16 August 2012
EMA/PDCO/422131/2012
Human Medicines Development and Evaluation

Paediatric Committee (PDCO)

Minutes of the 04-06 July 2012 meeting held at the
Paul Ehrlich Institut – Langen (Germany)

Chair: Daniel Brasseur

I Introduction

The President of Paul Ehrlich-Institut (PEI), Prof. Dr. Klaus Cichutek, welcomed the PDCO to Langen.

I.1 Adoption of the minutes from previous meeting

Adopted.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab

I.2 Adoption of the Agenda

Adopted

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab

I.3 Declaration of Conflict of Interest

See Annex I

I.4 External attendance

Please refer to the July 2012 PDCO monthly report published in the EMA Website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab

I.5 Leaving/New Members and Alternates

- Please refer to the July 2012 PDCO monthly report published in the EMA Website:

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An agency of the European Union

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab

II Opinions

II.1 Opinions on Products D120 and D60

II.2 Opinions on Compliance Check

II.3 Opinions on Modification of an Agreed PIP

Please refer to the July 2012 PDCO monthly report published in the EMA Website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab

III Discussion of applications

The PDCO discussed 85 procedures in total[1], of which:

- 42 PIP applications
- 12 product-specific waiver applications
- 3 compliance check procedures (interim and final)
- 27 requests for modifications of an agreed PIP
- 1 re-examination request

IV Nomination of Rapporteurs and Peer reviewers

• List of letters of intent received for submission of applications with start of procedure September 2012[1]for Nomination of Rapporteur and Peer reviewer • Nomination of Rapporteur for requests of confirmation on the applicability of the EMA decision on class waiver	The PDCO approved the lists of Rapporteurs and Peer Reviewers.

V Finalisation and adoption of opinions

All opinions taken at this meeting (relating to adoption of opinions, recommendations, requests for modifications and applicability of class waivers) were made in the presence of the required quorum of members.

The opinions adopted during the Paediatric Committee meeting of July are published in the same month's meeting report published in the EMA website: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000192.jsp&mid=WC0b01ac0580028eab.

[1] The procedures discussed by the PDCO are on-going and therefore are considered confidential. Additional details on these procedures will be disclosed in the PDCO Committee meeting reports (after the PDCO Opinion is adopted), and on the Opinions and decisions on paediatric investigation plans webpage (after the EMA Decision is issued).

VI DISCUSSION OF THE APPLICABILITY OF CLASS WAIVER

Class waiver number	Active substance	Condition	Outcome (confirmed / not confirmed)
EMEA-25-2012	(6R)-4, 5, 6, 7-tetrahydro-N6-propyl-2, 6-benzothiazolediamine dihydrochloride monohydrate (Dexpramipexole)	Treatment of amyotrophic lateral sclerosis	Confirmed
EMEA-26-2012	Perindopril tosilate/Amlodipine besilate	Treatment of coronary atherosclerosis	Not confirmed
EMEA-17-2012	Autologous tumour-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin (EMEA-001274-PIP01-12)	Treatment of follicular lymphoma	Confirmed

VII Other topics

Guidelines	
Revision* of the Note for Guidance on Clinical Investigation of Medicinal Products for Treatment of Asthma	The discussion focused on the paediatric chapter within the guideline, which has been previously discussed and already adopted by the PDCO. In the meantime some comments regarding the lower cut-off age of the younger children as well the use of spacers were received by members of the respiratory drafting group. The PDCO agreed to consistently divide the paediatric population in children below 6 years, and 6 years and older. The PDCO further confirmed their previous position, already pointed out in the paediatric chapter, that in children the use of pressurised metered-dose inhaler (pMDI) should be evaluated only in combination with an age-appropriate spacer device.
Advice to EC* on the revision of the 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	The Committee was informed that a proposal for modifications* to the EC guideline on the format and content of the PIP/waiver applications will be circulated in the next post-mail, for comments and proposal. Comments are particularly expected from the nominated working group. Discussions on the proposed modifications will be held in September, with a view for possible adoption in September or October.
Paediatric addendum* to the Note for Guidance on clinical investigation of medicinal products in the treatment of lipid disorders	The PDCO proposed some revisions regarding the endpoints and the duration of the open label extension for CHMP consideration.

