09 January 2017
EMA/COMP/704981/2016
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Committee for Orphan Medicinal Products (COMP)

## Minutes for the meeting on 03-04 November 2016

Chair: Bruno Sepodes – Vice-Chair: Lesley Greene

03 November 2016, 08:30-18:00, room 2F

04 November 2016, 09:00-15:30, room 2F

**Disclaimers**

Some of the information contained in these minutes are 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 COMP meeting reports once the procedures are finalised.

Of note, these minutes are a working document primarily designed for COMP members and the work the Committee undertakes.

Further information with relevant explanatory notes can be found at the end of this document.

**Note on access to documents**

Some documents mentioned in these 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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# 1. Introduction

## 1.1. Welcome and declarations of interest of members and experts

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 based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

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 and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 23 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

## 1.2. Adoption of agenda

The agenda for 3-4 November 2016 was adopted with no amendments.

## 1.3. Adoption of the minutes

COMP commented that the minutes from the 4-6 October 2016 plenary meeting should mention divergent positions expressed during the vote on Ninlaro. The amended minutes will be circulated after the meeting for adoption via written procedure before publication on the EMA website.

[*Post meeting note: minutes from the COMP October meeting were adopted on 14 November 2016 after written procedure*]

# 2. Applications for orphan medicinal product designation

## 2.1. For opinion

### 2.1.1. Avelumab - EMA/OD/170/16

Merck Serono Europe Limited; Treatment of gastric cancer

COMP coordinator: Bożenna Dembowska-Bagińska

As agreed during the previous meeting, a list of issues was sent to the sponsor for response.

The sponsor was asked to clarify the following issues:

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of gastric cancer, the sponsor should further elaborate on:

- the individual outcome data in both patient groups (SwM and 2L+) – and how they compare favourably versus bibliographical data from the published literature;
- the previous treatments that the enrolled patients received and the individual outcomes;
- the outcome of only the 2nd line patients without inclusion of enrolled patients, who were not in second line, if a comparison to historical data on 2nd line is attempted;
- the contextualisation of data from patients that were in later lines.

- Number of people affected

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

The sponsor should present a full point prevalence at the time of application and not refer to a partial 5-year prevalence.

- Significant benefit

The sponsor should provide answers to the above questions in order to establish the medical plausibility and to provide a list of previous treatments. This additional information will be taken into consideration to assess significant benefit versus all authorised products.

In the written response, and during an oral explanation before the Committee on 4 November 2016, the sponsor presented updated preliminary clinical data. The previous lines of treatment of the enrolled patient population were presented and it was acknowledged that the best standard of care was employed by using combination therapies including authorised treatments. The sponsor also further contextualised the study outcomes in the switch maintenance setting and in the later lines setting. The median overall survival figures of the switch maintenance setting were calculated from the start of the first line therapy. This clinically relevant measure compared favourably to published median overall survival data of first line therapies. Regarding the second line setting, the sponsor demonstrated that the median overall survival of treated patients compared favourably to published data with the authorised product ramucirumab. In totality, the COMP considered that the presented indirect comparisons were sufficient to support both assumptions of medical plausibility and significant benefit.

Regarding the prevalence, the sponsor presented a new overview of published literature reporting that the average survival time of patients affected by the condition is 2.8 years. In addition, the sponsor presented literature reports showing a decline in disease incidence. The sponsor concluded on a new prevalence estimate of 4.5 per 10,000, which was calculated taking into consideration the EUCAN 2012 incidence figure and the average disease duration. The COMP acknowledged the decline in incidence, but was also of the opinion that the 2.8 years might not be considered to be the most conservative assumption of disease duration. Additionally, the COMP expressed uncertainty regarding the presented prevalence figure in comparison with the previously presented 5-year partial prevalence reported by EUCAN (2.3 per 10,000) and agreed that a range could be used.

The Committee agreed that the condition, treatment of gastric cancer, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing avelumab was considered justified based on preliminary clinical data showing that treatment improved overall survival of patients affected by the condition.

The condition is life-threatening with poor overall survival.

The condition was estimated to be affecting 2.3 to 4.5 in 10,000 persons in the European Union, at the time the application was made. The upper prevalence level is based on a conservative partial prevalence taking into account EU incidence figures that are reported to be in decline.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing avelumab will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data demonstrating that treatment improves overall survival in patients in a first line switch-maintenance setting and in patients, who have received 2 or more previous lines of treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for avelumab, for treatment of gastric cancer, was adopted by consensus.

### 2.1.2. - EMA/OD/134/16

Treatment of multiple myeloma

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 25 October 2016, prior to responding to the list of issues.

### 2.1.3. Adeno-associated viral vector serotype 8 encoding engineered rhodopsin DNA-binding repressor and human rhodopsin expression cassettes - EMA/OD/165/16

Fondazione Telethon; Treatment of retinitis pigmentosa

COMP coordinator: Armando Magrelli

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Intention to diagnose, prevent or treat

The sponsor presented preclinical data to demonstrate that the mechanism of action of the product and the feasibility of delivering the product to the eye. Functional endpoints, such as visual acuity, were not measured in a model of the condition and the full product has not been tested in a disease model either.

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of retinitis pigmentosa, the sponsor should further elaborate on:

- the relevance of the preclinical model used for the treatment of retinitis pigmentosa, and the interpretation of the results obtained in the experiments,

- any data from the preclinical models used which would indicate a functional improvement of the sense of vision.

- Number of people affected

The sponsor performed a literature search but did not specify what would be the estimated number of patients suffering from retinitis pigmentosa in the EU (in an "x per 10,000" format).

