06 July 2012
EMA/PDCO/347509/2012
Human Medicines Development and Evaluation

Paediatric Committee (PDCO)

Minutes of the 06-08 June 2012 meeting

Chair: Daniel Brasseur

I Introduction

I.1 Adoption of the minutes from previous meeting

Adopted

I.2 Adoption of the Agenda

Adopted with modifications.

The agenda of the Paediatric Committee is 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.3 Declaration of Conflict of Interest

See Annex I

I.4 External attendance

Please refer to the June 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 June 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

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II Opinions

II.1 Opinions on Products

II.2 Opinions on Compliance Check

II.3 Opinions on Modification of an Agreed Paediatric Investigation Plan

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

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III Discussion of applications

The PDCO discussed 101 current procedures in total[1], of which:

- 49 paediatric investigation plan applications;
- 12 product-specific waiver applications;
- 3 compliance check procedures (interim and final);
- 35 requests for modifications of an agreed paediatric investigation plan.
- 2 re-examination requests.

IV Nomination of Rapporteurs and Peer reviewers

• List of letters of intent received for submission of applications with start of procedure August 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

The opinions adopted during the Paediatric Committee meeting of June 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-16-2012	Levodopa, carbidopa, entacapone	Treatment of Parkinson's disease (non-juvenile)	Confirmed
EMEA-18-2012	lisinopril dihydrate (EMEA-001291-PIP01-12)	Treatment of coronary atherosclerosis and peripheral atherosclerosis	Confirmed
EMEA-19-2012	Gabapentin	Treatment of climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause	Confirmed
EMEA-20-2012	Trastuzumab emtansine	Treatment of gastric adenocarcinoma	Confirmed
EMEA-21-2012	6-ethynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-one (CK-2017357, Tirasemtiv)	Treatment of amyotrophic lateral sclerosis	Not confirmed
EMEA-22-2012	HLA class I/II binding tumour associated peptides (ADF-APO-CCN-GUC-K67-MET- MMP-MUC-RGS) [Abbreviated Chemical Name] (IMA-RGS-001)	Treatment of kidney and renal pelvis carcinoma	Confirmed
EMEA-23-2012	Dacomitinib	Treatment of lung carcinoma (small cell and non-small cell carcinoma)	Confirmed
EMEA-24-2012	Solanezumab	Treatment of Alzheimer's disease	Confirmed

VII Other topics

Guidelines	
Guideline for clinical investigation of medicinal products for the treatment of cutaneous and systemic lupus erythematosus*	The PDCO endorsed the draft of the paediatric section of this guideline*. This is to be forwarded to the Rheumatology/Immunology Working Party.
Working groups	
Formulation: PDCO FWG list of criteria for screening PIPs*	The PDCO was informed that all starting PIP applications (D0) are currently reviewed by the EMA Quality of Medicines staff, who are screening PIPs against this proposed list of criteria for referring or not PIPs to the Formulation working group for discussion before the D30 PDCO plenary discussion. A further 3-month pilot phase was agreed to check the robustness of the approach, after which the criteria can be

	formally adopted by the PDCO. It was also reminded that even if a PIP has not been referred to Formulation working group initially, there is always the possibility for the Rapporteur / Peer Reviewer / PDCO / Paediatric-coordinator to add it to the following month agenda for discussion.
Non-Clinical	No non-product related issues where reported to the Committee
Extrapolation	N/A
Other topics	
Feedback on extrapolation at FDA	Julia Dunne gave a presentation to PDCO on the work of the FDA working group on the extrapolation of efficacy to the paediatric population. The outcome of the working group was published in the journal Pediatrics. (J. Dunne, W. Rodriguez, M.D. Murphy et al. (2011). Extrapolation of Adult Data and Other Data in Pediatric Drug-Development programs. *Pediatrics, Vol. 128 No. 5,* e1242-e1249*)* The exercise performed was a retrospective analysis of paediatric studies submitted to FDA between 1998 and 2008 in response to Written Requests issued by FDA. 370 paediatric studies were submitted to the FDA in response to 159 written requests (166 products) issued under the Pediatric Exclusivity Provision. Cases in which efficacy was extrapolated from adult data or other data were identified and the type of paediatric data required to support extrapolation was categorised. In addition the authors determined whether the data resulted in new paediatric labelling. The working group concluded that the ability to extrapolate and the level of paediatric evidence required to support extrapolation depended on the degree of certainty underlying the assumptions of similarity between the adult and the paediatric populations. In addition, the use of extrapolation of efficacy to the paediatric population is evolving and approaches may change with increasing knowledge and experience. Although it is difficult to quantify, extrapolation can decrease the paediatric resource needed in paediatric drug development. For some years, the Pediatric Review Committee of the FDA has considered extrapolation of efficacy systematically when discussing proposed paediatric study requests (PPSRs) and written requests at its weekly meetings, and ensures a consistent approach while at the same time developing the institutional memory regarding extrapolation. EMA is about to publish a CP on the extrapolation of efficacy and safety in medicines development. This will be a general paper and will not confine itself to the extrapolation of efficacy to the paediatric population. Differences between European and US approaches to extrapolation have been highlighted (e.g.: In accordance with US legislation, FDA cannot extrapolate safety from adults to the paediatric population, whereas extrapolation of safety to children is being discussed at the European level). EMA will liaise with FDA in due time to work towards a common approach.

