20 January 2023
EMA/PDCO/3263/2023
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 13-16 December 2022

Chair: Brian Aylward – Vice-Chair: Sylvie Benchetrit

Health and safety information

In accordance with the Agency's health and safety policy, delegates were briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in this set of minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published 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).

Of note, this set of minutes is a working document primarily designed for PDCO members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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1. Introductions

1.1. Welcome and declarations of interest of members, alternates and experts

The Chair opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) pandemic, and the associated EMA Business Continuity Plan (BCP), the meeting was held in-person with some members connected remotely (hybrid setting).

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics.

Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Chair welcomed the new member and thanked the departing members for their contributions to the Committee.

1.2. Adoption of agenda

The agenda for 13-16 December 2022 meeting was adopted.

1.3. Adoption of the minutes

The minutes for 8-11 November 2022 meeting were adopted and will be published on the EMA website.

2. Opinions

Some information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

2.1. Opinions on Products

2.1.1. 2'-MOE antisense oligonucleotide targeting apoC-III (ISIS 678354) - EMEA-003177-PIP01-21

Ionis Pharmaceuticals, Inc; Treatment of familial chylomicronaemia syndrome

Day 120 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and the additional clarifications received from the applicant, and further discussions at the Paediatric Committee, all issues were considered resolved and a positive opinion including a deferral was adopted by the PDCO for the PIP for 2'-MOE antisense oligonucleotide targeting apoC-III (ISIS 678354) for the paediatric population from 2 years to less than 18 years of age in the condition of treatment of familial chylomicronaemia syndrome.
The PDCO recommended granting a waiver for 2'-MOE antisense oligonucleotide targeting apoC-III (ISIS 678354) for the paediatric population from birth to less than 2 years of age on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).
The PDCO also recommended granting a deferral for completion of all studies contained in the paediatric investigation plan.

2.1.2. Asundexian - EMEA-003144-PIP01-21

Bayer AG; Prevention of arterial thromboembolism

Day 120 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and the additional clarifications received from the applicant, and further discussions at the Paediatric Committee, all issues were considered resolved and a positive opinion including a deferral was adopted by the PDCO for the PIP for asundexian for the paediatric population from 6 months to less than 18 years of age in the condition of prevention of arterial thromboembolism.
The PDCO recommended granting a waiver for asundexian for the paediatric population from birth to less than 6 months of age on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.3. Perflubutane - EMEA-003037-PIP02-22

GE Healthcare AS; Diagnostic evaluation of focal hepatic lesions

Day 120 opinion

Diagnostic / Oncology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for perflubutane for all paediatric patients from birth to less than 18 years of age in the condition of diagnostic evaluation of focal hepatic lesions. The PDCO granted a deferral for the completion of this PIP.

2.1.4. Avexitide acetate - Orphan - EMEA-003125-PIP02-21

EigerBio Europe Limited; Treatment of congenital hyperinsulinism

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

Based on the assessment of this application and the additional clarifications received from the applicant, and further discussions at the Paediatric Committee, all issues were considered resolved and a positive opinion was adopted by the PDCO for the PIP for avexitide acetate for all subsets of the paediatric population (birth to 18 years of age) in the condition of treatment of congenital hyperinsulinism.

2.1.5. Triheptanoin - Orphan - EMEA-001920-PIP04-19

Ultragenyx Germany GmbH; Treatment of long-chain fatty acid oxidation disorders

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

In the written response the applicant addressed the remaining issues raised by the Committee at Day 90.
Based on the assessment of this application and the additional information provided by the applicant a positive opinion on a PIP for triheptanoin for children from birth to less than 18 years of age in the condition of 'treatment of long-chain fatty acid oxidation disorders' was adopted.

2.1.6. Depemokimab - EMEA-003051-PIP05-22

GlaxoSmithKline Trading Services Limited; Treatment of hypereosinophilic syndrome (HES)

Day 120 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO discussed at Day 120, during the December 2022 plenary meeting, an application for a paediatric investigation plan with a waiver and a deferral for depemokimab for treatment of hypereosinophilic syndrome (HES).
The Committee confirmed all conclusions reached at Day 90 and took into consideration further information provided by the applicant between Day 90 and Day 120.
The PDCO adopted a positive opinion on a paediatric investigation plan with a deferral and a waiver for children under the age of 6 years on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible in the treatment of hypereosinophilic syndrome.

2.1.7. Satralizumab - Orphan - EMEA-001625-PIP04-22

Roche Registration GmbH; Treatment of autoimmune encephalitis

Day 120 opinion

Neurology

Summary of Committee discussion:

The PDCO discussed at Day 120, during the December 2022 plenary meeting, an application for a paediatric investigation plan for satralizumab for the treatment of autoimmune encephalitis.
The Committee took into consideration the conclusions reached at Day 90 as well as the information that the applicant provided between Day 90 and Day 120 and adopted a positive opinion at Day 120 on a paediatric investigation plan for the treatment of autoimmune encephalitis with a deferral and a waiver for children less than 2 years of age on the grounds that the disease for which the medicinal product is intended does not occur in the specified paediatric subset.

2.1.8. Troriluzole (hydrochloride) - Orphan - EMEA-003084-PIP03-22

Biohaven Pharmaceutical Ireland DAC; Treatment of hereditary spinocerebellar ataxia

Day 120 opinion

Neurology

Summary of Committee discussion:

In the written response, the applicant addressed the remaining issues raised by the Committee. Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for the proposed medicine for the age subset from 11 years to less than 18 years of age in the condition of treatment of hereditary spinocerebellar ataxia was adopted. The PDCO agreed on a waiver in a subset of children on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible. The PDCO granted a deferral for the completion of this PIP.

2.1.9. Autologous CD4+ and CD8+ T cells transduced with lentiviral vector encoding a chimeric antigen receptor (CAR) directed against CD19 and preserving the T cell

phenotype of the leukapheresis starting material (YTB323) - EMEA-003212-PIP01-22

Novartis Europharm Limited; Treatment of mature B cell neoplasms

Day 120 opinion

Oncology

Summary of Committee discussion:

The PDCO discussed at Day 120, during the December 2022 plenary meeting, an application for a paediatric investigation plan for autologous CD4+ and CD8+ T cells transduced with lentiviral vector encoding a chimeric antigen receptor (CAR) directed against CD19 and preserving the T cell phenotype of the leukapheresis starting material (YTB323) for the treatment of mature B cell neoplasms.
The PDCO agreed with all conclusions reached at Day 90 and adopted at Day 120 a positive opinion on a paediatric investigation plan for the treatment of mature B cell neoplasms with a deferral and a waiver for children weighing less than 6 kg on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for these paediatric patients.