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

The sponsor should justify the choice of the sources selected for the estimation of the prevalence of the condition. The sponsor should describe and justify the methodology used for the prevalence calculation.

In the written response, the sponsor provided additional data to support medical plausibility. Data with the use of the product in a valid preclinical model of the condition were added, demonstrating improvement in electroretinograms, which can be considered indicative of improved visual acuity. In addition, the sponsor provided a prevalence calculation and proposed the estimated prevalence of retinitis pigmentosa to be 2.3 in 10,000 persons in the EU. The committee considered these responses satisfactory and found that the oral explanation was not necessary. Consequently, the oral hearing was cancelled and the committee adopted a positive opinion.

The Committee agreed that the condition, treatment of retinitis pigmentosa, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing adeno-associated viral vector serotype 8 encoding engineered rhodopsin DNA-binding repressor and human rhodopsin expression cassettes was considered justified based on preclinical data demonstrating improved electroretinogram measurements which are predictive of preserved visual function following treatment with the product.

The condition is chronically debilitating due to the development of nyctalopia and tunnel vision that progresses to total blindness.

The condition was estimated to be affecting approximately 2.3 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for adeno-associated viral vector serotype 8 encoding engineered rhodopsin DNA-binding repressor and human rhodopsin expression cassettes, for treatment of retinitis pigmentosa, was adopted by consensus.

### 2.1.4. Propranolol - EMA/OD/166/16

The Anticancer Fund; Treatment of soft tissue sarcoma

COMP coordinator: Brigitte Bloechl-Daum

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Intention to diagnose, prevent or treat

The sponsor is invited to amend the proposed condition to the previously accepted soft tissue sarcoma. Should the sponsor disagree, angiosarcoma should be justified as a distinct medical entity or a valid subset. The sponsor's attention is drawn to the Orphan regulations and guidelines to clarify this (especially section A of ENTR/6283/00).

In addition, the sponsor is requested to discuss the available clinical data in the context of the expected responses to the treatment with authorised products. More data which would help tease apart the effects of propranolol and the chemotherapy administered in the clinical case studies would allow establishing the medical plausibility of the product.

- Number of people affected

The sponsor proposed the estimate of prevalence of angiosarcoma. The calculation should be amended taking into consideration the amended orphan condition, soft tissue sarcoma.

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

- Significant benefit

The sponsor presented data from clinical studies where the product is used in combination with chemotherapy in patients who have relapsed after previous treatment regimens.

The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition.

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from clinical studies to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan indication, including the product authorised for a similar group of patients, pazopanib. The sponsor is also requested to include detailed description of patient characteristics in the presented clinical studies as well as the study design, in order to justify the significant benefit arguments for the intended target population.

In the written response, and during an oral explanation before the Committee on 3 November 2016, the sponsor agreed to broaden the orphan drug designation to soft tissue sarcoma. This will not oblige the sponsor to develop the product in all subsets of the condition but will allow for exploratory studies in several groups of patients within the umbrella of soft tissue sarcoma. The only published case study with the use of propranolol as monotherapy (Chow et al. 2015) suggested a potential of the product to reduce proliferative index of the tumour and to induce clinical responses. Although there is scarcity of other in vivo data with propranolol as monotherapy, the committee accepted the evidence presented as supportive of medical plausibility in addition to published in vitro data in cell lines. In addition the sponsor presented data from a clinical study ongoing in India, in which the product is used in combination with vincristine and methotrexate to treat advanced and recurrent angiosarcoma. The overall survival of patients receiving this treatment regimen could be indirectly compared to survival times of patients receiving pazopanib, and was significantly improved.

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of soft tissue sarcoma.

The Committee agreed that the condition, treatment of soft tissue sarcoma, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing propranolol was considered justified based on clinical data demonstrating partial responses in patients with angiosarcoma.

The condition is chronically debilitating with a high recurrence and metastasis rate, and life-threatening with an overall 5-year survival rate of approximately 60%.

The condition was estimated to be affecting approximately 3.5 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing propranolol will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that the product can be used in combination with chemotherapy and that the progression free survival in patients with advanced, recurrent angiosarcoma receiving combination treatments compare favourably to the progression free survival in patients receiving pazopanib. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for propranolol, for treatment of soft tissue sarcoma, was adopted by consensus.

### 2.1.5. - EMA/OD/188/16

Treatment of pulmonary arterial hypertension

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Significant benefit

The sponsor is invited to present any available clinical data with the proposed product-device combination that support the claims of significant benefit versus the currently authorized product and versus the currently used administration pumps.

In absence of additional data to the ones already presented it is not possible to assess the significant benefit of the proposed product and therefore orphan designation cannot be granted.

In the written response, and during an oral explanation before the Committee on 3 November 2016, the sponsor further explained the device that is part of the proposed product, and its potential advantages as compared to the already authorized formulation of the product.

The sponsor described a report published in the Journal of Heart and Lung Transplantation (2010) based on a survey of 97 PAH Clinicians & 18 PAH Specialty Nurses, highlighting that serious errors in medication administration were reported by respondents using the currently available administration pumps

The COMP discussed the significant benefit grounds proposed by the sponsor. While the survey data showing errors with the existing the product formulations are informative, it was the opinion of the Committee that the advantage was linked only to the device and not

to the pharmacological and pharmaceutical characteristics of the active substance; therefore it would not justify a designation given to the substance. Furthermore the COMP was not aware of major signals from clinical practice and the literature of major public health problems, e.g. patients with PAH not being able to receive adequate treatment in the EU due to problems related to the current devices. While an improvement of the pharmaceutical formulation of the product compared to what currently available is a welcome feature, the COMP did not consider that the advantages brought were to be considered sufficient for the product to have a "significant" benefit.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 4 November 2016, prior to final opinion.

