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EUROPEAN COMMISSION

COMMUNICATION FROM THE COMMISSION

Guideline on the format and content of applications for agreement or modification of a paediatric investigation plan and requests for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies

(Text with EEA relevance)

(2014/C 338/01)

1. INTRODUCTION

1.1. Scope

This guideline, which replaces the previous version from 2008 ([1]), sets out:

— detailed arrangements for the format and content of applications for agreement on or modification of a paediatric investigation plan (PIP) and requests for waivers and deferrals, in accordance with Article 10 of Regulation (EC) No 1901/2006 of the European Parliament and of the Council on medicinal products for paediatric use ([2]) (hereinafter 'the Paediatric Regulation');

— arrangements for the operation of the compliance check referred to in Articles 23 and 28(3) of the Paediatric Regulation; and

— pursuant to Article 45(4) of the Regulation, the criteria for assessing the significance of studies started before and completed after its entry into force.

1.2. Definitions

For the purposes of this guideline, the following definitions apply:

(a) condition: 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;

(b) paediatric investigation plan indication: proposed indication in the paediatric population for the purpose of a PIP, and at the time of submission of the PIP, within a specific condition;

(c) proposed indication: the indication for use in adults as proposed by an applicant at the time of submission of the PIP/waiver application. In cases of a completed or ongoing adult development, this is the starting point for identifying the condition for potential paediatric use;

(d) measure: any study or other obligation (for example, a requirement to set up a registry), which is included in the PIP, with a view to ensuring that, in accordance with Article 15(2) of the Paediatric Regulation, the necessary data are generated to demonstrate the quality, safety and efficacy of the medicinal product in the paediatric population;

([1]) OJ C 243, 24.9.2008, p. 1.

([2]) Regulation (EC) No 1901/2006 of the European Parliament and of the Council on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (OJ L 378, 27.12.2006, p. 1).

(e) study: any measure that is designed to answer a specific scientific question, and is performed in accordance with a predefined methodology. This includes, for example, interventional and non-interventional studies, non-clinical studies, extrapolation studies, modelling and simulation studies, development of specific paediatric pharmaceutical forms and formulations;

(f) extrapolation study: a study involving the use of extrapolation to support the use of the medicinal product in children ([1]). An extrapolation study may be based on case series, meta-analyses, systematic reviews and modelling and simulation studies;

(g) modelling and simulation study: a study with the objective of quantifying the medicine/system/experimental design, in order to:

— understand and estimate its properties;

— optimise and predict future experimental outcomes; and

— aid regulatory, medicinal product development and use decisions;

(h) key elements: each measure in a PIP may contain one or more specific key elements, as specified in the annex to this guideline; key elements are binding and provide the basis for the operation of the compliance check.

2. FORMAT AND CONTENT OF APPLICATIONS FOR AGREEMENT ON OR MODIFICATION OF A PAEDIATRIC INVESTIGATION PLAN AND REQUESTS FOR WAIVERS AND DEFERRALS

2.1. General principles and format

2.1.1. *Structure of application*

Applications for agreement on or modification of a PIP or requests for waiver or deferral and combinations thereof should be accompanied by particulars and documents in accordance with this guideline. Applications should consist of the following sections:

Part A: Administrative and product information

Part B: Overall development of the medicinal product

Part C: Application for a product-specific waiver

Part D: Proposed paediatric investigation plan

Part E: Request for deferral

Part F: Annexes

Sections and/or subsections that are not relevant for the specific application can be left empty.

The European Medicines Agency (hereinafter 'the Agency') publishes templates and online forms based on this guideline. In addition, procedural advice is available on the Agency's website (www.ema.europa.eu).

2.1.2. *Supporting information*

The application should be based on all available information relevant to the evaluation, whether favourable or unfavourable to the product and its development. This includes details of any incomplete or discontinued pharmaco-toxicological test or clinical trials or other studies relating to the medicinal product, and/or completed trials concerning indications not covered by the application.

The amount of available information relevant to applications will differ substantially, depending on whether a medicinal product is in early clinical development or already authorised, and is being investigated for new or extended uses. Therefore, the level of detail expected in the application may differ significantly in line with the specific development stage of the product when the application is submitted.