2.1.10. Fianlimab - EMEA-003207-PIP01-22

Regeneron Ireland DAC; Treatment of melanoma

Day 120 opinion

Oncology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for fianlimab for patients from 12 years to less than 18 years of age in the condition of treatment of melanoma. The PDCO agreed on a waiver in patients less than 12 years of age on the grounds that the disease does not occur in this age subset. The PDCO granted a deferral for the completion of this PIP.

2.1.11. Naxitamab - Orphan - EMEA-002346-PIP01-18

Y-mAbs Therapeutics A/S; Treatment of neuroblastoma

Day 120 opinion

Oncology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for naxitamab for patients from 1 year to less than 18 years of age in the condition of treatment of neuroblastoma. The PDCO agreed on a waiver in children below 1 year of age on the ground that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset. The PDCO granted a deferral for the completion of this PIP.

2.1.12. Tirzepatide - EMEA-002360-PIP02-22

Eli Lilly and Company; Treatment of obesity

Day 120 opinion

Other

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for the proposed medicine for children and adolescents from 6 years to less than 18 years of age, in the condition of treatment of obesity was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 6 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments. The PDCO granted a deferral for the completion of this PIP.

2.1.13. Landiolol (hydrochloride) - EMEA-001150-PIP03-22

AOP Orphan Pharmaceuticals GmbH; Treatment of ventricular tachycardia and ventricular fibrillation

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

The PDCO confirmed the outcome of Day 30 discussion and based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant´s request for a waiver.
The PDCO recommended granting a waiver for landiolol hydrochloride for all subsets of the paediatric population (from birth to less than 18 years of age) for the condition of treatment of ventricular tachycardia and ventricular fibrillation on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need.

2.1.14. Ziltivekimab - EMEA-002840-PIP02-22

Novo Nordisk A/S; Treatment of heart failure

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for ziltivekimab for all subsets of the paediatric population (birth to 18 years of age) in the condition of treatment of heart failure on the grounds that

this medicinal product is likely to be ineffective in this condition. With the applicant's agreement the PDCO extended the waiver to all pharmaceutical forms and all routes of administration.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.15. Efgartigimod alfa - EMEA-002597-PIP09-22

argenx BV; Treatment of bullous pemphigoid

Day 60 opinion

Dermatology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for efgartigimod alfa for all subsets of the paediatric population (birth to less than 18 years of age) in the condition of bullous pemphigoid on the grounds of lack of safety for patients from birth to less than 2 years of age and on the grounds lack of significant therapeutic benefit for from 2 to less than 18 years of age.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.16. Setanaxib - Orphan - EMEA-003310-PIP01-22

Calliditas Therapeutics France SAS; Treatment of primary biliary cholangitis

Day 60 opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

Based on the assessment of this application and discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for setanaxib for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of primary biliary cholangitis on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s). The PDCO in agreement with the applicant extended the waiver to all pharmaceutical forms and all routes of administration.

2.1.17. Acetylsalicylic acid / rivaroxaban - EMEA-003308-PIP01-22

Alfred E. Tiefenbacher (GmbH & Co. KG); Prevention of atherothrombotic events

Day 60 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for acetylsalicylic acid / rivaroxaban for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of atherothrombotic events.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.18. Icerguastat - Orphan - EMEA-003312-PIP01-22

InFlectis BioScience S.A.S; Treatment of amyotrophic lateral sclerosis

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for icerguastat for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of amyotrophic lateral sclerosis.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.19. Retifanlimab - Orphan - EMEA-002798-PIP03-22

Incyte Biosciences Distribution B.V.; Treatment of Merkel cell carcinoma

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the December 2022 plenary meeting, a request for a product-specific waiver for retifanlimab for the treatment of Merkel cell carcinoma on the grounds that the disease does not occur in paediatric patients.
The PDCO confirmed all conclusions reached at Day 30 and adopted a positive opinion at Day 60 on a product specific waiver for this product for all subsets of the paediatric population (from birth to less than 18 years of age) in the conditions of “treatment of Merkel cell carcinoma” on the grounds that the disease does not occur in paediatric patients.

The applicant agreed for the waiver to be extended to all pharmaceutical forms and all routes of administration.

2.1.20. EMEA-003319-PIP01-22

Treatment of borderline personality disorder (BPD)

Day 60 opinion

Psychiatry

Note: Withdrawal request received on 29 November 2022

2.1.21. Tetanus toxoid - EMEA-003311-PIP01-22

IBSS BIOMED S.A.; Prevention of infectious disease caused by *Clostridium tetani*

Day 60 opinion

Vaccines

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the December 2022 plenary meeting, a request for a product-specific waiver for tetanus toxoid for the prevention of infectious disease caused by *Clostridium tetani* on the grounds of lack of significant therapeutic benefit. The PDCO confirmed all conclusions reached at Day 30 and adopted a positive opinion at Day 60 on a product specific waiver for this product for all subsets of the paediatric population (from birth to less than 18 years of age) in the conditions "prevention of infectious disease caused by *Clostridium tetani*" on the grounds that the medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2.1.22. Live attenuated varicella virus - EMEA-003317-PIP01-22

Prevention of varicella

Day 60 opinion

Vaccines / Infectious Diseases

Note: Withdrawal request received on 16 December 2022

2.1.23. Fenofibrate / rosuvastatin - EMEA-003332-PIP01-22

Laboratoires SMB s.a.; Prevention of cardiovascular events / Treatment of elevated cholesterol with elevated triglycerides

Day 30 discussion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric

Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for fenofibrate / rosuvastatin calcium for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of elevated cholesterol with elevated triglycerides and prevention of cardiovascular events.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.24. Candesartan cilexetil / amlodipine / hydrochlorothiazide - EMEA-002024-PIP02-22

Adamed Pharma S.A.; Treatment of hypertension

Day 30 discussion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for candesartan cilexetil / amlodipine / hydrochlorothiazide for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of hypertension.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.25. Diclofenac / orphenadrine citrate - EMEA-003337-PIP01-22

