EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, European Medicines Agency

Brussels,
SANCO/D5/FS/ci D(2013) 396156

DELEGATED ACT ON POST-AUTHORISATION EFFICACY STUDIES

REPLIES TO THE PUBLIC CONSULTATION

This document summarises the contributions made by stakeholders to DG Health and Consumer's public consultation on a delegated act on post-authorisation efficacy studies.

1. BACKGROUND OF THE CONSULTATION

The EU pharmacovigilance legislation has recently been subject to a major review that led to the adoption of new legislation in 2010, namely Directive 2010/84/EU[1] and Regulation (EU) No 1235/2010[2]. While the main focus of pharmacovigilance is the safety of the product, any new information received or new pharmacovigilance signals detected may have a potential impact on the overall product assessment and more particularly on its benefit-risk balance.

In order to streamline and clarify the regulatory tools of competent authorities for imposing certain obligations on marketing authorisation holders, Directive 2001/83/EC and Regulation (EC) No 726/2004 summarise the conditions, restrictions and obligations under which a marketing authorisation may be granted or which may be requested following the granting of the initial marketing authorisation.

In this context, the new pharmacovigilance legislation refers to the possibility of requesting the marketing authorisation holder to conduct post-authorisation efficacy studies (PAESs), complementing efficacy data that are available at the time of the initial authorisation.[3] In order to determine the situations in which post-authorisation efficacy studies may be required, the Commission is mandated to adopt, by means of a delegated

[1] Directive 2010/84/EU of 15 December 2010 amending, as regards pharmacovigilance Directive 2001/83/EC, OJ L 348, 31.12.2010, p. 74.

[2] Regulation (EU) No 1235/2010 amending, as regards pharmacovigilance Regulation (EC) No 726/2004, OJ L 348, 31.12.2010, p. 1.

[3] Articles 9(4)(cc) and 10a(1) of Regulation (EC) No 726/2004 and Articles 21a and 22a(1) of Directive 2001/83/EC.

Commission européenne/Europese Commissie, 1049 Bruxelles/Brussel, BELGIQUE/BELGIË - Tel. +32 22991111
Office: DM24 02/137 - Fax +32 229-98046

Sanco-pharmaceuticals-D5@ec.europa.eu

act, measures supplementing the provisions of Directive 2001/83/EC and Regulation (EC) No 726/2004[4].

The public consultation has been conducted with a view of receiving feedback from stakeholders on this issue.

2. CONTRIBUTORS

The Commission received 33 contributions. The majority of responses were received from stakeholder organisations representing pharmaceutical undertakings or individual companies, as well as public institutions including regulatory agencies and health technology assessment bodies. Additionally, healthcare professionals, academia and other associations contributed. A list detailing all contributors is provided in the Annex to this document.

All contributions and comments received provided valuable information for the Commission services. However, in some cases, the contributions submitted went beyond the scope of the public consultation and could not therefore be taken into account.

3. SUMMARY OF CONTRIBUTIONS

As regards **consultation item No. 1**, i.e. whether a delegated act on post-authorisation efficacy studies would be of added-value, the majority of respondents agreed, arguing that such act may provide legal certainty, increase predictability and contribute to a focussed dialogue between regulatory authorities and marketing authorisation holders and/or applicants. However, several respondents advised against such an act. It was highlighted that the imposition of such post-authorisation studies will be still a case-by-case decision, which would be difficult to frame by a measure of general scope. Moreover, once established a strict and inflexible framework may prevent regulatory authorities from reacting to new emerging situations, which have not already been addressed in the act concerned. Finally, it is feared that a delegated act could be understood by regulatory authorities as an invitation to regularly impose post-authorisation efficacy studies, making it the rule rather than the exception.

Consultation item No. 2, i.e. on whether generally-speaking post-authorisation efficacy studies should focus on generating efficacy data, was controversially discussed in the different replies received with no clear consensus emerging.

It was noted that the study design should be suited to the scientific question and boundaries between different concepts are vague.

