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COMMISSION GUIDELINE ON THE FORMAT AND CONTENT OF APPLICATIONS FOR PAEDIATRIC INVESTIGATION PLANS

REPLIES TO THE PUBLIC CONSULTATION

This document summarises stakeholders' responses to the Commission's public consultation on updating its guideline on the format and content of applications for agreeing on and modifying a paediatric investigation plan and of requests for waivers or deferrals.

1. BACKGROUND TO THE CONSULTATION

In accordance with Article 10 of the Paediatric Regulation (Regulation (EC) No 1901/2006), in consultation with the Member States, the European Medicines Agency and other interested parties, the Commission must draw up detailed arrangements concerning the format and content applications for agreeing on or modifying a paediatric investigation plan and requests for waivers or deferrals must take in order to be considered valid, and concerning the operation of the compliance check.

The Commission published the relevant guideline in September 2008.[1] It has been in use for the last five years. In its recent report on the Paediatric Regulation,[2] the Commission undertook to review the guideline in order to take into account the experience gained in the matter, including the considerable number of requests to modify paediatric investigation plans.

It therefore asked the Paediatric Committee of the European Medicines Agency to suggest amendments to the guideline which they considered appropriate. The content of the document for public consultation was based on but not identical to that of those suggestions.

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1 Communication from the Commission — Guideline on the format and content of applications for agreement or modification of a paediatric investigation plan and requests for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies, OJ C 243, 24.9.2008, p. 1.

2 *Better Medicines for Children — From Concept to Reality*, COM(2013) 443 final.

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The purpose of the public consultation was to receive feedback from stakeholders on this matter.

2. RESPONDENTS

The Commission received 26 responses from stakeholder organisations representing pharmaceutical undertakings or individual companies, as well as public institutions including regulatory agencies and national ministries. Healthcare professionals, academia, research networks and other associations also contributed. There is a list of all respondents in the annex to this document.

All responses and comments provided valuable information for the Commission. In some cases however, they went beyond the scope of the public consultation and could therefore not be taken into account.

To better analyse their responses, respondents were classified in the following categories: industry (individual entities and associations of companies), public authorities, academia and the healthcare sector, contract research organisations and others.

The annex gives an overview of the responses by sector and geographical origin.

3. SUMMARY OF RESPONSES

This document presents a factual summary of the responses to the public consultation. It does not present the views of the European Commission.

The Commission guideline on the format and content of an application for paediatric investigation plans was considered an important administrative document regarding the data required to substantiate applications to the European Medicines Agency in individual cases. Most respondents agreed that it was time to review the current guideline in view of the experience acquired from implementing the Paediatric Regulation in the last five years.

Many respondents used the opportunity (mainly under **consultation item number 5**) to raise issues not directly related to the application documents for a paediatric investigation plan, but linked to the current legal framework and to changes that should be considered. Those responses mostly went beyond the scope of this public consultation and contained a broad spectrum of opinions on the extent of the changes required. They mainly concerned the following.

- Requests for ensuring that any adult medicinal product is tested in children whenever the mechanism of action suggests it could be effective (including the repeal of all class waivers).

- Requests for changes to the point in time at which companies are requested to submit a paediatric investigation plan.

- Requests for a staggered evaluation of paediatric R&D projects, including the Paediatric Committee's right to modify an agreed paediatric investigation plan at its own discretion.

- Requests to align EU paediatric requirements with requirements in other parts of the world.

- Requests to change the process for agreeing on and monitoring paediatric R&D projects in relation to the category of products concerned (e.g. paediatric-only products, advanced therapy medicinal products).

Some respondents also stressed the need to ensure that the study concepts developed and agreed with a paediatric investigation plan are feasible in practice. In this context, it was suggested that applicants consider involving clinical research networks at an early stage in preparing paediatric investigation plans by discussing feasibility and patient recruitment issues with them. Others suggested broadening the scope of pre-submission meetings between applicants and the European Medicines Agency in order to facilitate the subsequent preparation and scrutiny of the application by the Agency and its Paediatric Committee.

With regard to **consultation item number 1**, the format and content of applications for agreeing on or modifying a paediatric investigation plan and requests for waivers or deferrals, detailed comments were received on many aspects of the matter. They included comments on the definitions used in the draft, terminology and the level of detail regarding the information required.

Several respondents said they appreciated the guideline's increased focus on extrapolation. They were also pleased with the flexibility it provided in relation to timelines for starting and completing studies.

Some responses suggested better covering specific product categories such as orphan products, advanced therapy medicinal products or vaccines.

It was mainly respondents from industry and public authorities who commented on the compliance check under **consultation item number 2**. Industry respondents wanted the compliance check to be simplified from an administrative point of view. This included involving the Paediatric Committee only if compliance is a bone of contention. Additionally, comments were received on the scope of an 'interim' compliance check, done in the context of regulatory submissions assessed before the completion of the full paediatric R&D programme. They also commented on the requirement to submit a final study reports for verifying compliance.

