EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

General update on Paediatric medicines

New and ongoing activities of relevance for Industry stakeholders

EMA-Stakeholders meeting, 11 May 2015, London

Presented by Paolo Tomasi on 11 May 2015
Head of Paediatric Medicines

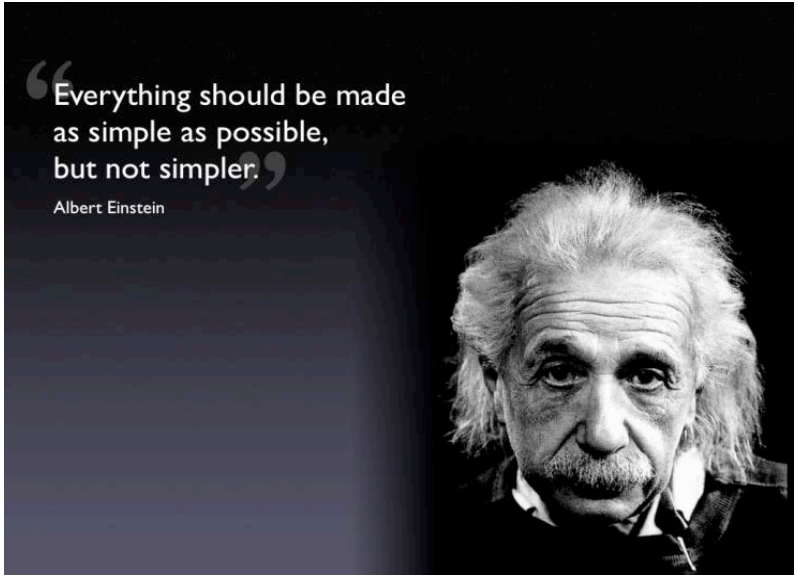
Today's agenda

EUROPEAN MEDICINES AGENCY

Class waiver list review: I. Motivation, methodology and outcome **II.** Consequences for regulatory submissions III. Industry stakeholders: Comments	Ralf Herold
Early interaction: • Presentation of plans and practicalities for early interactions to foster paediatric medicine development • Industry stakeholders: Comments • Discussion	Chrissi Pallidis
Public summary of the evaluation of a proposed PIP or product-specific waiver: I. Industry stakeholders: Questions • Information on public summaries	Paolo Tomasi
PIP Compliance check during submission validation: I. Industry stakeholders: Questions • Information on compliance check	Paolo Tomasi

Principles of action of the Paediatric Medicines Office

- Simplification of administrative tasks while maintaining and facilitating high-quality scientific assessment and outcomes
- Provide timely, correct and helpful procedural advice to applicants
- Provide timely, correct and helpful responses to queries from all stakeholders
- Reliable respect of the legal timelines for adoption of opinions and decisions



Recent relevant initiatives / improvements - 1

EUROPEAN MEDICINES AGENCY

- Talks on possible TIGRE cooperation with FDA (Rare and ultra-rare paediatric diseases initiative) – ongoing
- Annual EnprEMA meeting (28 May 2015)
- Launch of International Neonatal Consortium at EMA and involvement (C-Path) – next week
- Update of procedural advice on EMA website, including on compliance check and simplification for modification (and relevant forms, Jan 2015)
- Simplifications for applicants in new EC guideline (Sep-Dec 2014)
- New intelligent EnprEMA form, database and direct web publishing

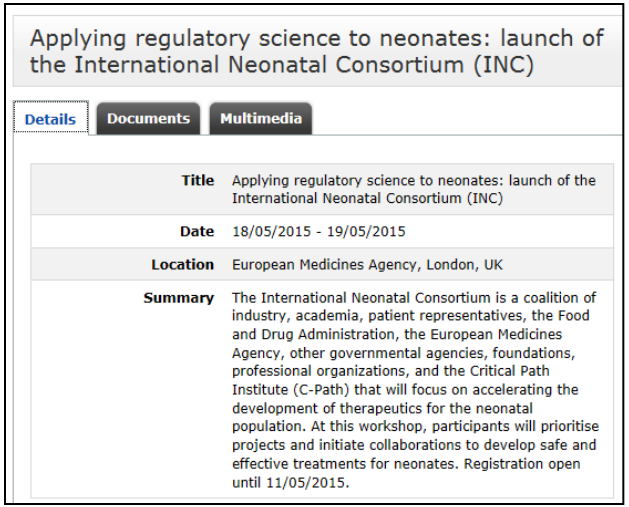

EnprEMA
European network of paediatric research at the European Medicines Agency

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

04 March 2015
EMA/150699/2015 Corr.1
Product Development Scientific Support Department

Draft agenda of the 2015 annual workshop of the European network of paediatric research at the European Medicines A (Enpr-EMA)