Verisfield Single Member S.A.; Treatment of pain

Day 30 discussion

Pain

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The condition proposed by the applicant is considered too narrow though, as the grounds for the waiver are applicable to all pain-related indications. The PDCO therefore recommended granting a waiver for diclofenac / orphenadrine citrate for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of pain.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.26. Thiocolchicoside / diclofenac - EMEA-003339-PIP01-22

Verisfield Single Member S.A.; Treatment of pain

Day 30 discussion

Pain

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The condition proposed by the applicant is considered too narrow though, as the grounds for the waiver are applicable to all pain-related indications. The PDCO therefore recommended granting a waiver for thiocolchicoside / diclofenac for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of pain.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.27. Pyridoxine hydrochloride / diclofenac sodium / thiamine hydrochloride / cyanocobalamin - EMEA-003292-PIP02-22

Verisfield Single Member S.A.; Treatment of inflammatory rheumatic diseases / Treatment of inflammatory pain

Day 30 discussion

Pain

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for pyridoxine hydrochloride / diclofenac sodium / thiamine hydrochloride / cyanocobalamin for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of inflammatory pain and treatment of inflammatory rheumatic diseases.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.2. Opinions on Compliance Check

2.2.1. Ivacaftor [N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide] - EMEA-C-000335-PIP01-08-M14

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

Day 60 opinion

Other

Note: Withdrawal request received on 2 December 2022

2.2.2. Methylphenidate (hydrochloride) - EMEA-C-003189-PIP01-22

Laboratorios Lesvi S.L.; Treatment of attention-deficit hyperactivity disorder

Day 30 opinion

Psychiatry

Note: Withdrawal request received on 20 December 2022

2.2.3. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA-C-001830-PIP01-15-M02

Seqirus S.r.l.; Prevention of influenza infection

Day 30 opinion

Vaccines

Summary of Committee discussion:

The PDCO agreed that all studies are compliant with the agreed PIP.

2.2.4. Empagliflozin - EMEA-C-000828-PIP01-09-M09

Boehringer Ingelheim International GmbH; Treatment of type 2 diabetes mellitus

Day 30 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

The PDCO agreed all studies were conducted in compliance with the agreed PIP.

2.2.5. Linagliptin - EMEA-C-000498-PIP01-08-M10

Boehringer Ingelheim International GmbH; Treatment of type 2 diabetes mellitus

Day 30 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

The PDCO agreed all studies were conducted in compliance with the agreed PIP.

2.2.6. Avacopan - EMEA-C4-002023-PIP01-16-M06

ChemoCentryx Ireland Ltd.; Treatment of anti-neutrophil cytoplasmic auto-antibody

(ANCA)-associated vasculitis

Day 30 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

The PDCO discussed at Day 30 the completed Study 5 and considered that the study is compliant with the latest Agency's decision (P/0266/2022) of 27 July 2022.
The PDCO finalised this partially completed compliance procedure on 16 December 2022.

2.2.7. Oteseconazole - EMEA-C-002392-PIP01-18-M02

Gedeon Richter Plc.; Treatment of vulvovaginal candidiasis

Day 30 opinion

Infectious Diseases

Summary of Committee discussion:

The PDCO adopted on 16 December 2022 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's decision (P/0460/2021) of 29 October 2021.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Macitentan - Orphan - EMEA-001032-PIP01-10-M05

Janssen-Cilag International NV; Treatment of systemic sclerosis / Treatment of pulmonary arterial hypertension / Treatment of idiopathic pulmonary fibrosis

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

The applicant addressed all outstanding issues satisfactorily prior to Day 60 of the procedure.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency’s latest decision (P/0480/2021 of 3 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.2. Rocatinlimab - EMEA-002886-PIP01-20-M02

Amgen Europe B.V.; Treatment of atopic dermatitis

Day 60 opinion

Dermatology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0168/2022 of 13 May 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Avatrombopag maleate - EMEA-001136-PIP01-11-M02

Swedish Orphan Biovitrum AB; Treatment of chronic immune thrombocytopenia

Day 60 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0373/2019 of 22 November 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Crovalimab - EMEA-002709-PIP01-19-M01

Roche Registration GmbH; Treatment of paroxysmal nocturnal haemoglobinuria / Treatment of atypical haemolytic uremic syndrome

Day 60 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

The applicant addressed all outstanding issues prior to Day 60.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0124/2021 of 17 March 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.5. Garadacimab - Orphan - EMEA-002726-PIP01-19-M03

CSL Behring GmbH; Prevention of hereditary angioedema attacks

Day 60 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO discussed at Day 60, during the December 2022 plenary meeting, a request for modification for garadacimab for the treatment of hereditary angioedema attacks.
Based on the review of the documentation submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be acceptable. Therefore, the PDCO adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0249/2022 of 8 July 2022). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. Allogeneic bone marrow derived mesenchymal stromal cells, ex-vivo expanded - Orphan - EMEA-002706-PIP01-19-M02

medac Gesellschaft für klinische Spezialpräparate mbH; Treatment of acute graft-versus-host disease

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0033/2022 of 1 February 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.7. Avibactam / ceftazidime - EMEA-001313-PIP01-12-M13

Pfizer Europe MA EEIG; Treatment of urinary tract infections / Treatment of intra-abdominal infections / Treatment of pneumonia / Treatment of infections due to aerobic gram-negative organisms

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0001/2022 of 7 January 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Aztreonam / avibactam - EMEA-002283-PIP01-17-M04

Pfizer Europe MA EEIG; Treatment of infections caused by aerobic gram-negative bacteria

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0185/2022 of 13 May 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.9. Cobicistat / atazanavir sulphate - EMEA-001465-PIP01-13-M05

Bristol-Myers Squibb Pharma EEIG; Treatment of human immunodeficiency virus (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

In the written response the applicant provided further information as required by the Committee.
Based on the review of the rationale, submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that some delay of PIP completion date was justified.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0041/2022 of 29 January 2022).

