EMA “ARTICLE 58” SCIENTIFIC OPINION: A TOOL FOR INTERNATIONAL COLLABORATION & ACCELERATION OF ACCESS TO ESSENTIAL MEDICINES AND VACCINES

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Article 58 of Regulation (EC) No. 726/2004

“1. The Agency may give a **scientific opinion**, in the context of cooperation with the World Health Organization, for the evaluation of certain medicinal products for human use intended exclusively for markets outside the Community. For this purpose, an application shall be submitted to the Agency in accordance with the provisions of Article 6. The Committee for Medicinal Products for Human Use may, after consulting the World Health Organisation, draw up a scientific opinion in accordance with the provisions of Articles 6 to 9. The provisions of Article 10 shall not apply.

2. The said Committee shall establish specific procedural rules for the implementation of paragraph 1, as well as for the provision of scientific advice.”
2005 CHALLENGES?

- EMA-WHO-NRA COLLABORATION?
- SCOPE/PRODUCTS?
- PROCEDURE?
- STANDARDS?
- PRE-POST-OPINION PHASES?
EMA “ARTICLE 58” SCIENTIFIC OPINIONS

SCOPE

• Responds to unavailability of medicinal products in EU for commercial reasons

• Responds to the need to protect public health

• Give scientific assistance in the context of cooperation with WHO

• Allowing rapid access to those countries for important new medicinal products

PRODUCTS

• Vaccines used or of possible use:
  - WHO Expanded Programme on Immunization (EPI) or
  - WHO public health priority disease or
  - part of a WHO managed stock pile for emergency response

• Medicinal products for WHO target diseases such as:
  - HIV/AIDS, malaria, tuberculosis trachoma, leishmaniasis, African trypanosomiasis (sleeping sickness), dengue fever, Chagas disease, leprosy etc...
**SAME EU AND ART.58 SO PROCEDURES**

**PRINCIPLES APPLIED**

- **SAME PROCEDURE**
  - Scientific Advice, Paediatric development, SME, Inspection (GCP/GLP), consultation with WPs/Expert Groups, Transparency, Post-“authorisation” etc...

- **SAME STANDARDS**
  - As EU CP MPs taking into account possible adjustments/adaptations as appropriate (e.g. stability conditions, formulations, RMP etc...). In absence of EU/ICH guidelines, or otherwise justified WHO guidelines apply

- **SAME TIMELINES**
  - 210 days can be accelerated

**ADAPTATIONS**

- **INITIATION/ELIGIBILITY**
- **EXPERTS PARTICIPATION**
EMA ART.58 SO – 2010 CHANGES

2010 CHALLENGES?

• DIVERSITY AND COMPLEXITY OF PRODUCTS
• INCREASED DEMAND FOR INVESTIGATION SAFETY & QUALITY ISSUES WORLDWIDE
• GLOBAL NEED TO BETTER USE RESOURCES/SCIENTIFIC EXPERTISE

2010 EMA & WHO STEPWISE REVIEW PROCEDURES

<table>
<thead>
<tr>
<th>EMA “Art. 58” process vaccines</th>
<th>Standard WHO PQ vaccines process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility</td>
<td>Screening</td>
</tr>
<tr>
<td>Dossier review</td>
<td>Dossier review</td>
</tr>
<tr>
<td>Inspections</td>
<td>Site audits</td>
</tr>
<tr>
<td>Risk / Benefit</td>
<td>Consistency Lot testing</td>
</tr>
<tr>
<td>~ 10 months</td>
<td>~ 12months</td>
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</tbody>
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EMA: European Medicines Agency
WHO: World Health Organization
PQ: Prequalification

EMA "Art. 58" process vaccines:
- ~ 10 months

Standard WHO PQ vaccines process:
- ~ 12 months

Screening, Dossier review, Site audits, Consistency Lot testing
WHO-EMA-NRAs COLLABORATION: PROCEDURAL ALIGNMENT

"ART. 58" WITHOUT WHO PRE-QUALIFICATION

Joint scientific advice

ELIGIBILITY

PRE SUBMISSION

SUBMISSION VALIDATION

PRIMARY EVALUATION

CLOCK STOP

SECONDARY EVALUATION

Art. 58 SO

Since 2012 "ART. 58" WITH WHO PRE-QUALIFICATION

WHO NRA EXPERTS/ OBSERVERS

WHO/QSS

WHO/QSS and QSM

NEW!