([1]) See Concept paper on extrapolation of efficacy and safety in medicine development, available at: www.ema.europa.eu

2.1.3. *Paediatric population*

Applications subject to the requirements of Article 7 or 8 of the Paediatric Regulation should cover all subsets of the paediatric population ([1]) unless there are grounds for a waiver. The paediatric population encompasses several subsets, as defined e.g. in international guidelines ([2]):

— pre-term and term neonates from 0 to 27 days;

— infants (or toddlers) from 1 month to 23 months;

— children from 2 years to 11 years; and

— adolescents from 12 up to 18 years.

However, when it is considered more appropriate to use different subsets (e.g. based on gender or stage of pubertal development), this may be acceptable, but the choice of subsets should be explained and justified.

A PIP application intended to support a future paediatric use marketing authorisation (PUMA) may be limited to certain paediatric subsets; it is not required to address all subsets.

2.1.4. *Coverage of application*

A single application should cover the proposed research and development programme for a future single marketing authorisation application. Where the product is developed in stages and for different conditions, the applicant may apply for separate PIPs. Applications for authorised products which will fall within the scope of Article 8 of the Paediatric Regulation should cover all existing and new indications, pharmaceutical forms and routes of administration with a view to agreement on a single comprehensive PIP.

The application may include a request for a product-specific waiver. Additionally, a PIP may include a request for deferring some or all of the measures.

2.1.5. *Preparing the application*

Applicants are advised to request a pre-submission meeting to discuss the timing of submission of the application and to facilitate successful validation and assessment.

Applicants are encouraged to consult the paediatric research community, for example via the European networks for paediatric research at the Agency, as early involvement may facilitate the development of a PIP.

2.2. **Part A: Administrative and product information**

All sections of Part A should be completed; where information is not available, this should be stated. Part A information should be submitted using the form published by the Agency.

2.2.1. *Name or corporate name and address of the applicant and contact person*

The name and address of the applicant should be provided, together with the contact details of the person authorised to communicate with the Agency on behalf of the applicant.

As Agency decisions will be made public, the applicant is encouraged to provide a contact point (telephone number and/or e-mail address) for enquiries from interested parties. The Agency will make this public with its decisions. Personal e-mail addresses should be avoided.

Where the applicant qualifies as a micro, small or medium-sized enterprise within the meaning of Commission Recommendation 2003/361/EC ([3]), this should be stated.

([1]) The paediatric population is defined in Article 2 of the Paediatric Regulation as 'that part of the population aged between birth and 18 years'. This is understood to mean up to but not including 18 years.
([2]) ICH Guideline E11, available at www.ich.org
([3]) OJ L 124, 20.5.2003, p. 36.

2.2.2. *Name of the active substance*

The active substance should be stated by its recommended international non-proprietary name (INN), accompanied by its salt or hydrate form if relevant. If no 'recommended' INN exists, the European Pharmacopoeia name should be provided or, if the substance is not in the European Pharmacopoeia, the usual common name should be used. In the absence of a common name, the exact scientific designation should be given. Substances without an exact scientific designation should be described by a statement of how and from what they were prepared, supplemented where appropriate by any relevant details.

In addition to the common name or scientific designation, the applicant may also submit the company or laboratory code.

Preliminary names only may be provided if necessary in view of the deadline for submission of the applications.

2.2.3. *Type of product*

The type of product for which the application is made (e.g. a chemical entity, a biological product, a vaccine, a gene therapy product, a somatic cell therapy medicinal product) should be specified. In addition, the pharmacological target and mechanism of action should be specified where possible. Where a pharmaco-therapeutic group and anatomical therapeutic chemical (ATC) code have been assigned, these should be included.

2.2.4. *Details of the medicinal product*

Information on all different pharmaceutical forms, formulations, strengths and routes of administration under development, irrespective of future use in the paediatric population, should be provided. For the paediatric product development, information on the proposed strength, pharmaceutical form, route of administration and formulation (including details on the proposed excipients) should be provided.

2.2.5. *Marketing authorisation status of the medicinal product*

Information on the marketing authorisation status of the medicinal product should be provided in tabular format.

For medicinal products authorised in the EU, the marketing authorisation status, including information on all authorised indications, strengths, pharmaceutical forms and routes of administration, should be provided and, as regards authorisation status outside the EU, only information on authorisations in children should be included.

For products being developed for PUMAs, information should be provided on medicinal products authorised in the EU that contain the same active substance.

For medicinal products not yet authorised in the EU, the marketing authorisation status in adults and children outside the EU should be provided.