2.3.10. Cobicistat / darunavir - EMEA-001280-PIP01-12-M05

Janssen-Cilag International NV; Treatment of human immunodeficiency virus type 1 infection

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered with some specifications added in the opinion that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0254/2021 of 9 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Lamivudine (3TC) / abacavir (ABC) / dolutegravir (DTG) - EMEA-001219-PIP01-11-M06

ViiV Healthcare UK Limited; Treatment of human immunodeficiency virus (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted, also taking into account that they were requested retrospectively to accommodate what was actually done in the completed study IMPAACT 2019 (Study 3 of the PIP).
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0116/2021 of 17 March 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Tazobactam / ceftolozane - EMEA-001142-PIP02-16-M01

Merck Sharp & Dohme (Europe), Inc.; Treatment of pneumonia

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes (a delay of the completion date of the PIP by 2 years and 10 months) could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0277/2017 of 4 October 2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.13. Tenofovir alafenamide / emtricitabine / cobicistat / darunavir - EMEA-001825-PIP01-15-M04

Janssen-Cilag International NV; Treatment of human immunodeficiency virus type-1 (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0198/2021 of 10 May 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Isoflurane - EMEA-002320-PIP01-17-M03

Sedana Medical AB; Sedation of mechanically ventilated patients

Day 60 opinion

Neonatology - Paediatric Intensive Care

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, including the responses submitted since Day 30, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0086/2022 of 11 March 2022). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Fordadistrogene movaparvovec - Orphan - EMEA-002741-PIP01-20-M01

Pfizer Europe MA EEIG; Treatment of Duchenne muscular dystrophy

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0518/2020 of 21 December 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Galcanezumab - EMEA-001860-PIP03-16-M08

Eli Lilly and Company Limited; Prevention of migraine headaches

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0142/2022 of 13 April 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Evoncabtagene pazurgedleucel - EMEA-002881-PIP01-20-M01

CRISPR Therapeutics AG; Treatment of B-lymphoblastic leukaemia/lymphoma / Treatment of mature B cell neoplasms

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the December 2022 plenary meeting, a request for modification for evoncabtagene pazurgedleucel for the treatment of B-lymphoblastic leukaemia/lymphoma and for the treatment of mature B cell neoplasms.
The PDCO confirmed all the conclusions reached at Day 30 and took into consideration the information the applicant provided between Day 30 and Day 60.
Based on the review of the documentation submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be acceptable. Therefore, the PDCO adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0321/2021 of 11 August 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.18. Calcium chloride / aprotinin / thrombin / fibrinogen - EMEA-001079-PIP01-10-M06

Kedrion S.p.A.; Treatment of haemorrhage resulting from a surgical procedure / Prevention of haemorrhage resulting from a surgical procedure

Day 60 opinion

Other

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted. The scope of the PIP has been amended to a waiver in all subsets of the paediatric population from birth to less than 18 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0199/2018 of 19 July 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.19. Lanadelumab - Orphan - EMEA-001864-PIP03-19-M01

Takeda Pharmaceuticals International AG Ireland Branch; Prevention of attacks of idiopathic non-histaminergic angioedema (INHA)

Day 60 opinion

Other

Summary of Committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO amended the scope of the waiver of its own motion to cover all subsets of the paediatric population, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0476/2020 of 1 December 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.20. Azelastine hydrochloride / mometasone furoate - EMEA-003122-PIP01-21-M01

Lek Pharmaceuticals d.d.; Treatment of seasonal allergic rhinitis

Day 60 opinion

Oto-rhino-laryngology

Summary of Committee discussion:

The applicant submitted a new proposal after Day 30 discussion.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0347/2022 of 10 August 2022).

2.3.21. Zuranolone - EMEA-003119-PIP01-21-M01

Biogen Netherlands B.V.; Treatment of postpartum depression

Day 60 opinion

Psychiatry

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that proposed changes to the timelines of Study 1 could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0358/2022 of 22 August 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.22. Mirabegron - EMEA-000597-PIP02-10-M09

Astellas Pharma Europe B.V.; Treatment of idiopathic overactive bladder

Day 60 opinion

Uro-nephrology

Summary of Committee discussion:

Between Day 30 and Day 60, the PDCO received responses from the applicant.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0350/2019 of 30 September 2019).

2.3.23. Nedosiran - Orphan - EMEA-002493-PIP01-18-M05

Dicerna Ireland Limited; Treatment of primary hyperoxaluria

Day 60 opinion

Uro-nephrology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0541/2021 of 31 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.24. *Neisseria meningitidis* serogroup B fHbp subfamily B / *Neisseria meningitidis* serogroup B fHbp subfamily A / *Neisseria meningitidis* group Y polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group W-135 polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group C polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group A polysaccharide conjugated to tetanus toxoid carrier protein - EMEA-002814-PIP02-21-M01

Pfizer Europe MA EEIG; Invasive disease caused by *Neisseria meningitidis* group A, B, C, W and Y from 12 months of age to less than 18 years of age

Day 60 opinion

Vaccines

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, and taking into account the additional information provided between Day 30 and Day 60, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0080/2022 of 11 March 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.25. SARS-CoV-2 virus, beta-propiolactone inactivated adjuvanted with CpG 1018 (VLA2001) - EMEA-003077-PIP01-21-M01

Valneva Austria GmbH; Prevention of coronavirus disease 2019 (COVID-19)

Day 60 opinion

Vaccines

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, including responses received between Day 30 and Day 60, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0184/2022 of 13 May 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.26. Ivacaftor - EMEA-000335-PIP01-08-M15

Vertex Pharmaceuticals (Ireland) Ltd; Treatment of cystic fibrosis

Day 30 opinion

Other

Summary of Committee discussion:

The PDCO discussed at Day 30 during the December plenary meeting a modification request for ivacaftor for the treatment of cystic fibrosis.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that even though the proposed changes to the evaluation of the acceptability and palatability of the formulation, the procedure for dose selection and the lung clearance index were not welcomed, these changes could be accepted in view of the patient population concerned.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0163/2020 of 17 April 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.4. Opinions on Re-examinations

No item

2.5. Opinions on Review of Granted Waivers

No item

2.6. Finalisation and adoption of Opinions

No item

2.7. Partial Compliance Checks completed by EMA

The following partial compliance checks have been identified by the PME coordinator and PDCO rapporteur as not needing to be referred to the PDCO for discussion. The PDCO has been informed in writing.