Thursday 28 May 2015, Room 3A


Applying regulatory science to neonates: launch of the International Neonatal Consortium (INC)

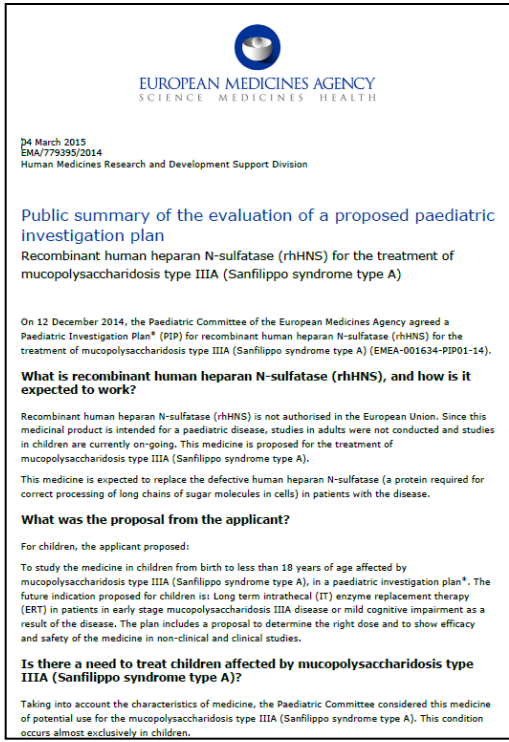
Details | Documents | Multimedia

Title	Applying regulatory science to neonates: launch of the International Neonatal Consortium (INC)
Date	18/05/2015 - 19/05/2015
Location	European Medicines Agency, London, UK
Summary	The International Neonatal Consortium is a coalition of industry, academia, patient representatives, the Food and Drug Administration, the European Medicines Agency, other governmental agencies, foundations, professional organizations, and the Critical Path Institute (C-Path) that will focus on accelerating the development of therapeutics for the neonatal population. At this workshop, participants will prioritise projects and initiate collaborations to develop safe and effective treatments for neonates. Registration open until 11/05/2015.

Recent relevant initiatives / improvements - 2

EUROPEAN MEDICINES AGENCY

- Implementation of Summary of the PDCO Evaluation (response to the E.O.)
- Systematic involvement in SA procedures of PDCO volunteer and Paediatric Medicines Scientific Officer (2014)
- Systematic reporting and discussion of SAWP procedures at PDCO (2014)
- Start of joint PDCO-COMP focus group, regular meetings and interactions (2014)
- Start of joint PDCO-PRAC focus group, regular meetings and interactions (2014)
- First round table with European Commission on initiatives to facilitate Clinical Trials in children (June 2014) – several ongoing activities



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

04 March 2015
EMA/779395/2014
Human Medicines Research and Development Support Division

Public summary of the evaluation of a proposed paediatric investigation plan

Recombinant human heparan N-sulfatase (rhHNS) for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A)

On 12 December 2014, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for recombinant human heparan N-sulfatase (rhHNS) for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A) (EMEA-001634-PIP01-14).

What is recombinant human heparan N-sulfatase (rhHNS), and how is it expected to work?

Recombinant human heparan N-sulfatase (rhHNS) is not authorised in the European Union. Since this medicinal product is intended for a paediatric disease, studies in adults were not conducted and studies in children are currently on-going. This medicine is proposed for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A).

This medicine is expected to replace the defective human heparan N-sulfatase (a protein required for correct processing of long chains of sugar molecules in cells) in patients with the disease.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in children from birth to less than 18 years of age affected by mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A), in a paediatric investigation plan*. The future indication proposed for children is: Long term intrathecal (IT) enzyme replacement therapy (ERT) in patients in early stage mucopolysaccharidosis IIIA disease or mild cognitive impairment as a result of the disease. The plan includes a proposal to determine the right dose and to show efficacy and safety of the medicine in non-clinical and clinical studies.

Is there a need to treat children affected by mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A)?

