12 May 2016
EMA/12429/2016
Product Development Scientific Support Department

Agenda – Workshop on extrapolation of efficacy and safety in medicine development across age groups

17 – 18 May 2016, European Medicines Agency, London

Background

The primary rationale for extrapolation is to avoid unnecessary studies in the target population for ethical reasons, for efficiency, and to allocate resources to areas where studies are the most needed.

Additionally, in situations where the feasibility of studies are restricted, extrapolation principles may be applied for rational interpretation of the limited evidence in the target population in the context of data from other sources.

The EMA is developing a framework to support the use of extrapolation approaches across the product life cycle until licensing. The framework shall set out a structured approach to be followed for each extrapolation exercise to improve interactions with stakeholders and to standardise the decision making across EMA committees.

Additionally, the revision of the ICH E11 (Clinical Investigation of Medicinal Products in the Paediatric Population) is ongoing with a focus on extrapolation.

Thus, it is important to provide drug developers with clear and compatible guidance specific to global product development and licensing of paediatric medicines.

Objectives of the workshop

Based on the EMA Reflection paper on extrapolation of efficacy and safety in paediatric medicine development, the goal of the meeting is to agree on recommendations for clinicians, modellers and statisticians which should result in an explicit and systematic approach for decision making alongside the life cycle; hence optimising the chances for successful development and approval.

This workshop is intended to gather input from European stakeholders with invited observers, including experts from the ICH E11 (R1) guideline.

The output from the workshop will be used for the finalisation of the EMA reflection paper on extrapolation across age groups.

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Tuesday, 17 May 2016

Item	Agenda item		
	Registration		08:30
	Introduction Head of the Human Medicines Research and Development Support Division	Zaide Frias	09:00
1	**Session 1: Setting the scene** Chair: Dirk Mentzer; EMA: Cécile Ollivier		
1.1	PDCO and the EMA Extrapolation Framework	Daniel Brasseur; Christoph Male	09:15
1.2	Paediatric Medicines Development: The Need for Different Approaches	Sam Maldonado	09:40
1.3	Patient representative	Marco Greco	09:55
1.4	Modelling and Simulation principles and tools for extrapolation	Ine Skottheim Rusten; Piet Van der Graaf; Amin Rostami	10:10
1.5	Statisticians perspectives on extrapolation	Rob Hemmings	10:45
1.6	FP7 projects- progress update	Nigel Stallard	11:00
	Coffee break		11:10
1.7	The quantitative challenges of extrapolation (on behalf of EFPIA)	Michael Looby; Frank Bretz	11:25
1.8	Q&A and Panel discussion	Joseph Standing; Christoph Gerlinger, Lynne Yao	11:50
1.9	Session 1 wrap-up	Chairs	12:30
	Lunch		12:45
2	**Session 2: Extrapolation concept** Chair: Tomas Salmonson; EMA: Efthymios Manolis		
2.1	• Clinical setting of paediatric Partial Onset Seizure • Case study: Briviact (UCB)	Catherine Chiron Jan-Peer Elshoff; Armel Stockis; Cynthia Beller; Coralie Domange	13:30

Item	Agenda item		
2.2	Bayesian prior elicitation: an application to the MYPAN trial in childhood polyarteritis nodosa	Lisa Hampson	14:10
2.3	MID3 Good practice on use of prior knowledge and setting up assumptions	Scott Marshall; Lutz Harnisch	14:25
2.4	Q&A and Panel discussion	Gerard Pons; S Y Amy Cheung; Ralph Bax; Piet van Der Graaf; Tim Friede; Angela Men (by TC)	14:50
	Coffee break		15:30
3	**Session 3: Extrapolation plan and PK/PD studies** Chair: Richard Vesely; EMA: Efthymios Manolis		
3.1	Extrapolation of dosing, efficacy and safety of biologics in JIA, IBD and psoriasis – EMA history	Richard Vesely	15:45
3.2	Extrapolation and paediatric development: A case study from paediatric ulcerative colitis (JnJ)	Richard Strauss; Joseph Adedokun	15:55
3.3	Case study: Cimzia (UCB)	Ruth Oliver; Laura Shaughnessy; Philippa Charlton	16:15
3.4	Design of PK/PD studies	Mats Karlsson	16:30
3.5	Q&A and Panel discussion	Ine Skottheim Rusten; Marco Greco; Martin Posch; Amin Rostami; Yeruk Mulugeta (TC)	17:00
3.6	Wrap up	Chairs	17:45
	End of Day 1		18:00

Wednesday, 18 May 2016

Item	Preliminary draft agenda		Mins
4	**Session 4: Extrapolation plan and statistical tools** Chair: Peter Volkers; EMA: Andrew Thomson		08:30
4.1	Use of extrapolation for rationale interpretation of limited evidence: Everolimus case study (Novartis)	Thomas Dumortier	08:35
4.2	On the road to clinical extrapolation	Armin Koch; Kristina Weber	09:00
4.3	• Paediatric Pulmonary Arterial Hypertension: clinical setting	Amani El Gazayerly	09:20
	• Case study: Extrapolation challenges in pediatric PAH (Actelion)	Marisa Bacchi; Per Nilsson; Adele Morganti	
4.4	Q&A and Panel discussion	Ralf Herold; Jan Regnstroem; Frank Bretz; Alexander Staab; Flora Musuamba	10:00
	Coffee break		10:45
5	**Session 5: Confirmation & extrapolation** Chair: Rob Hemmings; EMA: Andrew Thomson		
5.1	Statistical confirmation and uncertainties	Andrew Thomson	11:00
5.2	Confirmation of extrapolation based on PK/PD data and modelling	Jacob Brogren	11:15
5.3	General framework on uncertainties and RMP	Kevin Blake	11:30
5.4	Q&A and Panel discussion:	Sue Cole; Christoph Male; Lutz Harnisch	11:45
5.6	Wrap up	Chairs	12:30
	Lunch break		12:45
6	**Session 6: Paediatric development from challenges to opportunities** Chair: Daniel Brasseur; EMA: Cécile Ollivier		
6.1	Regulatory interactions expectations on extrapolation approaches – good practice	Lynne P. Yao	13:50
6.2	Considerations for Implementing the New EMA Extrapolation	Christina Bucci-	14:10