2.7.1. Concizumab - EMEA-C1-002326-PIP04-20

Novo Nordisk A/S; Treatment of congenital haemophilia A

Day 30 letter

Haematology-Hemostaseology

2.7.2. Odevixibat - EMEA-C1-002054-PIP03-20-M02

Albireo AB; Treatment of Alagille syndrome

Day 30 letter

Gastroenterology-Hepatology

2.7.3. Bosutinib - EMEA-C1-000727-PIP01-09-M06

Pfizer Europe MA EEIG; Treatment of chronic myeloid leukaemia

Day 30 letter

Oncology

2.7.4. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA-C3-002330-PIP01-18-M02

Pfizer Europe MA EEIG; Prevention of disease caused by *Streptococcus pneumoniae*

Day 30 letter

Vaccines

3. Discussion of applications

Some information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

3.1. Discussions on Products D90-D60-D30

3.1.1. Zilebesiran - EMEA-003218-PIP01-22

Treatment of hypertension

Day 90 discussion

Cardiovascular Diseases

3.1.2. Danuglipron - EMEA-002944-PIP02-22

Treatment of obesity

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.3. Insulin lispro - EMEA-003166-PIP01-21

Treatment of diabetes mellitus type 1 / Treatment of diabetes mellitus type 2

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.4. EMEA-003241-PIP01-22

Treatment of sickle cell disease

Day 90 discussion

Haematology-Hemostaseology

3.1.5. Adeno-associated virus serotype hu68 containing the human GLB1 gene - Orphan - EMEA-003102-PIP01-21

Passage Bio, Inc.; Treatment of GM1 gangliosidosis

Day 90 discussion

Neurology

Note: Withdrawal request received on 23 December 2022

3.1.6. Cemdisiran (sodium) - Orphan - EMEA-003237-PIP01-22

Regeneron Ireland DAC; Treatment of myasthenia gravis

Day 90 discussion

Neurology

3.1.7. Pozelimab - EMEA-003238-PIP01-22

Treatment of myasthenia gravis

Day 90 discussion

Neurology

3.1.8. Lutetium (177Lu) edotreotide - Orphan - EMEA-003245-PIP01-22

ITM Solucin GmbH; Treatment of gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs)

Day 90 discussion

Oncology

3.1.9. Obecabtagene autoleucel - Orphan - EMEA-003171-PIP01-21

Autolus GmbH; Treatment of acute lymphoblastic leukaemia

Day 90 discussion

Oncology

3.1.10. Humanised IgG2 monoclonal antibody against interleukin-6 - EMEA-003215-PIP01-22

Treatment of macular oedema

Day 90 discussion

Ophthalmology

3.1.11. Furosemide - EMEA-003316-PIP01-22

Treatment of fluid retention

Day 60 discussion

Cardiovascular Diseases

3.1.12. Barzolvolimab - EMEA-003327-PIP01-22

Treatment of chronic spontaneous urticaria

Day 60 discussion

Dermatology

3.1.13. Povorcitinib - EMEA-003313-PIP01-22

Treatment of hidradenitis suppurativa

Day 60 discussion

Dermatology

3.1.14. Rilzabrutinib - EMEA-002438-PIP03-22

Treatment of atopic dermatitis

Day 60 discussion

Dermatology

3.1.15. Ritlecitinib - EMEA-002451-PIP03-22

Treatment of vitiligo

Day 60 discussion

Dermatology

3.1.16. Upadacitinib - EMEA-001741-PIP07-22

Treatment of vitiligo

Day 60 discussion

Dermatology

3.1.17. Recombinant human glutamic acid dexarboxylase (rhGAD65) - EMEA-000609-PIP02-22

Prevention or delay of clinical type 1 diabetes mellitus / Prevention of type 1 diabetes mellitus

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.18. Ciraparantag - EMEA-003321-PIP01-22

Treatment of FXa inhibitor-associated haemorrhage / Prevention of FXa inhibitor-associated haemorrhage

Day 60 discussion

Haematology-Hemostaseology

3.1.19. Izokibep - EMEA-003325-PIP01-22

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis, and juvenile idiopathic arthritis)

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.20. EMEA-003326-PIP01-22

Treatment of infections caused by gram-negative organisms / Complicated urinary tract infections (cUTI) / Hospital associated pneumonia or ventilator associated pneumonia

Day 60 discussion

Infectious Diseases

3.1.21. Lenacapavir / bictegravir - EMEA-003324-PIP01-22

Treatment of human immunodeficiency virus (HIV-1) infection

Day 60 discussion

Infectious Diseases

3.1.22. Luminol - EMEA-003322-PIP01-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 60 discussion

Infectious Diseases

3.1.23. Posoleucel - Orphan - EMEA-002908-PIP02-22

Allovir International DAC; Prevention of viral disease in haematopoietic stem cell transplantation (HCT)

Day 60 discussion

Infectious Diseases

3.1.24. RNA replicase inhibitor - EMEA-003306-PIP01-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 60 discussion

Infectious Diseases

3.1.25. Uproleselan - Orphan - EMEA-003307-PIP01-22

GlycoMimetics, Inc.; Treatment of acute myeloid leukaemia

Day 60 discussion

Oncology

3.1.26. Vutrisiran - Orphan - EMEA-002425-PIP02-22

Alnylam Netherlands B.V.; Treatment of Stargardt disease

Day 60 discussion

Ophthalmology

3.1.27. Dersimelagon - EMEA-002850-PIP03-22

Treatment of systemic sclerosis

Day 60 discussion

Other

3.1.28. mRNA encoding modified human ornithine transcarbamylase - Orphan - EMEA-003315-PIP01-22

Arcturus Therapeutics Europe B.V.; Treatment of ornithine transcarbamylase deficiency / Treatment of ornithine transcarbamylase deficiency, which is characterised by episodes of hyperammonemia and consequent sequelae

Day 60 discussion

Other

3.1.29. Dexpramipexole - EMEA-003328-PIP01-22

Treatment of asthma

Day 60 discussion

Pneumology - Allergology

3.1.30. Pamrevlumab - EMEA-002979-PIP04-22

Treatment of interstitial lung diseases with fibrosis

Day 60 discussion

Pneumology - Allergology

3.1.31. EMEA-003319-PIP02-22

Treatment of major depressive disorder (MDD)

Day 60 discussion

Psychiatry

3.1.32. EMEA-003319-PIP03-22

Treatment of posttraumatic stress disorder (PTSD)

Day 60 discussion

Psychiatry

3.1.33. Influenza recombinant H7 haemagglutinin - EMEA-003314-PIP01-22

Prevention of influenza infection

Day 60 discussion

Vaccines

3.1.34. Phuket modRNA / Darwin modRNA / Austria modRNA / Wisconsin modRNA - EMEA-003318-PIP01-22

Prevention of influenza disease

Day 60 discussion

Vaccines

3.1.35. Single-stranded 5' capped mRNA encoding the respiratory syncytial virus glycoprotein F stabilised in the prefusion conformation - EMEA-003309-PIP01-22