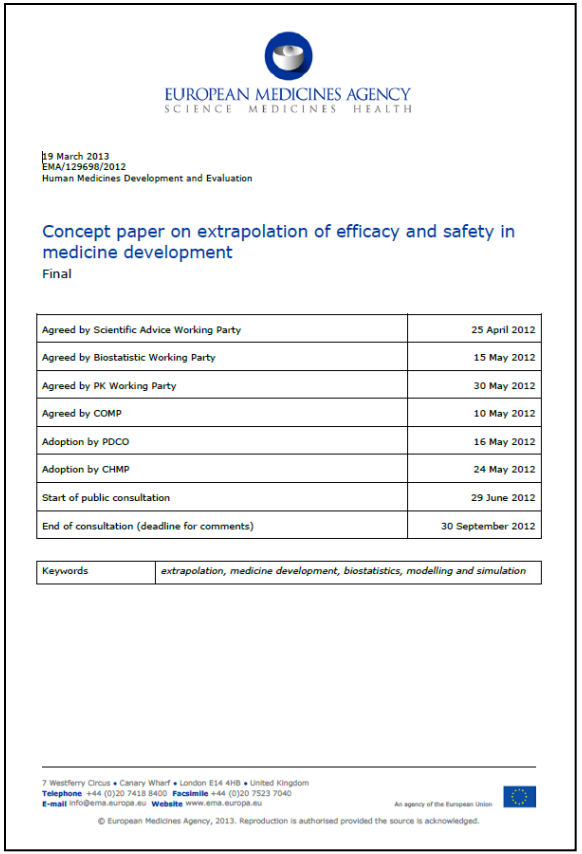
Taking into account the characteristics of medicine, the Paediatric Committee considered this medicine of potential use for the mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A). This condition occurs almost exclusively in children.

Work in progress – 1 - Extrapolation

EUROPEAN MEDICINES AGENCY

Extrapolation across age groups

- EMA Experts extrapolation workshop 30 Sep 2015
  - ✓ Draft agenda will be published in June 2015
  - ✓ Internal workshop with regulators and experts from FP7 funded projects
  - ✓ Cross-committees and working parties workshop, chaired by Rob Hemmings. FDA expected to participate
- EMA Industry extrapolation meeting Q1 2016
  - ✓ Open to industry
  - ✓ Associations to be contacted in Sep 2015 for expression of interest
  - ✓ Organised by EMA



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 March 2013
EMA/129698/2012
Human Medicines Development and Evaluation

Concept paper on extrapolation of efficacy and safety in medicine development
Final

Agreed by Scientific Advice Working Party	25 April 2012
Agreed by Biostatistic Working Party	15 May 2012
Agreed by PK Working Party	30 May 2012
Agreed by COMP	10 May 2012
Adoption by PDCO	16 May 2012
Adoption by CHMP	24 May 2012
Start of public consultation	29 June 2012
End of consultation (deadline for comments)	30 September 2012

Keywords	*extrapolation, medicine development, biostatistics, modelling and simulation*

7 Westferry Circus ♦ Canary Wharf ♦ London E14 4HB ♦ United Kingdom
Telephone +44 (0)20 7418 8400 Facsimile +44 (0)20 7523 7040
E-mail info@ema.europa.eu Website www.ema.europa.eu
An agency of the European Union

Work in progress - 2

- Revision of paediatric pages on EMA website, with improved guidance sorted by procedure
- List of paediatric disease designable as orphan conditions for Horizon 2020 funding
- Collaboration with FDA to develop a joint procedural advice on regulatory aspects of global paediatric development (similarities and differences, e.g. for content of application forms)
- Establishment of an Young Patients Advisory Group within the EMA Patients and Consumers Working Party
- Ongoing work to help EC on 10-yr report on paediatric regulation:
  - ✓ Collection of data ongoing (incl. from NCA), skeleton of the EMA report drafted
  - ✓ EMA to provide detailed report to EC by 30 April 2016
  - ✓ EC to submit report to Parliament and Council by Jan 2017

Review and Reconnect

- Process across Agency
- Analysis and proposals for optimisation of main procedure (PIP/waiver/modif/CC)
- Implementation of changes ongoing and to be completed by Q3 2015
- Aspects of relevance to applicants:
  - Optimisation of D60 request for modification from PDCO
  - Draft Opinion to be finalised earlier (*no modifications D90 to D120*)
  - New option: early interaction / initial consultation on paediatric development
  - Changes in structure of Summary Report (focus on key elements for Opinion, inclusion of original report[s] in modification procedures, other optimizations)
  - Updated Opinion template including updated Annex I

Any questions?