Details should be provided of any regulatory measures restricting for safety reasons the use of the medicinal product inside or outside the EU. This includes the suspension, revocation or non-renewal of the marketing authorisation, prohibition on supply, withdrawal of the medicinal product, a new contra-indication, a reduction in the recommended dose or a restriction on the indications of the medicinal product.

2.2.6. *Advice from a regulatory authority relevant to development in the paediatric population*

The Agency should be provided with any decisions, opinions or advice (including scientific advice) given by competent authorities, including those in non-EU countries, on the paediatric development of the medicinal product. This should include any written request for paediatric information issued by a regulatory body. Copies of any relevant documents should be annexed to the application.

2.2.7. *Orphan medicine status in the EU*

For orphan-designated products, the European Union Register of Orphan Medicinal Products number should be provided. If orphan designation is being sought, this should be indicated, and for pending applications the Agency's Orphan Designation Procedure number should be provided.

2.2.8. *Planned application for marketing authorisation/extension of marketing authorisation/variation*

The planned submission date for the marketing authorisation (or next variation/extension application under Article 8 of the Paediatric Regulation, as appropriate) should be provided, together with an indication of whether the intention is to submit the application via the centralised procedure or the procedures provided for by Directive 2001/83/EC [1].

[1] OJ L 311, 28.11.2001, p. 67.

For medicinal products not yet authorised which will fall under the requirements of Article 7 of the Paediatric Regulation, the planned or confirmed date of completion of the adult pharmaco-kinetic studies should be provided. Where an application is submitted more than six months after completion of such studies, a justification should be provided in this section.

2.2.9. *Application summary*

Applications for PIPs or waivers should be accompanied by an application summary of no longer than 1 000 words written in accordance with a template published by the Agency.

2.2.10. *Translations of the Agency decision*

If the Agency decision is requested in an official EU language other than English, the name of the active substance, the condition, the pharmaceutical form and route of administration should be provided in that language.

2.3. **Part B: Overall development of the medicinal product**

Part B should set out, for each existing indication and proposed condition/indication, and each subset of the paediatric population, how the requirements of the Paediatric Regulation will be met.

Where the medicinal product is developed for use in children only, some of the information requested in Part B may not be available. For products being developed for PUMAs, only the concerned paediatric subsets need to be addressed.

Applicants should provide:

— a general justification of the application submitted, including, where appropriate, the methodology chosen to identify potential conditions of paediatric need;

— a description of the condition in the paediatric population, including similarities between adult and paediatric populations and within the different paediatric subsets, prevalence, incidence, diagnosis and treatment methods, and alternative treatments;

— details of the condition that the medicinal product is intended to diagnose, prevent or treat. Diagnosis, prevention and treatment will generally be considered as separate conditions. For common, well-described paediatric conditions, reference can be made to paediatrics textbooks without submitting detailed information. Detailed information need not be provided on the condition in adults;

— where applicable, a reference to the condition according to an international disease classification system such as the WHO's International Classification of Disease (ICD) or another well recognised system.

The following points should be taking into account in the description of the condition. These points address, in particular, what constitutes a valid condition, as opposed to what would be considered as invalid subsets within a condition and how these elements are linked to existing treatments and to the proposed indication:

(a) The characteristics defining a condition should determine a group of patients in whom development of a medicinal product is plausible, based on the pathogenesis of the condition and pharmaco-dynamic evidence and assumptions;

(b) Recognised distinct medical entities would generally be considered as valid conditions. Such entities would generally be defined in terms of their specific characteristics, e.g. pathophysiological, histopathological, clinical characteristics;

(c) Different degrees of severity or stages of a disease would generally not be considered as distinct conditions;

(d) The fact that a subset of patients exists in whom the medicinal product is expected to show a favourable benefit/risk would generally not be sufficient to define a distinct condition; and

(e) Exceptionally, the need for a particular treatment modality (regardless of underlying diseases) can be considered a valid criterion to define a distinct condition, e.g. products to be used before or during bone marrow transplants, radiological or other diagnostic procedures.

2.3.1. *Discussion of similarities and differences in the condition between populations, and pharmacological rationale*

The application should briefly discuss any potential differences or similarities within the condition between the adult and the paediatric populations and/or between the different paediatric subsets.

These should be discussed with a view to extrapolating efficacy and/or pharmaco-kinetics, between adults and children, and the various paediatric subsets. Differences in aetiology, severity, symptoms, evolution, prognosis and response to therapy should be addressed where applicable.

