EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Regulatory update on guidelines relevant to paediatric formulations

Workshop on Paediatric Formulations II

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Are we walking in the dark?

"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."

General Guidelines

Reflection Paper: Formulations of choice for the paediatric population (EMEA/CHMP/PEG/194810/2005)

- Takes into account physiological and developmental issues that could be considered
- Does not specify regulatory requirements
- Reflection paper ≠ Regulatory guideline

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003782.pdf

General Guidelines

Excipients in the dossier for application for marketing authorisation of a medicinal product
(EMEA/CHMP/QWP/396951/2006)

- Key guideline on quality of excipients (in force since 2008)
- Not specifically focussed on paediatric formulations, general
- Good, well thought through formulation that fits for purpose is paramount for adults and for children

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003382.pdf

General Guidelines

ICH Q8: Note for guidance on pharmaceutical development (EMEA/CHMP/167068/2004)

- Overarching guideline on pharmaceutical development
- Very general, not specifically focussed on paediatric formulations
- Advice to select excipients for paediatric population with special care. Possible sensitivities of the different age groups should be taken into consideration

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/01/WC500059258.pdf

General Guidelines

Excipients in the label and package leaflet of medicinal products for human use (NtA Volume 3B)

- Acknowledges that excipients may also cause adverse reactions
- Relevant in context - *Quality in relation to Safety*
- Currently under revision to include paediatric specific information as well as new excipients

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003412.pdf

Paediatric Guidelines

Guideline on the investigation of medicinal products in the term and pre-term neonate (EMEA/536810/2008)

- Contains some specific Quality guidance since there was no quality guideline at that time
- Formulation aspects for neonates

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003750.pdf

Paediatric Guidelines

Guideline on pharmaceutical development of medicines for paediatric use
(EMA/CHMP/QWP/180157/2011)

- Draft guideline, consultation by end of 2011
- Fully dedicated to development of paediatric formulations
- Flags important issues/aspects which should be considered during development of paediatric formulations

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/06/WC500107908.pdf

Paediatric Guidelines

WHO Guideline: Development of paediatric medicines: Points to consider in pharmaceutical development

- Draft guideline, discussed and adopted in October at 46th Expert Committee meeting
- Fully dedicated to development of paediatric formulations
- Following the legal scrutiny will be published next year
- EMA contributed to its development

Other Sources of information

CHMP Scientific Opinions

- CHMP Scientific Article 5(3) Opinion on the potential risks of carcinogens, mutagens and substances toxic to reproduction when these substances are used as excipients of medicinal products for human use
    - Provides an overview of principles applied during the evaluation of excipients used in medicinal products for human use within the current legal and regulatory framework

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/10/WC500004013.pdf

Other Sources of information

- **Opinions and Reports for specific substances published by the European Food and Safety Agency (EFSA)**
- **Food legislation**
  - o Directive 2006/52/EC (food additives)
  - o Directive 94/35/EC (sweeteners)
  - o Directive 94/36/EC (colourants)
  - o Directive 2009/35/EC (colourants in medicines)
- **Other relevant sources: formularies, compendia, etc**

Conclusions

Paediatric Regulation (in force since 2007) stimulated development of paediatric focussed guidelines

Regulatory armamentarium improves, however there is still room for improvement

Development concepts from guidelines for adults may be applicable to some extend to paediatric formulations

Quality in relation to safety approach should be followed

Food legislation may be of help

Basic principle

- **Guidelines are not legally binding**

  - Their purpose is to set out principles and general requirements that should be followed
  - Important is the **spirit** of the guideline
  - **Derogations** can be **acceptable** provided that they are **adequately justified**




Thank you for your attention!

Questions?