Working groups	
Formulation	No non-product related issues where reported to the Committee.
Non-Clinical	No non-product related issues where reported to the Committee.
Extrapolation	N/A
Other topics	
Draft reflection paper on biomarkers* - PDCO comments	Following an internal review of biomarkers discussed at COMP level, the PDCO discussed the findings from this review, and in particular considered the need to conduct a similar review of the biomarkers used as endpoint in Opinions adopted. This work was considered to have important value and was set as a topic for further clarification of remit and discussion in the next PDCO meetings.
Harmonisation of vaccine schedules	Recognising that vaccination schedules are under national responsibility, the PDCO is concerned with in the multiple vaccine schedules across EU Member States for routine vaccinations, for 2 main reasons: • Discordant schedules create issues in view of the increasing mobility of children within Europe; • the unnecessary multiple paediatric clinical trials that are needed to comply with each of the schedules, and which require multiple blood sampling in large numbers of infants and children. Additionally, the PDCO has to identify the best schedule to require only the necessary trials in PIPs. As the EU Council had identified this as a significant problem, the Committee agreed that a small group of PDCO members will work on a proposal (for a model PIP) to be discussed and adopted by the whole Committee, and discussed with the EU Vaccination Task Force set up between ECDC, DG Sanco and other Scientific Committees/Working Groups of the EMA.
Improving D60 Requests for Modification	A presentation* was given to the Committee and the EMA staff, on how to improve the quality of the Request of Modification at D60. In particular, it was underlined that the Request should include the PDCO's position explicitly, and specific modifications desired, rather than simple requests for further information, leaving applicants without information on what is expected.
Propylene glycol Art. 5(3) - Joint AR for PDCO comments	The PDCO acknowledged the extensive work done by the CHMP and appreciated the quality of the investigations performed, as well as the literature review. One comment was related to the reference to the Commission Guideline on Excipients in the label and package leaflet: there seems to be a confusion between the threshold mentioned in the

	guideline, from which a wording is included in the package leaflet, and a safety limit. This will be brought to CHMP attention. In addition, the PDCO expects further answers to help them in making decisions with regard to future PIP applications for medicinal products containing propylene glycol. PDCO members were requested to provide comments in writing before 09 July 2012. Both PDCO conclusions* and comments received in writing* were transmitted to the CHMP.
Update on committees interactions project	The PDCO received an update on the latest initiatives to ensure coordination between the various EMA committees. A framework document* is being elaborated. Among the specific interactions, the first joint PDCO/SAWP procedure will be piloted from August 2012. A presentation on the operation of the procedure was given, including the draft Standard Operating Procedure*.
Executive Summary on applications	The data from 2011 and 2012 showed that the "Executive Summary project" has not been implemented consistently: approximately 15% of the new applications had an Executive Summary prepared by the Peer Reviewer. This is attributed to the very short time available to the Peer Reviewer to assess the application and prepare both presentation to the Committee and Executive Summary. Particularly difficult was also the update of the document for the following discussions. It was agreed to discontinue the preparation of this document. In replacement, D30 minutes will be prepared in a more structured manner (WIN* in preparation); additionally, public information on the justifications for PDCO Opinions is in preparation and will replace the information in the Executive Summary.

VIII Any other business

None

Note on access to documents

Documents marked with an asterisk* in these minutes cannot be released at present as they are currently in draft format. They will become public when adopted in their final form.

Annex I to the Minutes of the PDCO of July 2012

Documentation on Declaration of interest of members, alternates and experts

Based on the Declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of Committee members for the upcoming discussions.

In accordance with the Agency's revised Policy and Procedure on the handling of conflicts of interests, participants in this meeting were asked to declare any conflict of interests on the matters for discussion (in particular any changes, omissions or errors to the already declared interests).