Prevention of lower respiratory tract illness (LRTI) caused by respiratory syncytial virus

(RSV)

Day 60 discussion

Vaccines

3.1.36. Clazakizumab - EMEA-001371-PIP03-22

Prevention of cardiovascular events in patients with atherosclerosis

Day 30 discussion

Cardiovascular Diseases / Uro-nephrology

3.1.37. Clascoterone - EMEA-003330-PIP01-22

Treatment of acne vulgaris

Day 30 discussion

Dermatology

3.1.38. Encaleret - Orphan - EMEA-003348-PIP01-22

Calcilytix Therapeutics, Inc a BridgeBio Company; Treatment of hypoparathyroidism

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.39. Recombinant human tissue nonspecific alkaline phosphatase (TNSALP) fragment crystallizable (Fc) deca aspartate fusion protein - EMEA-003343-PIP01-22

Treatment of hypophosphatasia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.40. Sodium(4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop-1-ynyl)phenyl]allyloxy}-2-methylphenoxy)acetate - Orphan - EMEA-003331-PIP01-22

Reneo Pharmaceuticals Inc; Treatment of primary mitochondrial disorders

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.41. EMEA-003002-PIP03-22

Treatment of portal hypertension with compensated cirrhosis

Day 30 discussion

Gastroenterology-Hepatology

3.1.42. EMEA-003090-PIP02-22

Treatment of hereditary angioedema

Day 30 discussion

Haematology-Hemostaseology

3.1.43. Enpatoran - EMEA-003342-PIP02-22

Treatment of systemic lupus erythematosus

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.44. Enpatoran - EMEA-003342-PIP01-22

Treatment of cutaneous lupus erythematosus

Day 30 discussion

Immunology-Rheumatology-Transplantation / Dermatology

3.1.45. Trimodulin (human IgM, IgA, IgG solution) - EMEA-002883-PIP02-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Neonatology - Paediatric Intensive Care / Infectious Diseases

3.1.46. Recombinant human arylsulfatase A - Orphan - EMEA-002050-PIP02-22

Takeda Pharmaceuticals International AG Ireland Branch; Treatment of metachromatic leukodystrophy

Day 30 discussion

Neurology

3.1.47. Sodium ({(2S)-1,4-bis[2-(4-chloro-3-fluorophenoxy)acetamido]bicyclo[2.2.2]octan-2-yl}oxy)methyl hydrogen phosphate-2-amino-2-(hydroxymethyl)propane-1,3-diol (1/1/1) - Orphan - EMEA-003344-PIP01-22

Calico Life Sciences LLC; Treatment of vanishing white matter disease

Day 30 discussion

Neurology

3.1.48. Eftilagimod alpha - EMEA-002698-PIP02-22

Treatment of head and neck epithelial malignant neoplasms

Day 30 discussion

Oncology

3.1.49. Eftilagimod alpha - EMEA-002698-PIP03-22

Treatment of non-small cell lung cancer

Day 30 discussion

Oncology

3.1.50. Pembrolizumab - EMEA-001474-PIP03-22

Treatment of Hodgkin lymphoma / Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)

Day 30 discussion

Oncology

3.1.51. Sotorasib - EMEA-002690-PIP02-22

Treatment of malignant colorectal neoplasms

Day 30 discussion

Oncology

3.1.52. Upifitamab rilsodotin - EMEA-003340-PIP01-22

Treatment of primary peritoneal cancer / Treatment of fallopian tube cancer / Treatment of ovarian cancer

Day 30 discussion

Oncology

3.1.53. An acellular tubular graft composed of human collagen types I and III and other extracellular matrix proteins, including fibronectin and vitronectin - EMEA-003345-PIP01-22

Treatment of vascular injuries

Day 30 discussion

Other

3.1.54. Hemopexin, human - Orphan - EMEA-003333-PIP01-22

CSL Behring GmbH; Treatment of sickle cell disease

Day 30 discussion

Other

3.1.55. Camlipixant - EMEA-003334-PIP01-22

Treatment of refractory chronic cough

Day 30 discussion

Pneumology - Allergology

3.1.56. EMEA-003347-PIP01-22

Treatment of glomerulonephritis and nephrotic syndrome

Day 30 discussion

Uro-nephrology

3.1.57. Single-stranded 5' capped mRNA encoding the HAs of the influenza virus - EMEA-003346-PIP01-22

Prevention of influenza disease

Day 30 discussion

Vaccines

3.1.58. Varicella / Rubella virus (live, attenuated) / Measles virus (live, attenuated) / Mumps virus (live, attenuated) - EMEA-003341-PIP01-22

Prevention of measles, mumps, rubella and varicella

Day 30 discussion

Vaccines / Infectious Diseases

3.2. Discussions on Compliance Check

The following compliance checks have been identified for discussion and the members of the PDCO have been invited to comment on issues of possible non-compliance.

3.2.1. *Neisseria meningitidis* serogroup B fHbp subfamily B / *Neisseria meningitidis* serogroup B fHbp subfamily A / *Neisseria meningitidis* group A polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group W-135 polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group Y polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria*

meningitidis group C polysaccharide conjugated to tetanus toxoid carrier protein - EMEA-C1-002814-PIP02-21

Pfizer Europe MA EEIG; Treatment of invasive disease caused by *Neisseria meningitidis* group A, B, C, W and Y from 2 months of age

Day 30 discussion

Vaccines

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Crinecerfont; 2-Thiazolamine, 4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-2-propyn-1-yl; NBI-74788 - Orphan - EMEA-002700-PIP01-19-M01

Neurocrine Therapeutics Ltd.; Treatment of congenital adrenal hyperplasia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.2. Drospirenone / estetrol monohydrate - EMEA-001332-PIP01-12-M06

Estetra SRL; Prevention of pregnancy

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.3. Evinacumab - EMEA-002298-PIP01-17-M05

Ultragenyx Germany GmbH; Treatment of elevated cholesterol

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Ibutamoren mesilate - Orphan - EMEA-003032-PIP01-21-M01

Lumos Pharma, Inc.; Treatment of growth hormone deficiency

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.5. Baricitinib - EMEA-001220-PIP01-11-M07