### 2.1.6. - EMA/OD/163/16

Treatment of congenital adrenal hyperplasia

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Intention to diagnose, prevent or treat

For the purpose of orphan designation, the Committee for Orphan Medicinal Products (COMP) considered that the active substance must be renamed. This is because the descriptive name does not provide enough granularity to distinguish this chemical compound from other substances with similar activity (the sponsor is referred to the Guideline ENTR/6283/00 Rev 4). In the absence of the agreement to this change of name, the orphan drug designation cannot be granted.

The sponsor presented preliminary data in vitro to support the products mechanism of action. In addition, the sponsor presented Phase 1 clinical data to support the comparability of the proposed product to another product in the same pharmaceutical class. The comparator has been shown to have an effect on the relevant markers of the disease. No data with the use of the product in the condition or a model of the condition was presented.

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of congenital adrenal hyperplasia, the sponsor should further elaborate on:

  - the results obtained in vitro with the use of the product;
  - the relevance of the preclinical and clinical Phase 1 data for the treatment of congenital adrenal hyperplasia, and the interpretation of the results obtained in the experiments.

- Significant benefit

The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition.

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from preclinical studies to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.

Furthermore, it would be useful to obtain more information on the ongoing study/planned development.

In the written response, and during an oral explanation before the Committee on 3 November 2016, the sponsor provided additional data to support medical plausibility. The preclinical models used were not specific to the condition as applied for and the sponsor explained their relevance for the development of the product in congenital adrenal hyperplasia (CAH). In addition, the sponsor elaborated on the arguments to support the significant benefit over standard of care. The committee questioned the relevance of the models and endpoints presented, which were not directly related to CAH. The committee was of the opinion that data more specific to the condition should be provided to support the medical plausibility and significant benefit.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 3 November 2016, prior to final opinion.

### 2.1.7. 20% I.V. fat emulsion consisting of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water for injection - EMA/OD/062/16

Alan Boyd Consultants Ltd; Treatment of poisoning by local anesthetics

COMP coordinator: Violeta Stoyanova

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Proposed condition

The sponsor is invited to justify the proposed condition and in particular the exclusion of intravenous anaesthetic toxicity from the target population. The sponsor is also invited to discuss why the condition is not a complication in patients affected by other underlying entities.

- Stage of development

It would be useful to obtain more information on any preclinical or clinical studies that have been performed or initiated by the sponsor, in order to define the stage of development of the proposed product.

In the written response, and during an oral explanation before the Committee on 3 November 2016, the sponsor argued its position and the COMP discussed the following: The communication on Regulation (EC) No 141/2000 from the European Commission 2003/C 178/02 defines a condition in the context of designation as “any deviation from the normal structure or function of the body, as manifested by a characteristic set of signs and symptoms (typically a recognised distinct disease or a syndrome)”. In the context of this definition, the COMP considered that the proposed condition is not a recognised disease or syndrome.

The COMP reflected on older designations regarding opinions at the early days of the EU framework. The time lapsed from these designations was pointed out and it was noted that the standards have evolved, as reflected in the regulatory documents published since and the publicly available COMP minutes.

The COMP considered that the existence of an ICD-10 sub-code would not be a sufficient element in itself for qualifying as a proposed condition for the purpose of orphan designation, because this is not a condition delineated by a distinct aetiology,

pathophysiology and histopathology and clinical characteristics. In this respect reference was made to the guideline on the format and content of applications ENTR/6283/00 Rev 04.

Finally, it was considered that the proposed indication would also overlap with overdosing of lipophilic drugs, including inter alia antiarrhythmic substances of different classes. Such uses have not been taken into consideration for the purpose of orphan designation and, because of this, the prevalence calculation as submitted by the sponsor was not considered acceptable.

Therefore, even though the sponsor described a particular group of patients that may be managed by the proposed treatment, the COMP considered that these patients are not affected by a distinct disease valid for the purpose of orphan drug designation.

The intention to treat poisoning by local anaesthetics with the medicinal product containing 20% intravenous fat emulsion consisting of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water for injection was argued on the basis of preclinical and preliminary clinical data supporting increased survival in treated subjects affected by local anaesthetic toxicity; however, the sponsor has not established that the proposed product is intended to treat a distinct medical entity in terms of pathophysiology, histopathology and clinical characteristics.

As the sponsor excluded part of the possible target population in the prevalence calculation, the sponsor failed to establish that the proposed condition affects not more than 5 in 10,000 persons in the European Union, at the time the application was made.

The COMP also considered that the sponsor has established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by poisoning by local anaesthetics.

A negative opinion for 20% intravenous fat emulsion consisting of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water for injection, for treatment of poisoning by local anaesthetics, was adopted by consensus. The sponsor will have 90 days to appeal from the COMP decision.

*[Post-meeting note: The opinion was adopted by written procedure after its November meeting.]*

### 2.1.8. - EMA/OD/181/16

Treatment of plasma cell myeloma

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 19 October 2016, prior to responding to the list of issues.

### 2.1.9. Cabiralizumab - EMA/OD/169/16

Albany Regulatory Consulting Ltd; Treatment of tenosynovial giant cell tumour, localised and diffuse type

COMP coordinator: Daniel O'Connor

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Intention to diagnose, prevent or treat

In order to justify the medical plausibility of the proposed product the sponsor is invited to provide further and more recent details of the phase 1/2 clinical study.