Member, alternate, expert name	Outcome restriction following evaluation of electronic declaration of interest	Topics on the current Committee Agenda for which this restriction applies
Adriana Ceci	Restriction level 3	EMEA-000145-PIP01-07-M05
Adriana Ceci	Restriction level 3	EMEA-000548-PIP01-09-M03
Adriana Ceci	Restriction level 3	EMEA-000309-PIP01-08-M04
Adriana Ceci	Restriction level 3	EMEA-001222-PIP01-11
Adriana Ceci	Restriction level 3	EMEA-001217-PIP01-11
Adriana Ceci	Restriction level 3	EMEA-001039-PIP02-12
Dobrin Konstantinov	Restriction level 3	EMEA-000468-PIP02-12
Gerard Pons	Restriction level 3	EMEA-000116-PIP01-07-M05
Jaroslav Sterba	Restriction level 3	EMEA-001274-PIP01-12
Jaroslav Sterba	Restriction level 3	EMEA-001033-PIP02-11
Jaroslav Sterba	Restriction level 3	EMEA-000468-PIP02-12
Michal Odermarsky	Restriction level 3	EMEA-000222-PIP01-08-M06
Michal Odermarsky	Restriction level 3	EMEA-001288-PIP01-12
Andreas Teloudes	Restriction level 4	EMEA-001275-PIP01-12
Andreas Teloudes	Restriction level 4	EMEA-000468-PIP02-12
Christoph Male	Restriction level 4	EMEA-001024-PIP01-10-M01
Christoph Male	Restriction level 4	EMEA-001296-PIP01-12
Christoph Male	Restriction level 4	EMEA-001174-PIP02-12
Marek Migdal	Restriction level 4	EMEA-000525-PIP01-08-M01
Marek Migdal	Restriction level 4	EMEA-001249-PIP01-11

Member, alternate, expert name	Outcome restriction following evaluation of electronic declaration of interest	Topics on the current Committee Agenda for which this restriction applies
Matthias Keller	Restriction level 4	EMEA-001281-PIP01-12
Matthias Keller	Restriction level 4	EMEA-001279-PIP01-12
Michal Odermarsky	Restriction level 4	EMEA-000774-PIP01-09-M01
Paolo Rossi	Restriction level 4	EMEA-000558-PIP01-09-M01
Paolo Rossi	Restriction level 4	EMEA-001289-PIP01-12
Peter Szitanyi	Restriction level 4	EMEA-000300-PIP01-08-M03
Peter Szitanyi	Restriction level 4	EMEA-000301-PIP01-08-M03
Peter Szitanyi	Restriction level 4	EMEA-000054-PIP01-07-M03
Peter Szitanyi	Restriction level 4	EMEA-000302-PIP01-08-M03
Peter Szitanyi	Restriction level 4	EMEA-001300-PIP01-12
Peter Szitanyi	Restriction level 4	EMEA-001291-PIP01-12
Peter Szitanyi	Restriction level 4	EMEA-001278-PIP01-12
Peter Szitanyi	Restriction level 4	EMEA-001275-PIP01-12

Note: the procedures identified in the table above are on-going and therefore considered confidential. Additional details on these procedures will be disclosed in the PDCO Committee meeting reports (after the PDCO Opinion is adopted), and on the Opinions and decisions on paediatric investigation plans webpage (after the EMA Decision is issued).

No new or additional conflicts were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Scientific Committee members and, where relevant, experts attending the plenary meeting, as announced by the Scientific Committee Secretariat at the start of meeting.