Eli Lilly and Company Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.6. Baloxavir marboxil - EMEA-002440-PIP01-18-M04

Roche Registration GmbH; Treatment of influenza / Prevention of influenza

Day 30 discussion

Infectious Diseases

3.3.7. Relebactam monohydrate / cilastatin sodium / imipenem monohydrate - EMEA-001809-PIP01-15-M03

Merck Sharp & Dohme (Europe), Inc.; Treatment of gram-negative bacterial infections

Day 30 discussion

Infectious Diseases

3.3.8. Fremanezumab - EMEA-001877-PIP01-15-M03

Teva GmbH; Prevention of migraine headaches

Day 30 discussion

Neurology

3.3.9. Glycopyrronium bromide - EMEA-001366-PIP01-12-M03

Proveca Pharma Limited; Treatment of sialorrhoea

Day 30 discussion

Neurology

3.3.10. Quizartinib - Orphan - EMEA-001821-PIP01-15-M06

Daiichi Sankyo Europe GmbH; Treatment of acute myeloid leukaemia

Day 30 discussion

Oncology

3.3.11. Gilteritinib (as fumarate) - Orphan - EMEA-002064-PIP01-16-M04

Astellas Pharma Europe B.V.; Treatment of acute myeloid leukaemia

Day 30 discussion

Oncology / Haematology-Hemostaseology

3.3.12. Inotuzumab ozogamicin - Orphan - EMEA-001429-PIP01-13-M07

Pfizer Europe MA EEIG; Treatment of acute lymphoblastic leukaemia

Day 30 discussion

Oncology / Haematology-Hemostaseology

3.3.13. Afamelanotide - Orphan - EMEA-000737-PIP02-11-M02

Clinuvel Europe Limited; Treatment of erythropoietic protoporphyria

Day 30 discussion

Other

3.3.14. Selexipag - EMEA-000997-PIP01-10-M06

Janssen-Cilag International NV; Treatment of pulmonary arterial hypertension

Day 30 discussion

Other

3.3.15. Begelomab - Orphan - EMEA-001744-PIP01-14-M02

ADIENNE S.r.l SU; Treatment of acute graft-versus-host disease (aGvHD)

Day 30 discussion

Other / Immunology-Rheumatology-Transplantation

3.3.16. Methoxyflurane - EMEA-000334-PIP01-08-M11

Medical Developments UK Ltd; Treatment of acute pain

Day 30 discussion

Pain

3.3.17. Budesonide / glycopyrronium bromide / formoterol fumarate dihydrate - EMEA-002063-PIP01-16-M02

AstraZeneca AB; Treatment of asthma

Day 30 discussion

Pneumology - Allergology

3.3.18. Cariprazine hydrochloride - EMEA-001652-PIP01-14-M04

Gedeon Richter Plc.; Treatment of schizophrenia

Day 30 discussion

Psychiatry

3.3.19. Lumasiran sodium - Orphan - EMEA-002079-PIP01-16-M03

Alnylam UK Limited; Treatment of primary hyperoxaluria type 1

Day 30 discussion

Uro-nephrology

4. Nominations

Information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

4.1. List of submissions of applications with start of procedure 3 January 2023 for Nomination of Rapporteur and Peer reviewer

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.2. Nomination of Rapporteur for requests of confirmation on the applicability of the EMA decision on class waiver

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

5. Scientific Advice Working Party (SAWP) and Paediatric Committee (PDCO) Interaction

Information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

5.1. New Scientific Advice

No item

5.2. Final Scientific Advice (Reports and Scientific Advice letters)

No item

6. Discussion on the applicability of class waivers

6.1. Discussions on the applicability of class waiver for products

No item

7. Discussion on the inclusion of an indication within a condition in an agreed PIP/waiver

7.1. Discussion on the possibility to include an indication within a condition in an agreed PIP/waiver

No item

8. Annual reports on deferrals

The members of the PDCO took note of the products listed in the Annex B.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

9.1.1. PDCO membership

The Chair thanked Nora Kriauzaite for her contribution as a member for representing patients' organisations.

The Chair thanked Sara Galluzzo for her contribution as a member for Italy.

The Chair announced that Tomasz Grybek is the new member for representing patients' organisations, replacing Nora Kriauzaite.

9.1.2. Vote by Proxy

None

9.1.3. Strategic Review and Learning Meeting (SRLM)

No item

9.2. Coordination with EMA Scientific Committees or CMDh-v

9.2.1. Committee for Medicinal Products for Human Use (CHMP)

Summary of Committee discussion:

The list of PIP-related CHMP procedures starting in November 2022, was presented to the PDCO members. Feedback on ongoing CHMP procedures was provided to the Committee by the PDCO experts involved.

9.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

9.3.1. Non-clinical Working Party: D30 Products identified

PDCO member: Karen van Malderen

Summary of Committee discussion:

The Vice-Chair of the Non-clinical Working Party (NcWP) identified the products which will require NcWP evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward (*ad ínterim*)

Summary of Committee discussion:

The Chair of the Formulation Working Group (FWG) identified the products which will require FWG evaluation and discussion.

A list of PDCO Formulation Working Group experts was presented to PDCO for appointment for year 2023. The list was adopted during the plenary.

9.3.3. Modelling and Simulation Working Party (MSWP)

PDCO member: Kristin Karlsson

Summary of Committee discussion:

Upon request of the PDCO the MSWP had developed a Q&A on the current understanding of the role of modelling and simulation on paediatric development which was presented to the Committees. The PDCO congratulated the authors for the work done and recommended further discussion with other regulators at international level in the appropriate fora. This Q&A will be further refined and will be finally published on the EMA website. The PDCO will be kept up to date with progress.

9.3.4. Methodology Working Party (MWP)

Introduction of MWP to the Committees

PDCO member: Kristin Karlsson; MWP Chair: Christian Roes

Summary of Committee discussion:

The Committee was introduced to the new structures within the Methodology domain, as part of the Working Party Reorganisation. Specific focus was on the work of the Methodology Working Party itself. Operational support to PDCO remains seamless during any transitions.

9.3.5. Patients and Consumers Working Party (PCWP)/Healthcare Professionals Working Party (HCPWP)

No item

9.4. Cooperation within the EU regulatory network

9.4.1. European Network of Paediatric Research (Enpr) - European Medicines Agency (EMA)

No item

9.5. Cooperation with International Regulators

9.5.1. Paediatric Cluster Teleconference

Summary of Committee discussion:

The November 2022 minutes of the cluster were shared with the PDCO members for information.

