/BWP/157653/2009) entered into force in July 2009.
- Workshop on biosimilar MAbs organised at the Agency in July 2009.  
Participants: Regulators (EU and other regions, including US), Industry, academics, healthcare professionals.
- Concept Paper on the development of a guideline on biosimilar MAbs published in October 2009 (CHMP/BMWP/632613/2009).
  - Public consultation until 31 January 2010.
  - Most quality aspects are already addressed but guidance is needed on non clinical and clinical development.

18

## Guidelines on biological Investigational Medicinal Products

---

Important progress to provide an harmonised approach in EU for industry and regulators for assessment of quality of Investigational Medicinal Products (IMPs) during clinical development (especially beneficial for multi-centre studies)

Guideline on virus safety evaluation of biotechnological investigational medicinal products (adopted Jul 2008 – effective as of Feb 2009)

- Outlines the viral safety requirements applicable to all stages of clinical development of an IMP
- Covers monoclonal antibodies and recombinant DNA derived IMPs including recombinant subunit vaccines (but not other vaccines)

19

## Guidelines on biological Investigational Medicinal Products -continues

---

Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials (under development)

- Approval of clinical trials lies with National Competent Authorities of the EU Member States
- The guideline is aimed to find consistent approach in IMP dossier quality requirements across Europe
- A concept paper is available. At present the draft guideline is prepared to be released for external comments by the CHMP, estimated release in February 2010

20

## Contact details

---

European Medicines Agency  
Quality of Medicines Sector

**John Purves**  
Head of Sector

Email: [john.purves@ema.europa.eu](mailto:john.purves@ema.europa.eu)

Biologicals Section

**Peter Richardson**  
Section Head

Email: [peter.richardson@ema.europa.eu](mailto:peter.richardson@ema.europa.eu)

**Glenda Silvester**  
Principal Scientific Administrator  
Email: [glenda.silvester@ema.europa.eu](mailto:glenda.silvester@ema.europa.eu)  
Topic: BPWP, blood products, monoclonals

**Nick Gate**  
Principal Scientific Administrator  
Email: [nick.gate@ema.europa.eu](mailto:nick.gate@ema.europa.eu)  
Topic: BWP, vaccines