Item	Preliminary draft agenda		Mins
	Approach: A Global Drug Developers Perspective	Rechtweg	
6.3	EMA extrapolation framework – regulatory tools	Paolo Tomasi	14:30
6.4	Q&A and Panel discussions	Solange Rohou; Irmgard Eichler; Sabine Fuerst-Recktenwald	14:50
6.5	Workshop wrap up	Dirk Mentzer; Sam Maldonado	15:30
	Conclusion	Chairs	16:00

Organisation Committee:

EMA:

- Cecile Ollivier – ICH E11 working group
- Efthymios Manolis
- Andrew Thomson
- Kevin Blake
- Richard Vesely

Network:

- Rob Hemmings, Scientific Advice Working Party (SAWP, Chair)
- Dirk Mentzer, Paediatric Committee (PDCO, Chair) - ICH E11 working group
- Tomas Salmonson, Committee for Medicinal Products for Human Use (CHMP, Chair)
- Daniel Brasseur, Committee for Medicinal Products for Human Use (CHMP) - ICH E11 working group
- Ine Skottheim Rusten, Paediatric Committee (PDCO)- ICH E11 working group
- Armin Koch, Scientific Advice Working Party (SAWP)
- Flora Musuamba Tshinanu, Modelling and Simulation Working Group
- Gerard Pons, Modelling and Simulation Working Group
- Peter Volkers, Biostatistics Working Party (BSWP)
- Martin Posch, Biostatistics Working Party (BSWP)
- Jacob Brogren, Modelling and Simulation Working Group

Food and Drug Administration (FDA):

- Lynne Yao - ICH E11 working group

Industry Stakeholders:

- EFPIA: Solange Rohou- ICH E11 working group
- EFPIA MID3 workgroup
- EuropaBio: Nael Mostafa
- EUCOPE: John Watson
- Vaccines Europe: Richard Pilsudski
- Christina Bucci-Rechtweg, Novartis – ICH E11 working group

List of speakers:

(in the order of the agenda)

Zaide Frias, EMA

Dirk Mentzer, Paediatric Committee (PDCO, Chair)

Cecile Ollivier, EMA

Daniel Brasseur, Committee for Medicinal Products for Human Use (CHMP)

Christoph Male, Paediatric Committee (PDCO)

Sam Maldonado, Johnson & Johnson

Marco Greco, European Federation of Crohn's & Ulcerative Colitis Associations

Ine Skottheim Rusten, Paediatric Committee PDCO

Piet Van Der Graaf: Leiden University Hospital

Amin Rostami, University of Manchester

Rob Hemmings, Scientific Advice Working Party (SAWP, Chair)

Nigel Stallard, Warwick University

Michael Looby, Novartis

Frank Bretz, Novartis

Joseph Standing, Modelling and Simulation Working Group

Christoph Gerlinger, Bayer

Lynne Yao, Food and Drug Administration (FDA)

Tomas Salmonson, Committee for Medicinal Products for Human Use (CHMP, Chair)

Efthymios Manolis, EMA

Catherine Chiron, Hopital Necker

Jan-Peer Elshoff, UCB Pharma

Armel Stockis, UCB Pharma

Cynthia Beller, UCB Pharma

Coralie Domange, UCB Pharma

Lisa Hampson, Lancaster University

Scott Marshall, Pfizer EFPIA MID3

Lutz Hanisch, Pfizer EFPIA MID3

Ralph Bax, EMA

S Y Amy Cheung, AstraZeneca EFPIA MID3

Tim Friede, University of Warwick

Angela Men, Food and Drug Administration (FDA)

Richard Vesely, EMA

Richard Strauss, Johnson & Johnson

Joserph Adedokun, Johnson & Johnson

Ruth Oliver, UCB

Laura Shaughnessy, UCB

Philippa Charlton, UCB

Mats Karlsson, Uppsala University

Martin Posch, Biostatistics Working Party (BSWP)

Armin Koch, Scientific Advice Working Party (SAWP)

Yeruk Mulugeta, Food and Drug Administration (FDA)

Thomas Dumortier, Novartis

Kristina Weber, Medizinische Hochschule Hannover

Amany El-Gazayerly, Scientific Advice Working Party (SAWP)

Marisa Bacchi, Actelion

Per Nilsson, Actelion

Adele Morganti, Actelion

Ralf Herold, EMA

Jan Regnstrom, EMA

Alexander Staab, Boehringer-Ingelheim EFPIA MID3

Flora Musuamba Tshinanu, Modelling and Simulation Working Group

Andrew Thomson, EMA

Jacob Brogren, Modelling and Simulation Working Group

Kevin Blake, EMA

Christina Bucci-Rechtweg, Novartis

Paolo Tomasi, EMA

Solange Rohou, EFPIA

Irmgard Eichler, EMA

Sabine Fuerst-Recktenwald, F. Hoffmann La Roche LTD- ICH E11 EWG