9.5.2. Food and Drug Administration (FDA) – Introduction Liaison Official

Summary of Committee discussion:

The PDCO noted the introduction of the Liaison Official.

9.6. Contacts of the PDCO with external parties and interaction with the Interested Parties to the Committee

No item

9.7. PDCO work plan

PDCO Chair: Brian Aylward

Summary of Committee discussion:

The PDCO workplan for 2023 was adopted and has been published.

9.8. Planning and reporting

9.8.1. EMA Business Pipeline activity and Horizon scanning

Q4/2022 Update of the Business Pipeline report for the human scientific committees

Summary of Committee discussion:

The business pipeline report for Q4/2022 was provided for information.

10. Any other business

10.1. COVID-19 update

Summary of Committee discussion:

The update was cancelled.

10.2. Upcoming Innovation Task Force (ITF) meetings

Summary of Committee discussion:

Two ITF meetings taking place in December 2022 were presented for information.

10.3. ICH M11 Public Consultation

Summary of Committee discussion:

An update on the ICH M11 was provided to the group. The three deliverables, the Guideline, the protocol template and the Technical Specification have been published for public consultation.

Further information can be found on the ICH M11 page, including the three aforementioned documents available for download. The public consultation is open until 26 February 2023.

In parallel to the public consultation on the ICH M11 deliverables, a group has been set up to particularly review the integration of the E9 principles in the protocol template.

11. Breakout sessions

11.1. HIV

Summary of Committee discussion:

The group identified areas where focused discussion will be needed to streamline assessment and related presentation aspects of proposed HIV related PIPs, particularly for HIV Fix Dose Combination Products (FDC).

Further discussion on the issues raised will take place at the January 2023 meeting.

11.2. Neonatology

Summary of Committee discussion:

Discussion on organisational aspects of the planned revision of the neonatal guideline as well as debriefing from the recent INC workshop in November 2022.

11.3. Paediatric oncology

Summary of Committee discussion:

The group was informed about initiatives related to oncology of the Scientific Advice Working Party and Oncology Working Party. In addition, there was a discussion about ways for the PDCO to access Real World Evidence data in paediatric oncology.

The Chair thanked all participants and closed the meeting.

12. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 13-16 December 2022 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Brian Aylward	Chair	Ireland	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Marleen Renard	Member	Belgium	No restrictions applicable to this meeting	
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Zena Gunther	Member	Cyprus	No interests declared	
Tereza Bazantova	Alternate	Czechia	No interests declared	
Nanna Borup Johansen	Member	Denmark	No interests declared	
Louisa Braun Exner	Alternate	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Pauliina Lehtolainen-Dalkilic	Member	Finland	No interests declared	
Anne Paavola	Alternate	Finland	No interests declared	
Sylvie Benchetrit	Member (Vice-Chair)	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member	Germany	No interests declared	
Yuansheng Sun	Alternate	Germany	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Eleni Katsomiti	Member	Greece	No interests declared	
Anastasia Mountaki	Alternate	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP alternate)	Hungary	No interests declared	
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	
Vlasta Zavadova	Member	Liechtenstein	No interests declared	
Dovile Zacharkiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member	Luxembourg	No restrictions applicable to this meeting	
Olivier Moes	Alternate	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	
Roderick Houwen	Member	Netherlands	No participation in final deliberations and voting on:	2.7.2. Odevixibat - EMEA-C1-002054-PIP03-20-M02
Maaike van Dartel	Alternate	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Anette Solli Karlsen	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No restrictions applicable to this meeting	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Peter Sisovsky	Member	Slovakia	No interests declared	
Peter	Alternate	Slovakia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Szitanyi				
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesus Fernández Cortizo	Alternate	Spain	No interests declared	
Kristin Karlsson	Member	Sweden	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No interests declared	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Jose Ignacio Malagon Calle	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Jaroslav Sterba	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Tomasz Grybek	Member	Patients' Organisation Representative	No interests declared	
María Estela Moreno Martín	Expert - via telephone*	Spain	No interests declared	
Gaby Wangorsch	Expert - via telephone*	Germany	No interests declared	
Sara Galluzzo	Expert - via telephone*	Italy	No interests declared	
Pieter Colin	Expert - via telephone*	Netherlands	No restrictions applicable to this meeting	
Frederike Lentz	Expert - via telephone*	Germany	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Meeting run with support from relevant EMA staff				
*Experts were evaluated against the agenda topics or activities they participated in.				

13. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Paediatric investigation plan (PIP) (*section 2.1 Opinion on PIPs and section 3.1 Discussions on PIPs*)
A paediatric investigation plan (PIP) is a development plan aimed at ensuring that the necessary data are obtained through studies in children, when it is safe to do so, to support the authorisation of a medicine for children. Pharmaceutical companies submit proposals for PIPs to the European Medicines Agency's Paediatric Committee (PDCO). This Committee is responsible for agreeing or refusing the plan.

Compliance checks (*section 2.2 Opinions on Compliance check, section 3.2 Discussions on Compliance check*)
A compliance check may be necessary before any application for marketing authorisation (even for an adult indication) can be considered valid, if there was no deferral for at least one of the studies agreed in the PIP, or after the due date of initiation or completion of a study/measure. The same applies to some regulatory applications for authorised products, as described above.

Modification of an Agreed Paediatric Investigation Plan (*section 2.3 Opinions on Modification of an agreed PIP, section 3.3 Discussions on Modification of an agreed PIP*)
The development plan for a medicine can be modified at a later stage as knowledge increases. Modifications can also be made if the applicant encounters such difficulties with the implementation of a PIP, which render it unworkable or no longer appropriate.
In some cases, studies can be deferred until after the studies in adults have been conducted. This ensures that research in children is done only when it is safe and ethical to do so. Even when studies are deferred, the PIP will include details of the paediatric studies and their timelines.

Class waiver (*section 6 Discussion on the applicability of class waiver*)
As some diseases do not affect children (for example Parkinson's disease), the development of medicines for these diseases should not be performed in children. In these cases, a PIP is not required and it will be waived**.** For more information on the classes of diseases subject to waivers, see class waivers.

Annual reports on deferrals (*section 8*)
If the medicinal product is approved in the EU, annual reports on the deferred measures in the PIP must be submitted to the Agency.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/