Restriction levels:

Evaluation of the conflict of interest	
Outcome	**Impact**
1	**No involvement in activity**
2	**To be replaced for the discussions, final deliberations and voting** as appropriate in relation to the relevant product or a competitor product.
3	**Where Individual product involvement is declared:** - **No involvement** with respect to procedures involving the relevant product or a competitor product in the relevant indication, i.e. no part in discussions, final deliberations and voting as appropriate as regards these medicinal

Evaluation of the conflict of interest	
4	**Where Individual product involvement is declared:** - **Involvement in discussions only** with respect to procedures involving the relevant product or a competitor product, i.e. no part in final deliberations and voting as appropriate as regards these medicinal

Annex II to the Minutes of the PDCO of July 2012

List of Participants

Chair

Daniel BRASSEUR

Vice-chair

Dirk MENTZER

Members appointed by Member States or CHMP

Christoph MALE	Austria
Koenraad NORGA	Belgium
Dobrin KONSTANTINOV	Bulgaria
Marianne ORHOLM	Denmark
Irja LUTSAR	Estonia
Pirjo LAITINEN-PARKONNEN	Finland
Gerard PONS	France
Dirk MENTZER	Germany
Stefanos MANTAGOS	Greece
Agnes GYURASICS	Hungary
Kevin CONNOLLY	Ireland
Paolo ROSSI	Italy
Dina APELE-FREMIANE	Latvia
Carine de BEAUFORT	Luxembourg
Hendrik van den BERG	The Netherlands
Siri WANG	Norway
Marek MIGDAL	Poland
Helena FONSECA	Portugal
Vlasta KAKOSOVA	Slovak Republic
Janez JAZBEC	Slovenia
Fernando DE ANDRÉS TRELLES	Spain
Marta GRANSTRÖM	Sweden

Julia DUNNE	United Kingdom

Alternates appointed by Member States or CHMP

Karl Heinz HUEMER	Austria
Jacqueline CARLEER	Belgium
Ann Marie KAUKONEN	Finland
Sylvie BENCHETRIT	France
Birka LEHMANN	Germany
Brian AYLWARD	Ireland
Francesca ROCCHI	Italy
Johannes TAMINIAU	The Netherlands
Ine Skottheim RUSTEN	Norway
Jolanda WITKOWSKA-OZOGOWSKA	Poland
Hugo TAVARES	Portugal
Dana Gabriela MARIN	Romania
Viveca Lena ODLIND	Sweden

Members representing patients' organisations

Michal ODERMARSKY

Alternates representing patients' organisations

Gerard NGUYEN

Gerlind BODE

Members representing healthcare professionals

Adriana CECI

Jean Pierre ABOULKER

Alternates representing healthcare professionals

Paolo PAOLUCCI

Alexandra COMPAGNUCCI

Experts

Peter BAUER	Medical statistician

Observers

Igor Francetic	Croatia

European Medicines Agency

Agnes SAINT RAYMOND[+]	Head of Sector, Human Medicines Special Areas
Paolo TOMASI	Head of Section, Paediatric Medicines
Sophie OLIVIER	Scientific Administrator, Paediatric Medicines
Anne-Sophie HENRY-EUDE[+]	Scientific Administrator, Paediatric Medicines
Blanca QUIJANO RUIZ[+]	Scientific Administrator, Paediatric Medicines
Dobromir PENKOV[+]	Scientific Administrator, Paediatric Medicines
Elin HAF-DAVIES[+]	Scientific Administrator, Paediatric Medicines
Emilie DESFONTAINE[+]	Scientific Administrator, Paediatric Medicines
Gunter EGGER[+]	Scientific Administrator, Paediatric Medicines
Irmgard EICHLER[+]	Scientific Administrator, Paediatric Medicines
Janina KARRES	Scientific Administrator, Paediatric Medicines
Julia SAPERIA[+]	Scientific Administrator, Paediatric Medicines
Peter KÁROLYI[+]	Scientific Administrator, Paediatric Medicines
Ralf HEROLD	Scientific Administrator, Paediatric Medicines
Ralph BAX	Scientific Administrator, Paediatric Medicines
Richard VESELY[+]	Scientific Administrator, Paediatric Medicines
Thorsten OLSKI	Scientific Administrator, Paediatric Medicines
Ermanno ZORZOLI[+]	Scientific Administrator, Paediatric Medicines
Giovanni LESA[+]	Scientific Administrator, Paediatric Medicines
Isabel PEREZ	Assistant, Paediatric Medicines
Agustina POGGIO	Assistant, Paediatric Medicines

[+]Participation via teleconference from London