Compliance check

- EMA advises to request CC to PDCO always before submission of MAA
- EMA advises to request CC multiple times whenever indicated (e.g. after completion of individual paediatric trials), instead of just before a regulatory application

  This approach minimizes the risk of a delayed MA, due to possible non-validation of a regulatory application (MA or extension/variation applications) that triggers art. 7 or 8 of the paediatric regulation. It allows sufficient time for a potential modification of the agreed PIP in case of non-compliance.

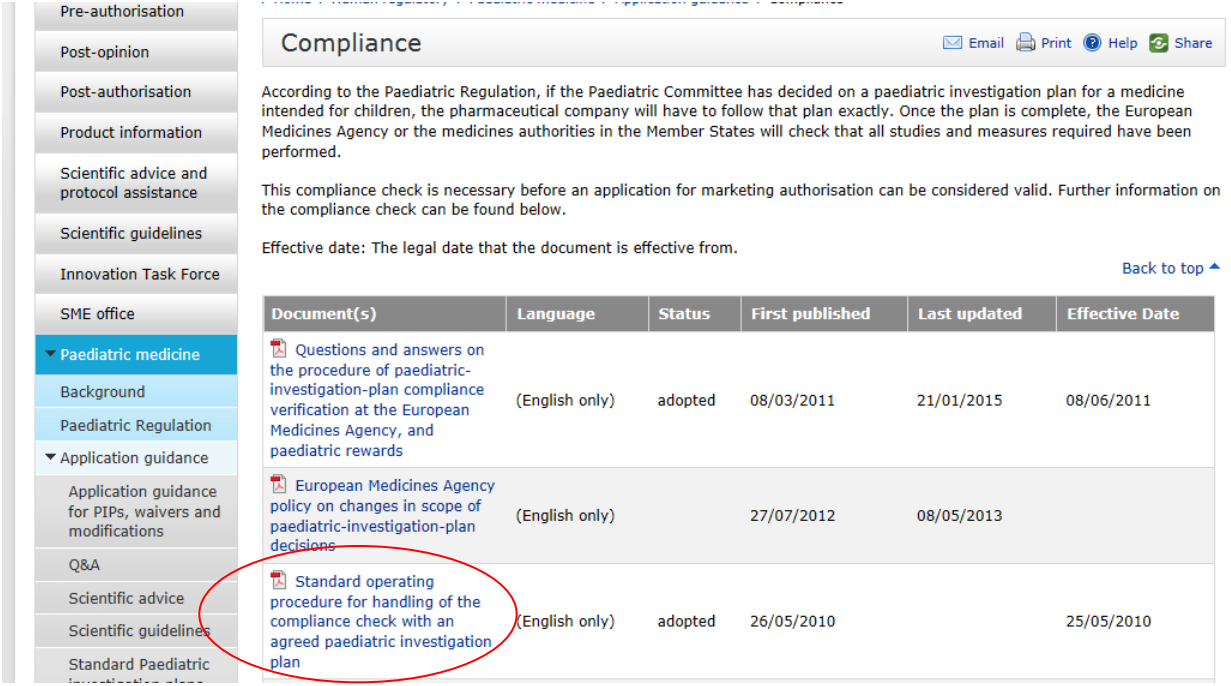
Compliance check done during the validation of the MAA (or other reg. proc.) can be done but is risky for applicant (if non-compliance detected)

Compliance check – Answers to questions from industry

Why is the internal EMA process for CC not available?

In fact SOP is published since 2010, and is currently being reviewed.

Changes however mainly for CC during validation (which is discouraged)



Compliance check – Answers to questions from industry

Is it possible to complete a partial CC each time a completed paediatric measure/study is submitted then a final partial compliance check at the time the final PIP measure is submitted?

Possible and recommended!

In procedural advice already

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 December 2014
EMA/PDCO/179892/2011 Rev. 2
Product Development Scientific Support
Paediatric Medicines

Questions and answers on the procedure of PIP compliance verification at EMA, and on paediatric rewards
(revised December 2014)