Additionally, applicants should provide:

— a sufficiently detailed description of the pharmacological properties and of the known or suspected mechanism of action;

— a discussion of the potential paediatric use of the product, based on its characteristics, in the relevant conditions; and

— data/assumptions and a discussion of the impact of maturation aspects of pharmaco-kinetics and pharmaco-dynamics where applicable.

2.3.2. *Current methods of diagnosis, prevention or treatment in paediatric populations*

For each condition covered by the application, the diagnosis, prevention and treatment interventions that are available in the EU should be identified, making reference to scientific literature or other relevant information. This should include unauthorised treatment methods, whether pharmacological, surgical, dietary or otherwise, if they represent the standard of care (e.g. if mentioned in internationally recognised treatment guidelines). This should be presented in tabular format.

In the case of authorised medicinal products, the list of available treatments identified should include those authorised by the national authorities and those authorised under the centralised procedure. This can be presented as an overview table. Information on generic medicinal products need not be provided if the reference medicinal product is identified.

For medical devices marketed in the EU, the invented name and the approved use should be provided.

If methods for diagnosis, prevention or treatment of the condition in question have been included in the inventory of therapeutic needs established pursuant to Article 43 of the Paediatric Regulation, this information should be highlighted.

2.3.3. *Significant therapeutic benefit and/or fulfilment of therapeutic need*

The Paediatric Committee will assess whether the specific medicinal product is expected to be of significant therapeutic benefit to children and/or to fulfil a therapeutic need in children. The application should include a comparison of the medicinal product in question with the current methods of diagnosis, prevention or treatment of the conditions that are the subject of the PIP indication.

When assessing significant therapeutic benefit, the Paediatric Committee will take into account the nature and seriousness of the paediatric condition to be treated (or diagnosed or prevented) and available data on the medicinal product concerned. Significant therapeutic benefit could be based on one or more of the following:

(a) reasonable expectation of safety and efficacy for an authorised or new medicinal product to treat a paediatric condition, where no authorised paediatric medicinal product is on the market;

(b) expected improvement in efficacy in a paediatric population, as compared with the current standard of care for the treatment, diagnosis or prevention of the condition concerned;

(c) expected improvement in safety, as regards adverse reactions or potential medication errors in a paediatric population as compared with the current standard of care;

(d) improved dosing scheme or method of administration (e.g. number of doses per day, oral compared with intravenous administration, reduced treatment duration) leading to improved safety, efficacy or compliance;

(e) availability of a new clinically relevant age-appropriate formulation or pharmaceutical form;

(f) different mechanism of action, with a scientific explanation of the potential advantage for the paediatric population in terms of improved efficacy or safety;

(g) unsatisfactory nature of existing treatments and need for alternative methods expected to involve an improved benefit-risk balance; and

(h) expected improvement in the quality of life of the child.

As experience with the use of the medicinal product in the paediatric population might be unavailable or very limited at the time of submission of the application, significant therapeutic benefit could also be based on well-justified assumptions. The application should explore these assumptions on the basis of reasoned arguments and relevant literature.

If the therapeutic need is included in the inventory of therapeutic needs pursuant to Article 43 of the Paediatric Regulation, the application should refer to the inventory.

2.4. **Part C: Applications for product-specific waivers**

2.4.1. *Overview of the waiver request*

A waiver may be issued with reference either to one or more specified subsets of the paediatric population, or to one or more specified indications/conditions, or to a combination of both. Requests for product-specific waivers should clearly define their scope in terms of paediatric subset and indication.

A product-specific waiver will not be required if the product and the proposed indication are already covered by a class waiver.

Companies are advised to ask the Agency to give advance confirmation of the applicability of a class waiver to a proposed development of a medicinal product in one or more adult conditions.

If applicants intend to claim that measures in the paediatric population are not feasible, appropriate and detailed justification should be provided to support the claim.

2.4.2. *Justification for a product-specific waiver*

2.4.2.1. Applications based on a likely lack of safety or efficacy in part or all of the paediatric population

In accordance with Article 11(1)(a) of the Paediatric Regulation, a waiver may be granted if 'the specific medicinal product or class of medicinal products is likely to be ineffective or unsafe in part or all of the paediatric population'. On this basis, a request for a waiver may be based on a pharmaceutical rationale or (preliminary) data suggesting lack of efficacy or safety in the paediatric population.