In addition the sponsor is invited to elaborate on the relevance of stable disease to the intended clinical efficacy of the product in a tumour that has slow progression.

In the written response, the sponsor presented more recent data from the ongoing phase 1/2 clinical trial in patients with inoperable (or operable, but where the surgery would result in unacceptable morbidity) tenosynovial giant cell tumour with measurable disease.

The data provided by the sponsor, showing responses in patients treated with the highest dose in the phase 1/2 study, were considered sufficient by the COMP to support the medical plausibility without the need of an oral explanation.

The Committee agreed that the condition, treatment of tenosynovial giant cell tumour, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing cabiralizumab was considered justified based on preliminary clinical data showing antitumor activity in patients affected by the condition that had not responded to surgery or in whom surgery was not indicated.

The condition is chronically debilitating due to loss of function of the affected joints and the development of secondary arthritis.

The condition was estimated to be affecting less than 3 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for cabiralizumab, for treatment of tenosynovial giant cell tumour, was adopted by consensus.

### 2.1.10. - EMA/OD/152/16

Treatment of Huntington's disease

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 18 October 2016, prior to responding to the list of issues.

### 2.1.11. - EMA/OD/177/16

Treatment of recurrent Clostridium difficile infection

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Intention to diagnose, prevent or treat

The sponsor is proposing a subset of a very common infection.

Recurrent CDI should be justified as a distinct medical entity or a valid subset. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is

drawn to the Orphan regulations and guidelines to clarify this (especially section A of ENTR/6283/00).

The sponsor should justify why the product would not have any pharmacodynamic effects in the excluded patients (treatment of CDI), and whether it may be used as a single therapy or together with antibiotics in first occurrence to shorten the duration of recovery and prevent further relapses.

- Number of people affected

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

The sponsor should justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition. The sponsor should describe and justify the methodology used for the prevalence calculation.

The sponsor should re-calculate the prevalence estimate based on relevant epidemiological studies and registers for the proposed orphan condition, and given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations.

An overall up-to-date figure for the annual incidence of Clostridium Difficile Infections in the EU is expected.

In the written response, and during an oral explanation before the Committee of 4 November 2016, the sponsor provided a discussion of the pathophysiology of the proposed condition. In particular the applicant described the disruption of intestinal flora diversity in recurrent CDI, but the COMP was of the opinion that the applicant has not advanced its position further considering recurrent CDI as a degree of severity of CDI. This is explicitly advised against in the guideline of applications. More importantly the sponsor acknowledged potential pharmacodynamic effects in the excluded populations, that invalidated subsetting per se. As such, recurrent CDI is not described neither as a distinct medical entity (because it is described as a more severe form of dysbiosis), nor as a valid subset of CDI (because effects cannot be ruled out in the excluded patients). Therefore the COMP considered that the broader CDI population should be examined for the purpose of prevalence calculations.

As for the issue of prevalence calculations, the applicant clarified the methods of estimation. The COMP considered that there were several limitations, including the calculation of non-hospitalised cases. The COMP considered that data on the national incidence of CDI should include all cases of CDI including hospital acquired and community acquired CDI. Some further data sources could also have been included e.g. in Sweden one nationwide study from 1995 (Karlström O et al.) that covered all laboratory confirmed cases in Sweden. In this study the incidence was 5.8/10 000 in 1995 (5133 CDI cases and SE population 8.8 million in 1995) and it was noted that 28% of all cases involved no recent hospitalization and were defined as community-acquired CDI. The national incidence for Sweden with regard to CDI is 7.9/ 10 000 (2014), 8.1/ 10 000 (2013), 8.5 / 10 000 (2012). It is very unlikely that other countries in the EU with higher prescription of antibiotics should have an incidence of CDI that is lower than what is seen in Sweden.

The COMP thus considered that the prevalence criterion was not justified.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 4 November 2016, prior to final opinion.

### 2.1.12. Arsenic trioxide - EMA/OD/208/16

Medsenic; Treatment of graft versus host disease

COMP coordinator: Frauke Naumann-Winter

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Significant benefit

The arguments on significant benefit are based on an alternative mechanism of action and the potential improved efficacy in the condition without reference to either preclinical or clinical data.

The sponsor should re-submit pre-clinical in vivo data in solid organ transplantation where their product was used in combination with cyclosporin. This data was submitted in a previous submission but deleted from the current application.

This sponsor should use this additional data to further discuss the arguments provided for significant benefit and to elaborate on the results from this study to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan indication.

In the written response, the sponsor re-submitted the requested pre-clinical in vivo data where they showed the combined effects of their product with cyclosporin. The results demonstrated prolonged grafts survival. The COMP was of the opinion that this data was sufficient to support a significant benefit on the basis of a clinically relevant advantage in the treatment of patients with graft vs host disease for orphan designation.

The Committee agreed that the condition, treatment of graft-versus-host disease, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing arsenic trioxide was considered justified based on pre-clinical in vivo models of the condition showing reduced inflammation and improved survival.

The condition is chronically debilitating and life-threatening in particular due to intestinal inflammation causing diarrhoea, abdominal pain, nausea and vomiting, as well as due to hepatotoxicity, skin and mucosal damage, sicca syndrome, cholestasis, arthritis, obliterative bronchiolitis and the need for immunosuppression that increases susceptibility to infections.