Other topics (cont.)	
Update on EMA Policy on conflict of interest	The revised EMA policy on conflict of interest has been presented with focus on the main changes as compared to previous policy (e.g., need to declare direct interest of the spouse). In addition, the new policy on Breach of Trust was presented. The Policy on conflicts of interest for experts and committee members is published on the EMA website: Handling conflicts of interests
Draft Reflection Paper on phthalates*	PDCO members were informed that the SWP has endorsed the draft reflection paper on phthalates*.
Draft Reflection Paper on parabens*	The PDCO was informed that the draft Reflection Paper on parabens* is still under review by the SWP.
Revision of the EC guideline on excipients in the label and package leaflet of medicinal products for human use	After the meeting which took place on the 6 June 2012 at the Agency with the Safety and Toxicity of Excipient for Paediatrics-Database (STEPS) and the European Study of Neonatal Excipient Exposure (ESNEE) project investigators, the PDCO was given a description of what these 2 projects are and what the collaboration between the drafting group and both projects could offer. It was agreed that there is common agreement on the current safety issues and ensure that relevant literature is available to assessor's and drafting group and that safety experts can comment on the methodology for ensuring quality of animal toxicology literature in both projects. An update of the status of the excipients guideline revision* was given to the PDCO. The drafting group is working on the first drafts on priority excipients, and a face to face meeting is scheduled in October.
Innovative Task Force (ITF) Briefing Meeting with Chiesi	The PDCO nominated two members to participate in this briefing meeting scheduled for 14 June 2012.
Update of the organisation in place to the delegates attending meetings abroad during the Olympics Games in London.	The organization put in place for the July PDCO meeting in Langen (Germany) was reviewed.
Policy - Use of agency's information and communication technology by external organisations	The PDCO members were reminded of the need to ensure the safety and confidentiality of the Agency data when assessing applications and that specific information is available in the public Policy - Use of agency's information and communication technology by external organisations.
Dealing with uncertainties in PIP evaluations and PDCO opinions	Experience gathered so far and suggestions were discussed for how to address uncertainties related to the development of a paediatric medicine, and how to share these in a more systematic and transparent way.

VIII Any other business

- A draft concept paper* on the participation of children / young people in PDCO activities was presented for consultation to all the members. Comments to be made by the July 8th. The topic will be re-discussed at the August PDCO.
- EU Ombudsman's press release on recommendation for more transparency concerning medicines for children (http://www.ombudsman.europa.eu/en/press/release.faces/en/11610/html.bookmark): A summary of the Ombudsman draft recommendation to EMA (May 2012) was presented to the PDCO. A complaint for maladministration was submitted to the Ombudsman in October 2009 by AstraZeneca and Takeda, following the refusal of the Waiver for candesartan in heart failure. The Ombudsman concluded that there was no unfair treatment of applicants from the part of the EMA, but requested that the grounds of PDCO opinions be made more transparent, so that applicants could understand why apparently different conclusions may be reached for products of the same therapeutic class. The Ombudsman concluded that the Agency should make available to the public a justification of the outcome of the assessment of PIPs and waivers. Of note, the Ombudsman concluded that the PDCO was entitled to require studies in heart failure, a high unmet paediatric need. This opinion is in line with the judgment from the Court of Justice of the European Union (Nycomed vs EMA T-52/09) concluded in Feb 2012. The Agency is working on a proposal to follow this recommendation, noting that this may require altering the agreed definition of commercially confidential information. The proposal could take the form of a lay language summary of the application made, with its outcome as decided by the PDCO. This summary could be available in the summary report and/or on the EMA website, once the Executive Director takes the EMA decision. The summary could facilitate understanding by stakeholders of the reasoning of the PDCO, but would not replace the scientific grounds discussed at length in the PDCO summary report, the latter being a part of the formal opinion of the Committee.
- The PDCO was informed that the Agency will start publishing the non-confidential part of the PDCO minutes from July 2012, starting with the present minutes of the June meeting (after their approval by the PDCO in July).