WHO NRA EXPERTS/ OBSERVERS

WHO/QSS

WHO - PQ

+ consistency lots
+ UN tender specifications
+ site audit (if not done by EMA)
+ assignment of VVM category
+ UN packaging requirements
### EURARTESIM - EMA SO/EU MA

**REGULATORY STATUS**

- EMA orphan medicinal product SO adopted by CHMP in June 2011 & EU Commission granted MA in October 2011

**COMPOSITION**

- Piperaquine tetraphosphate / dihydroartemisinin, 160mg/20mg, 320mg/40mg, Tablets

**INDICATION**

- For adults and children 6 months or over and **weighing 5Kg or more** to treat uncomplicated malaria, caused by *Plasmodium falciparum* parasite.

### PYRAMAX - EMA ART.58 SO/WHO PQ

**REGULATORY STATUS**

- EMA Art. 58 SO adopted by CHMP in February 2012 WHO PQ in May 2012

**COMPOSITION**

- Pyronaridine tetraphosphate / artesunate, 180mg/60mg, tablets

**INDICATION**

- For adults and children **weighing 20 kg or more** to treat uncomplicated malaria, caused by **two types** of malaria parasites, *Plasmodium falciparum* and *Plasmodium vivax*.

Pyramax is for use in parts of the world with low transmission of malaria and where the parasites are becoming resistant to artemisinin antimalarial medicines.
## PROCEDURAL COMPARISON

<table>
<thead>
<tr>
<th>Similar <strong>DOSSIER</strong> content (except PIP/ERA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Different <strong>ASSESSMENT TEAM</strong></td>
</tr>
</tbody>
</table>

## CONSULTATION

Ad Hoc Expert Group

## STANDARDS OF EVALUATION

### QUALITY
- Different presentations, Stability studies, GMP inspection

### CLINICAL
- Main pivotal studies outside EU
- GCP inspection routine or triggered
- Assessment clinical safety & Benefit taking into account different public health needs

## PHARMACOVIGILANCE & RISK MANAGEMENT PLAN
- Different requirements, systems, evaluation
EMA “ART. 58” MEDICINAL PRODUCTS PIPELINE

EMA ART. 58 SCIENTIFIC OPINION CENTRALISED EVALUATION PROCESS

SCIENTIFIC ADVICE
- 2 PNEUMOCOCCAL VACCINES
- 2 MICROBICIDES
- 3 ANTI-LEISHMANIOSIS
- 2 COMBINBED VACCINE
- 1 ONCHOCERCIASIS
- 1 HUMAN AFRICA TRYPANOSOMA

ELIGIBILITY
- 1 ANTI-MALARIA VACCINE
- 1 PERICOITIAL ORAL CONTRACEPTIVE
- 1 MP for OMPHALITIS IN NEW BORN INFANTS
- 1 Tetravalent VACCINE

EVALUATION
- GLOBORIX (DTP, HepB, Hib, Meningococcal) Vaccine
- 1 BPH

POST-ART. 58 SO /MARKETING
- 3 HIV:
  - Aluvia (lopinavir/ritonavir), Lamivudine ViiV (lamivudine), Lamivudine ViiV (lamivudine/zidovudine)
- 1 ANTI-MALARIA: Pyramax (pyronaridine/artesunate)
- 1 Multivalent Vaccine Hexaxim (DTP, HepB, Polio, Hib)

EMA webpage link:
TOWARDS FURTHER CHALLENGES...

**POST-MARKETING FOLLOW-UP**

- Implementation of **RISK MANAGEMENT PLANS**?
- Implementation of **CHANGES POST- ART. 58 OPINNION at National Level**?
- Adverse Events (ADRs) reporting/collection?

**COMMUNICATION & INTERACTION**

- **Organisation of** Health care systems and ADRs reporting systems?
- How to **inform patients**?
- How to **communicate with health care professionals**?

**NRAs RESPONSIBILITIES?**
CONCLUSIONS

ART. 58 SO – NOT A COMPETITIVE EVALUATION

Unique legal tool to **best use available global scientific expertise**

Built to **address targeted NRAs needs**

ART. 58 SO – REGULATORY CAPACITY TOOL

“Hand on” collaborative evaluation with NRAs participation

Use also for **regulatory and technical capacity building**

ART. 58 SO – ACCELERATE ESSENTIAL MEDICINES AVAILABILITY

EMA-WHO streamlining procedures

... NEED NEXT PHASE COLLABORATION DISCUSSIONS?
Thank you.