Some respondents argued that once a product is marketed real-world settings of studies would be more typical, while other respondents claimed that studies in everyday medicinal practice would be the exception rather than the rule. In this context, it was observed that post-authorisation efficacy studies should not repeat phase III/pivotal studies and not be seen as an alternative to the generation of appropriate clinical data during product development, as this would risk compromising the level of evidence expected for the granting of the initial marketing authorisation.

[4] Article 10b of Regulation (EC) No 726/2004 and Article 22b of Directive 2001/83/EC.

Several respondents pointed to the different remits between regulatory authorities on one side and health technology assessment and reimbursement bodies on the other. Noting this should be taken into account in the final shaping of the scope of any delegated measure.

As far as some of the key definitions of terminology used in the concept paper are concerned, several respondents pointed out an inconsistency with the terminology used in literature.

As far as **consultation item No. 3** is concerned (situations in which a post-authorisation efficacy studies may be required), the majority of respondents commented on the seven situations indicated. Some respondents highlighted some additional scenarios arguing that some important examples would be missing.

Not all respondents commented on **consultation item No. 4** (study design). It was however, argued by some that a delegated act should be supplemented by special guidance on methodology. Other respondents took the view that the study design should be part of the discussion between the marketing authorisation holder and the regulatory authority with a view to establishing the best way of generating the required data.

Some respondents disagreed with the statement in the concept paper that "interventional studies are expected to represent the majority of cases" of post-authorisation efficacy studies.

Finally, under **consultation item No 5** (any other issue) respondents referred to a number of aspects, including procedures and timelines for post-authorisation efficacy studies, involvement of independent scientific experts in those studies, collaboration with health technology assessment bodies, studies involving several marketing authorisation holders and the need for greater clarity in terminology.

All contributions received have been made available in the Pharmaceuticals website.

ANNEX: LIST OF CONTRIBUTORS TO THE PUBLIC CONSULTATION:

- **Industry Associations:**

(1) AESGP – Association of the European Self-Medication Industry

(2) BPI – German Pharmaceutical Industry Association

(3) EFPIA – European Federation of Pharmaceutical Industries and Associations

(4) EUCOPE – European Confederation of Pharmaceutical Entrepreneurs

(5) LEEM – Association of pharmaceutical industry in France

(6) PPTA – Plasma Protein Therapeutics Association

(7) Vaccines Europe

- **Individual Companies**

(8) Bausch+Lomb

(9) Janssen Pharmaceutical

(10) Leo Pharma

(11) Lundbeck

(12) Rosemont Pharmaceuticals Ltd.

(13) TEVA Europe

- **Public Institutions**

(14) AEMPS – Spanish Agency of Medicines and Medical Devices

(15) Arzenimittelkommission der deutschen Ärzteschaft – Drug Commission of the German Medical Association

(16) CBG-MEB – Dutch Medicines Evaluation Board, The Netherlands

(17) EMA – European Medicines Agency

(18) EUnetHTA – European Network for Health Technology Assessment

(19) France – Secretariat General des Affaires Européennes

(20) HAS - La Haute Autorité de Santé, France

(21) IQWIG – Institute for Quality and Efficency in Health Care, Germany

(22) MHRA – Medicines and Healthcare products Regulatory Agency, UK

(23) MPA – Swedish Medicinal Product Agency

(24) NICE – National Institute for Health and Clincial Excellence, UK

(25) RIZIV-INAMI, Belgium

- **Academia & Healthcare professionals**

(26) ENCEPP – European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

(27) ESCAMP – European Scientific Cooperative on Anthroposophic Medicinal Products

(28) ESC - European Society of Cardiology

(29) PGEU – Pharmaceutical Group of the European Union

(30) Van Staa, London School of Hygiene & Tropical Medicine

- **Other stakeholders and individuals**

(31) AEFI – Spanish Association of Pharmacists in Industry

(32) EUCROF - European CRO Federation

(33) Kosim, Marzena, MPharm.