The condition was estimated to be affecting approximately 0.5 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing arsenic trioxide will be of significant benefit to those affected by the condition. The sponsor has provided pre-clinical in vivo data that demonstrate the product could be used in combination with cyclosporine. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for arsenic trioxide, for treatment of graft-versus-host disease, was adopted by consensus.

## 2.2. For discussion / preparation for an opinion

### 2.2.1. Ivosidenib - EMA/OD/197/16

QRC Consultants Ltd; Treatment of acute myeloid leukaemia

COMP coordinator: Jens Ersbøll

The Committee agreed that the condition, treatment of acute myeloid leukaemia, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing ivosidenib was considered justified based on preliminary clinical data in patients with the condition showing complete and partial response.

The condition is life-threatening and chronically debilitating due to the consequences of the bone marrow dysfunction, such as intracranial or gastro-intestinal haemorrhagic episodes, disseminated intravascular coagulation, and the risk of severe infections. The condition progresses rapidly and is fatal within days to weeks or a few months if left untreated. The overall 5-year relative survival with the currently available treatments is approximately 22%.

The condition was estimated to be affecting approximately 1.1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing ivosidenib will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate a response in relapsed/refractory acute myeloid leukaemia patients. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for ivosidenib, for treatment of acute myeloid leukaemia, was adopted by consensus.

### 2.2.2. - EMA/OD/205/16

Treatment of Cockayne syndrome

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.3. - EMA/OD/212/16

Treatment of multiple myeloma

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.4. - EMA/OD/215/16

Treatment of glioma

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

## 2.2.5. 68Ga-DOTA-pABzA-DIG-dPhe-Gln-Trp-Ala-Val-Gly-His-NHCH[(CH2-CH(CH3)2]2 - EMA/OD/206/16

Advanced Accelerator Applications; Diagnosis of gastrointestinal stromal tumours

COMP coordinator: Bożenna Dembowska-Bagińska/Irena Rogovska

The Committee agreed that the condition, gastrointestinal stromal tumours, is a distinct medical entity and meets the criteria for orphan designation.

The intention to diagnose the condition with the medicinal product containing $^{68}$Ga-DOTA-pABzA-DIG-dPhe-Gln-Trp-Ala-Val-Gly-His-NHCH[($CH_2$-$CH(CH_3)_2$]$_2$ was considered justified based on in vivo data in xenotransplanted models of the proposed condition, showing visualization of the tumour with PET imaging.

The condition is chronically debilitating and life-threatening in particular due to the high rate of relapse and development of metastatic disease.

The population of patients eligible for diagnosis of the condition was estimated to be approximately 0.2 in 10,000 persons in the European Union, at the time the application was made.

In addition, no satisfactory methods of diagnosis of the condition have been authorised in the European Union.

A positive opinion for $^{68}$Ga-DOTA-pABzA-DIG-dPhe-Gln-Trp-Ala-Val-Gly-His-NHCH[($CH_2$-$CH(CH_3)_2$]$_2$, for diagnosis of gastrointestinal stromal tumours, was adopted by consensus.

## 2.2.6. Adeno-associated viral vector of serotype 8 containing the human *CNGA3* gene under the control of a cone arrestin promoter - EMA/OD/190/16

Universitätsklinikum Tübingen (UKT); Treatment of achromatopsia caused by mutations in the *CNGA3* gene

COMP coordinator: Irena Bradinova

The Committee agreed that the condition, treatment of achromatopsia caused by mutations in the *CNGA3* gene, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing adeno-associated viral vector serotype 8 containing the human *CNGA3* gene under the control of a cone arrestin promoter was considered justified based on preclinical data in a relevant disease model that show that treatment can improve electrical responses of retinal cells.

The condition is chronically debilitating due to the serious impairment of visual acuity in daylight, which is associated with limitations in normal day activities. Lack of visual acuity can be accompanied by severe photophobia, nystagmus, small central scotoma, eccentric fixation and reduced or complete loss of colour discrimination.

The condition was estimated to be affecting approximately 0.3 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for adeno-associated viral vector serotype 8 containing the human *CNGA3* gene, for treatment of achromatopsia caused by mutations in the *CNGA3* gene, was adopted by consensus.

## 2.2.7. - EMA/OD/214/16

Treatment of status epilepticus

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

## 2.2.8. - EMA/OD/200/16

Treatment of paediatric stroke

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

## 2.2.9. - EMA/OD/203/16

Treatment of Rett syndrome

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

## 2.2.10. Dantrolene sodium - EMA/OD/202/16

Alan Boyd Consultants Ltd; Treatment of Wolfram syndrome

COMP coordinator: Ingeborg Barisic/Vallo Tillmann

The Committee agreed that the condition, treatment of Wolfram syndrome, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing dantrolene sodium was considered justified based on improvement of glucose tolerance in an in vivo model of the proposed condition treated with dantrolene.

The condition is life-threatening due to a life-expectancy of 30 years and chronically debilitating due to the development of diabetes mellitus and optic atrophy.

The condition was estimated to be affecting not more than 0.2 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for dantrolene sodium, for treatment of Wolfram syndrome, was adopted by consensus.

## 2.2.11. - EMA/OD/213/16

Treatment of antiphospholipid syndrome

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.12. Ibudilast - EMA/OD/182/16

MediciNova (Europe) Limited; Treatment of amyotrophic lateral sclerosis

COMP coordinator: Violeta Stoyanova

The Committee agreed that the condition, treatment of amyotrophic lateral sclerosis, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing ibudilast was considered justified based on preliminary clinical data showing a reduction in the decline of motor and respiratory function over time.