8. How early before submission of the Regulatory Application can a compliance check be requested?

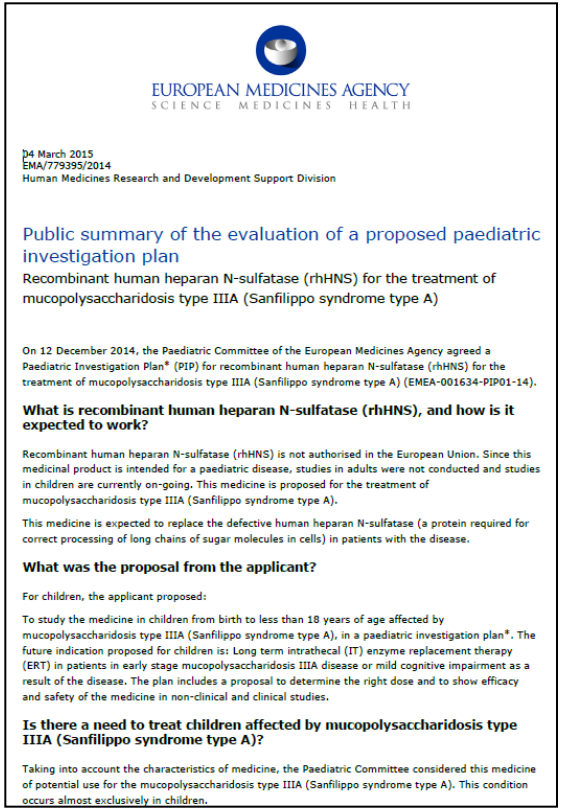
The Paediatric Regulation does not establish a timeframe for the compliance check prior to submission of the Regulatory Application.

To prevent delays at the time of validation of a Regulatory Application, applicants are encouraged to request compliance check by the PDCO at least 2 months prior to the planned submission of a Regulatory Application, in keeping with the submission timelines indicated on the Paediatric investigation plans: Templates, forms and submission dates page.

It is recommended that, when indicated, applicants submit separate sequential compliance check applications to the PDCO, before submission of the regulatory procedure (centralised or non-centralised). This is intended to confirm compliance for individual measures (or groups of measures) as early as possible, on an ongoing basis, and to allow applicants more time if changes are needed. For example, an applicant may submit one compliance check request after completing all the non-clinical studies, and another after completion of the first clinical trial in children, before submitting their MAA in adults.

Public Summary of the PDCO evaluation of the PIP/waiver application

- First published: July 2014. Written by PaedCo
- 75 published so far and increasing
- Applicants are given opportunity to point out factual errors (if any) or comment
- Only published for first PIP/waiver procedures so far
- To be updated after modifications of first PIPs agreed after July 2014
- Average time from Decision date to publication of Summary: 58.7 ± 26.9 days



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

04 March 2015
EMA/779395/2014
Human Medicines Research and Development Support Division

Public summary of the evaluation of a proposed paediatric investigation plan

Recombinant human heparan N-sulfatase (rhHNS) for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A)

On 12 December 2014, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for recombinant human heparan N-sulfatase (rhHNS) for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A) (EMEA-001634-PIP01-14).

What is recombinant human heparan N-sulfatase (rhHNS), and how is it expected to work?

Recombinant human heparan N-sulfatase (rhHNS) is not authorised in the European Union. Since this medicinal product is intended for a paediatric disease, studies in adults were not conducted and studies in children are currently on-going. This medicine is proposed for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A).

This medicine is expected to replace the defective human heparan N-sulfatase (a protein required for correct processing of long chains of sugar molecules in cells) in patients with the disease.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in children from birth to less than 18 years of age affected by mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A), in a paediatric investigation plan*. The future indication proposed for children is: Long term intrathecal (IT) enzyme replacement therapy (ERT) in patients in early stage mucopolysaccharidosis IIIA disease or mild cognitive impairment as a result of the disease. The plan includes a proposal to determine the right dose and to show efficacy and safety of the medicine in non-clinical and clinical studies.

Is there a need to treat children affected by mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A)?

Taking into account the characteristics of medicine, the Paediatric Committee considered this medicine of potential use for the mucopolysaccharidosis type IIIA (Sanfilippo syndrome type A). This condition occurs almost exclusively in children.

Public Summary of the PDCO evaluation of the PIP/waiver application – answers to questions from industry

- Consultation with stakeholders: Internal consultation done with the Medical and Health Information Service. Template built on the basis of existing Summaries of Opinion e.g. for OD or MA
- Difficult to find, language still technical: EMA is aware. Requirement for entire review of Paed Website pages ongoing. Discussion on greater involvement of MHSI ongoing.
- Process to update existing summaries: Yes. Update after every modification
- Plan to publish retrospective summaries: No.

Thank you for your attention

Further information

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Follow us on **@EMA_News**