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International Affairs

Improving the perception and use of the Article 58 procedure

An action plan for 2015-2017

1. Background

Article 58 was introduced in the 2004 revision of the Agency's founding regulation, and allows the Agency to give scientific opinions – in collaboration with the World Health Organization – on medicines for use outside of the European Union. The intention of the process is to increase access by low- and middle-income countries (LMICs) to medicines and improve public health.

Use of the procedure during its first decade has been disappointing, with only 8 products having completed the process.

With the financial support of the Bill & Melinda Gates Foundation, a study was commissioned from external consultants in April 2015. The study was jointly led by the EMA and DG SANTE, together with regular support and involvement of Dr Murray Lumpkin from the Gates Foundation and Tomas Salmonson.

The objectives of the study were to understand awareness, experience and views of stakeholders of Article 58 and its influence on manufacturers' decisions to use the procedure and the wider landscape of alternative regulatory tools and pathways.

The consultants delivered their final report in September 2015, together with a series of recommendations and proposals for consideration by EMA and DG SANTE.

2. Summary of recommendations made

The consultants were appointed and funded entirely by the Gates Foundation through their existing procurement and budgetary arrangements; neither the European Medicines Agency nor the European Commission were involved in the selection of the consultants.

The project was operated through a Working Group composed of representatives of EMA and DG SANTE, in close association with the Gates Foundation. The EMA was represented by Emer Cooke,

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Marie-Hélène Pinheiro, Martin Harvey with the involvement of Tomas Salmonson. DG SANTE was represented by Dagmar Stara and Agnès Mathieu.

Regular working group meetings were held at the Agency with the consultants. There were also a number of meetings with Andrzej Ryś, Sabine Jülicher, Murray Lumpkin, Guido Rasi and the working group to monitor progress.

The consultants structured their work in three main blocks: desk research and analysis, interviews, and case studies. They carried out 48 interviews with stakeholders, including NGOs, non-EU regulators, and companies that had been through the procedure and those who had decided not to do so.

The report sets out a comprehensive set of findings and recommendations, it should be noted that the study was finalised before the Mosquirix opinion.

While there have been substantial gains in public health in LMICs, few innovative products seeking regulatory approval have targeted LMICs only, meaning in part that 'Article 58' has been little used.

Among the 7 products that have gone through 'Article 58', participants appreciated the rigour and quality of the process:

- The few NRA observers to 'Article 58' have immensely benefited from capacity building aspects; and
- Manufacturers who have gone through 'Article 58' appreciate the scientific advice to shape their clinical plans, the responsiveness of EMA during the process and the technical/scientific rigour of the review.

However, other factors have contributed to the limited use of 'Article 58':

- Alternative pathways and incentives have sprung up (e.g. FDA priority review voucher and significant fee waivers);
- Five core barriers to 'Article 58' realising its full potential:
    1) Manufacturers are **unclear/unconvinced of its benefits**, and are reluctant to use it due to the lack of successful precedents;
    2) For many manufacturers, the **fees are burdensome** or prohibitive (particularly the annual maintenance fees);
    3) Many **NRAs are unaware** of 'Article 58' or consider it a lower grade review, given it does not confer EU marketing approval;
    4) Even where opinions are well accepted, the pace of **national assessment is no quicker** than with other Stringent Regulatory Authority approvals; and
    5) Poor **coordination between the EMA and WHO** – both in terms of general logistics, and the management of variations and pharmacovigilance – limits the potential impact of their collaboration for both NRAs and manufacturers.

3. Publication of the study

In line with the strategy objectives of promoting the Article 58 procedure and increasing its use, it is proposed that the Agency should publish at least part of the study and its intended strategy.

The study involved interviews with a number of industry and NGO stakeholders, together with information and input from the consultants. The final report contains commercially confidential information relating to product development strategies provided by companies in confidence, together with information provided by the consultants from their own research, which have not been verified by the Agency.

It is noted that the study is mentioned, including a reference to the Gates Foundation, in the minutes of the 11 June 2015 Management Board meeting.

Proposal is to publish the following:

- Executive summary (draft prepared by the consultants but requires revision);
- Full compendium slide deck (with commercially confidential information redacted and disclaimer saying that the content of the document does not necessarily reflect the views of the European Medicines Agency, the European Commission or the Bill & Melinda Gates Foundation);
- Summary 'final read-out' slide deck (with similar redaction and disclaimer); and
- Final strategy for Article 58 once agreed with the Commission and endorsed by Management Board.

4. Proposed next steps towards a future Article 58 action plan

Various concerned Divisions and Departments (D-RS-REA, E-HDiv, E-SR-AIV, etc.) will be consulted prior to discussion with Scientific Coordination Board (SciCoBo), CHMP and EMA Strategy Board, in addition to DG SANTE.

Many of the actions planned are included in the Work Programme 2016, to be adopted in December 2015, and the Board will be kept informed of developments. The action plan will fully take into account the globalisation and capacity building theme of the 'EU Medicines Agencies Network Strategy to 2020', as a component of promoting European practices in line with the network strategy.

The European Commission has indicated it is prepared to discuss and clarify the regulatory options in association with the use of Article 58.

In addition to activities described in the Work Programme 2016, the action plan will also focus on:

- Communication activities: developing communication tools to better explain the procedure and the Agency's capacity-building activities, looking at 're-branding' the procedure to find a more attractive way of promoting it, developing 'Questions and Answers' to use to help sponsors and other third parties, simplifying messages about the procedure and its advantages, etc.
- Stakeholder communication: improving communication and awareness with stakeholders such as NGOs, product development partnerships, and regulators in Africa and other target LMICs

- Regulator interactions: improving interactions with WHO and ensuring greater involvement of local regulators from target LMICs, better understanding UK visa entry requirements for LMIC experts nominated by WHO
- Regulatory issues: clarifying regulatory options in association with Commission relating to findings and recommendations in the study, to be included as appropriate in the revision of the November 2005 Article 58 guideline