The condition is life-threatening and chronically debilitating due to progressive degeneration of motor neurons, ultimately leading to paralysis and respiratory failure. The survival of patients is usually limited to 2-3 years.

The condition was estimated to be affecting approximately 0.6 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing ibudilast will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate a reduction in the decline in respiratory and motor function when the product is used in combination with riluzole. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for ibudilast, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

### 2.2.13. - EMA/OD/210/16

Prevention of necrotising enterocolitis

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.14. - EMA/OD/097/16

Treatment of primary hypogonadotropic hypogonadism

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.15. Metformin - EMA/OD/179/16

Centro de Investigación Biomédica en Red (CIBER); Treatment of progressive myoclonic epilepsy type 2 (Lafora disease)

COMP coordinator: Giuseppe Capovilla

The Committee agreed that the condition, treatment of progressive myoclonic epilepsy type 2 (Lafora disease), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing metformin was considered justified based on pre-clinical in vivo data in a valid model of the condition showing a reduction in Lafora bodies and improvements in behavioural tests.

The condition is life-threatening and chronically debilitating due to myoclonic seizures and generalized convulsions which follow and all escalate over time. This is also associated with cognitive decline. Individuals die within ten years of onset, usually from complications related to nervous system degeneration and status epilepticus.

The condition was estimated to be affecting approximately 0.01 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for metformin, for treatment of progressive myoclonic epilepsy type 2 (Lafora disease), was adopted by consensus.

## 2.2.16. - EMA/OD/192/16

Treatment of pulmonary arterial hypertension

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

## 2.2.17. PEGylated form of recombinant human IL-10 - EMA/OD/193/16

Larode Ltd; Treatment of pancreatic cancer

COMP coordinator: Brigitte Bloechl-Daum

Following review of the application by the Committee, it was agreed to broaden/rename the active substance to pegylated recombinant human interleukin-10.

The Committee agreed that the condition, treatment of pancreatic cancer, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing pegylated recombinant human interleukin-10 was considered justified based on clinical data demonstrating improved progression free survival when used in combination with FOLFOX chemotherapy in patients who progressed after treatment with gemcitabine.

The condition is chronically debilitating because of pain in the upper abdomen, loss of appetite, nausea, vomiting, weight loss, jaundice, fatigue, weakness and depression; and life-threatening with a median survival of about 6 months.

The condition was estimated to be affecting approximately 2.4 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing pegylated recombinant human interleukin-10 will be of significant benefit to those affected by the condition. The sponsor

has provided clinical data that demonstrate that the product can be used in combination with the standard of care in advanced pancreatic cancer patients who have progressed after gemcitabine treatment and that the progression free survival and responses in patients are improved compared to all authorised product regimens in this clinical setting. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for pegylated recombinant human interleukin-10, for treatment of pancreatic cancer, was adopted by consensus.

### 2.2.18. - EMA/OD/189/16

Treatment of acute sensorineural hearing loss

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.19. - EMA/OD/196/16

Treatment of Guillain-Barré syndrome

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.20. Recombinant self-complementary adeno-associated viral vector serotype 9 encoding the human *CLN3* gene - EMA/OD/195/16

Ser-mes Planificación SL; Treatment of neuronal ceroid lipofuscinosis type 3

COMP coordinator: Giuseppe Capovilla

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of neuronal ceroid lipofuscinosis and to broaden/rename the active substance to recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN3* gene.

The Committee agreed that the condition, treatment of neuronal ceroid lipofuscinosis, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN3* gene was considered justified based on preclinical data in a valid disease model of neuronal ceroid lipofuscinosis showing that treatment was able to improve motor-function and behaviour.

The condition is life-threatening with death in the third decade of life and chronically debilitating due to vision impairment and blindness, mental retardation, loss of motor control, speech impediment, behavioural problems, seizures, cerebral atrophy, parkinsonism, cardiac issues, and dementia.

The condition was estimated to be affecting approximately 0.3 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN3* gene, for treatment of neuronal ceroid lipofuscinosis, was adopted by consensus.

### 2.2.21. - EMA/OD/199/16

Treatment of pancreatic cancer

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December meeting.

### 2.2.22. Udenafil - EMA/OD/218/16

Mapi Ireland Limited; Treatment of functional single ventricle congenital heart disease

COMP coordinator: Eva Malikova/Olimpia Neagu

The Committee agreed that the condition, treatment of functional single ventricle congenital heart disease, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing udenafil was considered justified based on preliminary clinical data showing a trend to improvement of parameters reflecting cardiac function in patients affected by the condition.

The condition is chronically debilitating and life-threatening due to impaired cardiac ventricular function, atrial arrhythmias, and thrombotic events. Some patients also develop neurological and developmental deficits, and protein losing enteropathy. 30-year survival rates have been estimated to be approximately 43%.

The condition was estimated to be affecting approximately 0.3 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for udenafil, for treatment of functional single ventricle congenital heart disease, was adopted by consensus.

## 2.3. Revision of the COMP opinions

None

## 2.4. COMP opinions adopted via written procedure following previous meeting

### 2.4.1. Recombinant human acid sphingomyelinase – EMEA/OD/004/01, EU/3/01/056

Genzyme Europe BV; Treatment of Niemann-Pick disease

COMP coordinator: Pauline Evers

**Action**: For information

Document tabled:
Amended summary report

## 2.5. Appeal

None

## 2.6. Nominations

### 2.6.1. New applications for orphan medicinal product designation - Appointment of COMP coordinators

COMP coordinators were appointed for 35 applications submitted.