Only a minority of respondents commented on the proposed changes to section 3 of the current guideline, relating to the criteria for assessing the significance of studies started before the Paediatric Regulation entered into force (**consultation item number 3)**.

Some of the respondents questioned the continued need for the section given the transitional nature of this aspect. Most paediatric investigation plans would now contain only studies started after the Paediatric Regulation entered into force.

Respondents who commented on the suggested introduction of a list of key elements (**consultation item No 4)** generally agreed that such a list would provide added value. That is because it would help identify the main aspects of the plan a company must comply with. Most respondents thought that the suggested list gave a fair description of those parts, but that it would benefit from further streamlining and the clarification of terminology. Respondents also suggested stressing the fact that not every agreed paediatric investigation plan must necessarily contain all the key aspects listed in the

annex to the guideline. Only those considered relevant to the specific R&D project should be mentioned in the decision agreeing to the paediatric investigation plan. Some respondents also suggested allowing the addition of other aspects in justified cases.

All the responses have been published on the pharmaceuticals website.

ANNEX:

A. LIST OF RESPONDENTS TO THE PUBLIC CONSULTATION:

- **Industry associations**

(1) EFPIA — European Federation of Pharmaceutical Industries and Associations

(2) EuropaBio

(3) PPTA — Plasma Protein Therapeutics Association

- **Individual companies**

(4) Norgine Ltd

(5) Pfiser Ltd

(6) Teva Europe

(7) Therakind Ltd

- **Public institutions**

(8) AEMPS — Spanish Agency of Medicines and Medical Devices

(9) CBG-MEB — Dutch Medicines Evaluation Board

(10) The Czech Ministry of Health

(11) Inframed — Portuguese National Authority of Medicines and Health Products

(12) The Dutch Ministry of Foreign Affairs

(13) Swissmedic — Swiss Agency for Therapeutic Products

- **Academia and healthcare professionals**

(14) Enpr-EMA — European Network of Paediatric Research at the European Medicines Agency

(15) FINPEDMED — Finnish Investigators Network for Paediatric Medicines

(16) GRiP — Global Research in Paediatrics Network of Excellence

(17) ICR — The UK Institute of Cancer Research

(18) NPPG — Neonatal and Paediatric Pharmacy Group, UK

(19) The Portuguese Order of Nurses

- **Contract research organisations and other stakeholders and individuals**

(20) Cell Therapy Catapult Ltd, UK

(21) CRIG — Children's Research Industry Group

(22) The German Society of Paediatrics and Adolescent Medicine

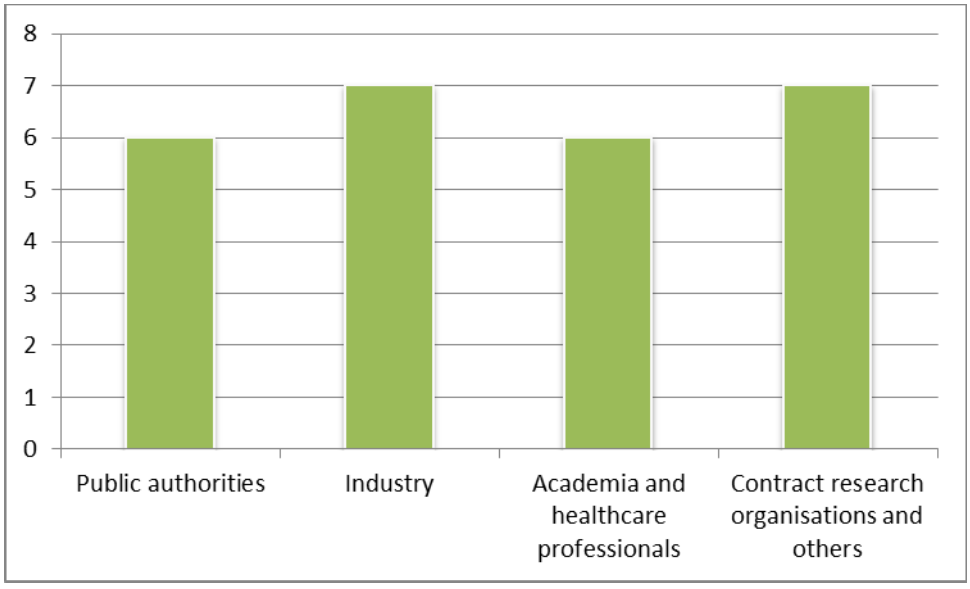
(23) EUCROF — European Contract Research Organisation Federation

(24) SciencePharma Ltd, Poland

(25) Teenage Cancer Trust, UK

(26) One individual

B. DISTRIBUTION OF RESPONSES BY SECTOR



C. DISTRIBUTION OF RESPONSES BY GEOGRAPHIC ORIGIN