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 June 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
Peter Szitanyi	Restriction level 4	EMEA-000006-PIP03-12
Peter Szitanyi	Restriction level 4	EMEA-000007-PIP04-12
Peter Szitanyi	Restriction level 4	EMEA-000063-PIP02-12
Adriana Ceci	Restriction level 3	EMEA-000715-PIP02-11
Adriana Ceci	Restriction level 3	EMEA-000118-PIP02-10-M01
Adriana Ceci	Restriction level 3	EMEA-001222-PIP01-11
Adriana Ceci	Restriction level 3	EMEA-001217-PIP01-11
Adriana Ceci	Restriction level 3	EMEA-C1-000431-PIP01-08-M04
Adriana Ceci	Restriction level 3	EMEA-000309-PIP01-08-M04
Adriana Ceci	Restriction level 3	EMEA-000548-PIP01-09-M03
Christoph Male	Restriction level 3	EMEA-000183-PIP02-12
Dobrin Konstantinov	Restriction level 3	EMEA-000191-PIP01-08-M04
Dobrin Konstantinov	Restriction level 3	EMEA-000468-PIP02-12
Gerard Pons	Restriction level 3	EMEA-000347-PIP01-08-M02
Gerard Pons	Restriction level 3	EMEA-000630-PIP02-09-M02
Gerard Pons	Restriction level 3	EMEA-000662-PIP02-09-M02
Jaroslav Sterba	Restriction level 3	EMEA-000468-PIP02-12
Jaroslav Sterba	Restriction level 3	EMEA-001033-PIP02-11
Jaroslav Sterba	Restriction level 3	EMEA-001274-PIP01-12
Marek Migdal	Restriction level 3	EMEA-000184-PIP01-08-M01

Member, alternate, expert name	Outcome restriction following evaluation of electronic declaration of interest	Topics on the current Committee Agenda for which this restriction applies
Michal Odermarsky	Restriction level 3	EMEA-000774-PIP01-09-M01
Michal Odermarsky	Restriction level 3	EMEA-001005-PIP01-10-M01
Andreas Teloudes	Restriction level 4	EMEA-000006-PIP03-12
Andreas Teloudes	Restriction level 4	EMEA-000007-PIP04-12
Andreas Teloudes	Restriction level 4	EMEA-000063-PIP02-12
Andreas Teloudes	Restriction level 4	EMEA-000144-PIP01-07-M03
Andreas Teloudes	Restriction level 4	EMEA-000406-PIP01-08-M03
Andreas Teloudes	Restriction level 4	EMEA-001275-PIP01-12
Andreas Teloudes	Restriction level 4	EMEA-000468-PIP02-12
Christoph Male	Restriction level 4	EMEA-001139-PIP01-11-M01
Christoph Male	Restriction level 4	EMEA-000428-PIP01-08-M01
Christoph Male	Restriction level 4	EMEA-000312-PIP01-08-M04
Marek Migdal	Restriction level 4	EMEA-000525-PIP01-08-M01
Matthias Keller	Restriction level 4	EMEA-001279-PIP01-12
Matthias Keller	Restriction level 4	EMEA-001281-PIP01-12
Paolo Rossi	Restriction level 4	EMEA-000872-PIP01-10-M01
Paolo Rossi	Restriction level 4	EMEA-001110-PIP01-10-M01
Paolo Rossi	Restriction level 4	EMEA-000558-PIP01-09-M01
Peter Szitanyi	Restriction level 4	EMEA-001268-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
Igor Francetic	Restriction level 4	EMEA-001185-PIP01-11
Igor Francetic	Restriction level 4	EMEA-001230-PIP01-11
Igor Francetic	Restriction level 4	EMEA-000235-PIP02-10-M01

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 webpage (after the PDCO Opinion is adopted), and on the Opinions and decisions on paediatric investigation plans webpage (after the EMA Decision is issued).

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
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 June 2012

List of Participants

Chair

Daniel BRASSEUR

Vice-chair

Dirk MENTZER

Members appointed by national agencies or CHMP

Christoph MALE	Austria
Koenraad NORGA	Belgium
Dobrin KONSTANTINOV	Bulgaria
Jaroslav STERBA	Czech Republic
Marianne ORHOLM	Denmark
Irja LUTSAR	Estonia
Pirjo LAITINEN-PARKONNEN	Finland
Dirk MENTZER	Germany
Stefanos MANTAGOS	Greece
Agnes GYURASICS	Hungary
Gylfi OSKARSSON	Iceland
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
Marta GRANSTRÖM	Sweden
Julia DUNNE	United Kingdom

Alternates appointed by national agencies or CHMP

Karl Heinz HUEMER	Austria
Jacqueline CARLEER	Belgium
Peter SZITANYI	Czech Republic
Ann Marie KAUKONEN	Finland
Sylvie BENCHETRIT	France
Birka LEHMANN	Germany
Francesca ROCCHI	Italy
Herbert LENICKER	Malta
Johannes TAMINIAU	The Netherlands
Ine Skottheim RUSTEN	Norway
Jolanda WITKOWSKA-OZOGOWSKA	Poland
Dana Gabriela MARIN	Romania
Pending	Slovenia
Maria Jesus FERNANDEZ CORTIZO	Spain
Viveca Lena ODLIND	Sweden

Members representing patients' organisations

Tsveta SCHYNS-LIHARSKA

Alternates representing patients' organisations

Gerard NGUYEN

Members representing health care professionals

Adriana CECI

Jean Pierre ABOULKER

Anthony James NUNN

Alternates representing health care professionals

Paolo PAOLUCCI

Experts

Peter BAUER

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
Cecile OLLIVIER	Scientific Administrator, Paediatric Medicines
Dobromir PENKOV	Scientific Administrator, Paediatric Medicines
Elin Haf DAVIES	Scientific Administrator, Paediatric Medicines
Emma SALA SORIANO	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
Isabel PEREZ	Assistant
Agustina POGGIO	Assistant