## 2.7. Evaluation on-going

Thirty applications for orphan designation will not be discussed as evaluation is on-going.

**Action**: For information

Notes:
See 6.8.1. Table 6. Evaluation Ongoing.

# 3. Requests for protocol assistance with significant benefit question

## 3.1. Ongoing procedures

### 3.1.1. -

Treatment in haematopoietic stem cell transplantation

The Committee was briefed on the significant benefit issues. The COMP adopted the proposed answers on the significant benefit issues.

## 3.2. Finalised letters

### 3.2.1. -

Treatment of tuberculosis

The finalised letter was circulated for information.

## 3.3. New requests

### 3.3.1. -

Treatment of acromegaly

The new request was noted.

# 4. Review of orphan designation for orphan medicinal products for marketing authorisation

## 4.1. Orphan designated products for which CHMP opinions have been adopted

### 4.1.1. Chenodeoxycholic acid sigma-tau - chenodeoxycholic acid – EMA/OD/196/14, EU/3/14/1406, EMEA/H/C/004061

Sigma-tau Arzneimittel GmbH; Treatment of inborn errors of primary bile acid synthesis

The COMP appointed new COMP co-ordinators in the eventuality of an appeal from the sponsor following the negative opinion adopted by COMP on 17 October 2016.

### 4.1.2. Cystadrops (mercaptamine) - EMA/OD/036/08, EU/3/08/578, EMEA/H/C/003769

Orphan Europe S.A.R.L.; Treatment of cystinosis

COMP noted the ongoing discussion with European Commission.

## 4.2. Orphan designated products for discussion prior to adoption of CHMP opinion

### 4.2.1. - trientine tetrahydrochloride – EMA/OD/001/15, EU/3/15/1471, EMEA/H/C/004005

GMP-Orphan SA; Treatment of Wilson's disease

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the meeting closer to the CHMP final opinion.

### 4.2.2. - eryaspase – EMEA/OD/033/06, EU/3/06/409, EMEA/H/C/004055

ERYTECH Pharma S.A.; Treatment of acute lymphoblastic leukaemia

The status of the procedure at CHMP was noted.

### 4.2.3. - dinutuximab beta – EMA/OD/112/12, EU/3/12/1062, EMEA/H/C/003918

APEIRON Biologics AG; Treatment of neuroblastoma

The status of the procedure at CHMP was noted.

### 4.2.4. - aceneuramic acid – EMA/OD/126/11, EU/3/12/972, EMEA/H/C/004176

Ultragenyx UK Limited; Treatment of GNE myopathy

COMP coordinator: Ingeborg Barisic/ Michel Hoffmann / Josep Torrent-Farnell

The COMP discussed whether the product still meets the criteria for orphan designation in anticipation of the CHMP decision expected in December 2016 and concluded that:

The proposed therapeutic indication, *treatment of Hereditary Inclusion Body Myopathy (HIBM)* falls entirely within the scope of the orphan indication of the designated orphan medicinal product, treatment of GNE myopathy.

The prevalence of GNE myopathy (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded in to be less than 0.1 in 10,000 persons in the European Union, at the time of the review of the designation criteria.

The condition is chronically debilitating due to progressive limb muscle weakness leading to difficulties climbing stairs or getting up from sitting, and weakness of the hands and shoulder muscles. The condition usually causes complete functional impairment over 10–20 years, leading to a wheelchair-bound state.

There is, at present, no satisfactory treatment that has been authorised in the European Union for patients affected by the condition

An opinion not recommending the removal of the product from the EC Register of Orphan Medicinal Products was adopted by consensus.

The COMP opinion is based on the review of criteria for orphan designation and is not predictive of the outcome of CHMP discussions.

### 4.3. On-going procedures

COMP co-ordinators were appointed for 3 applications.

### 4.4. Public Summary of Opinion

The draft public summaries of the COMP opinions adopted last month were endorsed for publication on the EMA website.

## 5. Application of Article 8(2) of the Orphan Regulation

None

## 6. Organisational, regulatory and methodological matters

### 6.1. Mandate and organisation of the COMP

#### 6.1.1. Strategic Review & Learning meetings

Report from COMP Strategy Review & Learning meetings, 17-18 October 2016, Rome, Italy

Documents used during the meeting were circulated for information.

#### 6.1.2. Protocol Assistance Working Group

Cancelled

#### 6.1.3. COMP Drafting Group

Cancelled

### 6.1.4. Preclinical Models Working Group

None

### 6.1.5. Recommendations on eligibility to PRIME – report from CHMP

Documents were circulated in MMD.

Document(s) tabled:
PRIME eligibility requests - list of adopted outcomes October 2016

### 6.1.6. COMP Membership

The COMP welcomed Melinda Sobor as new member representing Hungary.
The COMP welcomed Kerstin Westermark as new member nominated by the European Commission on EMA's recommendation.

## 6.2. Coordination with EMA Scientific Committees or CMDh-v

### 6.2.1. PDCO/COMP Working Group

Cancelled

## 6.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

### 6.3.1. Working Party with Patients' and Consumers' Organisations (PCWP)

None

### 6.3.2. Working Party with Healthcare Professionals' Organisations (HCPWP)

None

## 6.4. Cooperation within the EU regulatory network

### 6.4.1. The European Network of Centres for Pharmacoepidemiology & Pharmacovigilance (ENCePP)

Dinah Duarte was appointed for a second term to represent the COMP at the Steering Group of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP).

## 6.5. Cooperation with International Regulators

### 6.5.1. Food and Drug Administration (FDA)

The draft agenda of the monthly teleconference with FDA held on 11 October 2016 is available in MMD for information.

