The European Strategy for Influenza A/H1N1 Vaccine Benefit-Risk Monitoring

Report on meeting of 17 September 2009,

EMEA

Objectives of meeting of 17 September

- To provide an overview of the EU Strategy, in particular as regards research needs
- To learn about planned or existing projects on the safety and effectiveness of A/H1N1 vaccines that may contribute to the strategy, especially those to be carried-out at the EU level
- To agree on principles of communication and collaboration to be promoted in the Strategy
- To brainstorm about needs for research
- To brainstorm about principles of a possible consortium to answer gaps in knowledge
- NOT to discuss details of studies performed/planned by each participant.

Today

- Overview of the EU Strategy
- Principles of communication and collaboration to be promoted in the Strategy
- Needs for research
- Principles of a possible consortium to answer gaps in knowledge

Starting point:

The CHMP Recommendations for the pharmacovigilance plan as part of the risk management plan for pandemic influenza vaccines

The core Risk Management Plan

European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 25 June 2009
Doc. Ref: EMEA/359381/2009

CHMP Recommendations for the Pharmacovigilance Plan as part of the Risk Management Plan to be submitted with the Marketing Authorisation Application for a Pandemic Influenza Vaccine

Adopted by CHMP in November 2006

Revision 1.0 adopted by CHMP on 25 June 2009

http://www.emea.europa.eu/pdfs/human/pandemicinfluenza/35938109en.pdf

- Recommendations developed by Pharmacovigilance Working Party, the EMEA and vaccine manufacturers.
- This document describes additional pharmacovigilance activities and additional risk minimisation activities that should be presented by vaccine manufacturers in the Risk Management Plan.
- Recommendations can be made legally mandatory in the European Commission Decision.

Main components of the CHMP recommendations to vaccine manufacturers of pandemic influenza vaccines

Spontaneous reporting

- **Definition of Adverse events of special interest**

Monthly simplified Periodic update safety report

Prospective safety cohort study

- **At least 9,000 subjects for each vaccine to be recruited at the start of the vaccination campaign**

Rare adverse events (GBS)

Special populations (children, pregnant women, immunocompromised subjects)

Effectiveness studies

Immunological studies

The European Strategy for Influenza A/H1N1 Vaccine Benefit-Risk Monitoring

- developed by the EMEA, the ECDC and the PhVWP
- still a draft to be revised by PhVWP and adopted by the CHMP

Objectives

- To define and describe the activities that would be useful to detect and assess promptly new information on the benefits and risks of A/H1N1 vaccines.
- To propose roles and responsibilities of different partners in these activities.

Scope

- The main responsibility for the monitoring of the safety and effectiveness of vaccines lies within vaccine manufacturers.
- During the course of mass vaccination, data may also be generated by hospitals, academic research institutions, sentinel networks and other groups in relation to the safety and effectiveness of A/H1N1 vaccines. These data are important for the identification and evaluation of new safety issuee that may arise during the vaccination.
- This document proposes to establish interactions between these various groups, national competent authorities (NCA), public health institutions, the EMEA and the ECDC in order to strengthen the monitoring of the benefits and risks of the vaccines.
- Recommendations- no legal obligation

Three pillars

- Safety
- Effectiveness
- Immunogenicity

➔ **Benefit-risk evaluation**

Roles and responsibilities

- Vaccine manufacturers
- Member States (national competent authority, public health institution or other relevant authority)
- CHMP and Working parties
- Rapporteurs
- The EMEA
- The ECDC
- “Research groups”

1. Roles and responsibilities of “Research groups”

Communication with national competent authority

To inform their national competent authority of :

- **any survey, registry or study they intend to initiate in the context of the pandemic influenza vaccination (preferably with a copy of the protocol).**
- **interim and final results of these studies**
- **suspected adverse reactions to pandemic vaccines**
- **any information which may impact on the benefit-risk profile of the pandemic vaccines.**

To collaborate with their national competent authority on any further investigations.

2. Need for research in addition to requirements in RMP

- Monitoring of vaccine safety in vulnerable populations (children, pregnant women, immuno-compromised subjects)
  - **Pregnant women**
    - immunogenicity and effectiveness of vacines in pregnant women
    - background data on pregnant women vaccinated (nbr, period, timing) in each country
    - miscarriages
    - data on non-malformed controls (for case-control analyses)
  - **Immunocompromised subjects**
    - safety and immunogenicity in patients with autoimmune diseases
    - immunocompromised: e.g. HIV
    - diabetes/obesity
- Surveillance of rare adverse events
  - Guillain-Barre syndrome: many projects – signal evaluation
  - other AESIs/ rare adverse events (signal detection)
  - agreement on codes for extracting AESIs from databases
  - exposure data

Need for research in addition to requirements in RMP(2)

- **Investigation of emerging safety issues**
  - methods for “rapid” investigation of emerging safety issues which may arise
    - what is “rapid”
    - signal detection vs. signal evaluation
      - if use of databases or case-control surveillance: periodicity for analysing data (data mining ?)

- **Benefit-risk assessment/modelling**
  - mid-term project: to collect disease and vaccine outcomes at the patient level in a same population using large databases
  - basis for research work on epidemiology of influenza and influenza vaccines

3. Proposal for a possible consortium

Consortium to be established jointly by the EMEA and the ECDC

Research groups to be invited to participate, with nomination or election of a Coordinator

Terms of reference

- to establish a network of centres able to perform rapidly specific studies to elucidate safety signals or answer questions raised by the CHMP, NCAs and public health authorities
- to design, develop, assess the feasibility (a) benefit-risk study(-ies) in large databases
- to conduct studies based on an agreed protocol.

Principles for a possible consortium

Funding

- Consortium made up of a coordinating centre and individual research centres
- Each vaccine manufacturer would contribute to a central fund managed by the Coordinator attended by an Oversight Committee. The fund would only supplement the main funding for the Coordinating Centre and the core funding of individual participating centres to carry-out the studies which address requests from the CHMP or EMEA or ECDC.
- Additional funding might be provided by the EMEA.
- Scientific independence - Scientific Steering Committee.
- Vaccine manufacturers may be involved in some way.
- Amount of the contribution for each VM would be defined by the scope of the studies.

Principles for a possible consortium

Discussion

- Why “new” consortium ?
- Extension of existing consortium ?
- Timelines ?
- Conflicts of interest in relation to funding ?
- Idea to be further developed ?

Thank you !