Document tabled:
Draft Agenda October 11, 2016

### 6.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

### 6.5.3. The Therapeutic Goods Administration (TGA), Australia

None

### 6.5.4. Health Canada

None

## 6.6. Contacts of the COMP with external parties and interaction with the Interested Parties to the Committee

None

## 6.7. COMP work plan

### 6.7.1. COMP Work Plan 2016

Documents were circulated in MMD.

Document(s) tabled:
COMP Work Plan 2016
6-7-1 COMP Work plan tracking tool 2016

### 6.7.2. COMP Work Plan 2017

Documents were circulated in MMD.

Document(s) tabled:
COMP draft Work Plan 2017

## 6.8. Planning and reporting

### 6.8.1. List of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2016

An updated list of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2016 were circulated.

### 6.8.2. Overview of orphan marketing authorisations/applications

An updated overview of orphan applications for Marketing Authorisation was circulated.

# 7. Any other business

None

## List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 03-04 November 2016 meeting.

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Bruno Sepodes | Chair | Expert recommended by EMA | No interests declared | |
| Brigitte Blöchl-Daum | Member | Austria | No interests declared | |
| Irena Bradinova | Member | Bulgaria | No interests declared | |
| Dinko Vitezic | Member | Croatia | No restrictions applicable to this meeting | |
| Jens Ersbøll | Member | Denmark | No interests declared | |
| Vallo Tillmann | Member | Estonia | No interests declared | |
| Karri Penttilä | Member | Finland | No interests declared | |
| Annie Lorence | Member | France | No interests declared | |
| Frauke Naumann-Winter | Member | Germany | No interests declared | |
| Nikolaos Sypsas | Member | Greece | No restrictions applicable to this meeting | |
| Melinda Sobor | Member | Hungary | No interests declared | |
| Sigurdur B. Thorsteinsson | Member | Iceland | No interests declared | |
| Geraldine O'Dea | Member | Ireland | No interests declared | |
| Armando Magrelli | Member | Italy | No interests declared | |
| Irena Rogovska | Member | Latvia | No interests declared | |
| Aušra Matulevičienė | Member | Lithuania | No interests declared | |
| Michel Hoffmann | Member | Luxembourg | No interests declared | |
| Robert Nistico | Member | Malta | No interests declared | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Violeta Stoyanova-Beninska | Member | Netherlands | No interests declared | |
| Ingrid Wang | Member | Norway | No interests declared | |
| Bożenna Dembowska-Bagińska | Member | Poland | No restrictions applicable to this meeting | |
| Dinah Duarte | Member | Portugal | No interests declared | |
| Olimpia Neagu | Member | Romania | No interests declared | |
| Eva Malikova | Member | Slovak Republic | No interests declared | |
| Josep Torrent-Farnell | Member | Spain | No interests declared | |
| Dan Henrohn | Member | Sweden | No restrictions applicable to this meeting | |
| Daniel O'Connor | Member | United Kingdom | No interests declared | |
| Pauline Evers | Member | Patients' Organisation Representative | No interests declared | |
| Lesley Greene | Member (Vice-Chair) | Patients' Organisation Representative | No interests declared | |
| Kerstin Westermark | Member | Expert recommended by EMA | | |
| Ingeborg Barisic | Member | Expert recommended by EMA | No restrictions applicable to this meeting | |
| Giuseppe Capovilla | Member | Expert recommended by EMA | No interests declared | |
| Virginie Hivert | Expert - in person* | Patients' Organisation Representative | No restrictions applicable to this meeting | |
| Meeting run with support from relevant EMA staff | | | | |

* Experts were only evaluated against the agenda topics or activities they participated in.

## Explanatory notes

The notes below give a brief explanation of the main sections and headings in the COMP agenda and should be read in conjunction with the agenda or the minutes.

### Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use
COMP: Committee for Orphan Medicinal Products
EC: European Commission
OD: Orphan Designation
PA: Protocol Assistance
PDCO: Paediatric Committee
PRAC: Pharmacovigilance and Risk Assessment Committee
SA: Scientific Advice
SAWP: Scientific Advice Working Party

**Orphan Designation** (*section 2 Applications for orphan medicinal product designation*)

The orphan designation is the appellation given to certain medicinal products under development that are intended to diagnose, prevent or treat rare conditions when they meet a pre-defined set of criteria foreseen in the legislation. Medicinal products which get the orphan status benefit from several incentives (fee reductions for regulatory procedures (including protocol assistance), national incentives for research and development, 10-year market exclusivity) aiming at stimulating the development and availability of treatments for patients suffering from rare diseases.

Orphan Designations are granted by Decisions of the European Commission based on opinions from the COMP. Orphan designated medicinal products are entered in the Community Register of Orphan Medicinal Products.

**Protocol Assistance** (*section 3 Requests for protocol assistance with significant benefit question*)

The protocol assistance is the help provided by the Agency to the sponsor of an orphan medicinal product, on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of the medicinal product in view of the submission of an application for marketing authorisation.

**Sponsor**

Any legal or physical person, established in the Community, seeking to obtain or having obtained the designation of a medicinal product as an orphan medicinal product.

**Maintenance of Orphan Designation** (*section 4 Review of orphan designation for orphan medicinal products for marketing authorisation*).

At the time of marketing authorisation, the COMP will check if all criteria for orphan designation are still met. The designated orphan medicinal product should be removed from the Community Register of Orphan Medicinal Products if it is established that the criteria laid down in the legislation are no longer met.

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