The application should take account, for the different paediatric subsets, of the seriousness of the condition and the availability of other methods as stated in Part B. All available evidence should be submitted to illustrate the likely lack of efficacy in the paediatric population as a whole or in subsets, as applicable. The justification should be based on effects observed in non-clinical models and studies, where available, or on a review of scientific literature.

The justification for a waiver based on the likelihood or evidence that the product is likely to cause harm may differ depending on experience with the product. Justification for a waiver on these grounds may include the pharmacological properties of the product or class of product, results of non-clinical studies, clinical trials or post-marketing data. The applicant should signal specific known or suspected safety issues.

The absence of available data on the safety or efficacy in the paediatric population will not be accepted as the sole justification for a waiver.

2.4.2.2. Applications based on the disease or condition not occurring in the specified paediatric subset

In accordance with Article 11(1)(b) of the Paediatric Regulation, a waiver may be granted if 'the disease or condition for which the specific medicinal product or class is intended occurs only in adult populations'. On this basis, a justification for a waiver may be based on a detailed description of the incidence or prevalence of the condition in different populations. For waivers covering the totality of the paediatric population, the justification should focus particularly on the earliest age of onset of the condition. For waivers for specific subsets of the paediatric population, the justification should focus on the incidence or prevalence in the paediatric subsets identified in Part B.

2.4.2.3. Applications based on lack of significant therapeutic benefit

In accordance with Article 11(1)(c) of the Paediatric Regulation, a waiver may be granted if 'the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients'. On this basis, the justification for a waiver may be based on a lack of significant therapeutic benefit.

Justification for such a waiver should be based on a detailed discussion of the existing treatment methods. Reference can be made to the discussion under point 2.3.3.

In particular, where existing medicinal products are authorised for use in children, applicants intending to request a waiver on this ground should justify in detail why the new product would lack significant benefit over the existing treatments.

2.5. **Part D: Proposed paediatric investigation plan**

Part D should focus on the development of the medicinal product for the paediatric population. While applicants can discuss possible choices, there is no need to propose separate alternative developments in the application.

2.5.1. *Existing data and overall strategy proposed for the paediatric development*

2.5.1.1. Paediatric investigation plan indication

The PIP indication should be described for the paediatric subsets included in the paediatric investigation plan. This part should specify whether the medicinal product is intended for the diagnosis, prevention or treatment of the conditions in question.

2.5.1.2. Selected paediatric subsets

The age ranges to be studied should be justified, and may vary depending on the pharmacology of the product, the manifestation of the condition in various age groups and other factors. In addition to age, the classification of the paediatric population may be based on other variables, such as gestational age, pubertal stages, gender and renal function.

2.5.1.3. Information on quality, non-clinical and clinical data

The application should outline the development of the medicinal product, including the pharmaceutical development which is relevant for paediatric development, completed clinical studies in adults and the results where available. A brief outline of the planned studies in adults should also be provided. This information may be provided in tabular format.

The full study reports of completed non-clinical and clinical studies do not need to be provided; a summary of the results and a discussion of the implications for paediatric development should be sufficient. Full reports should be made available upon request. The application should take into account any existing scientific guidance/advice and standard PIP published by the Agency and justify any deviation for the paediatric development.

In addition, the application should include a review of any information on the product in the paediatric population, making reference to scientific and medical literature or other relevant information, such as reports on use outside the terms of a marketing authorisation, medication errors, accidental exposures or known class effects.

2.5.2. *Paediatric formulation development*

2.5.2.1. General strategy

This section should address selected aspects related to the administration of the product to the relevant paediatric subsets.

Guidelines on pharmaceutical development should be consulted to decide which measures could be relevant within the proposed strategy ([1]).

The addition of a paediatric indication may result in the need for an age-appropriate pharmaceutical form, e.g. a dispersible form rather than a large tablet, or a mini-tablet of a new strength, because the existing pharmaceutical form, excipients or strength may be unsuitable for use in all or part of the relevant paediatric populations. This means that the suitability of the existing formulation, strength and pharmaceutical form should be discussed in the PIP. Consideration may be given to ethnic or cultural differences as regards acceptability, route of administration, acceptable dosage forms and excipients, in relation to the specific characteristics of the product.

([1]) See Guideline for pharmaceutical development of medicines for paediatric use, available at www.ema.europa.eu

The discussion should take into account the existing or proposed pharmaceutical development of the product and address critical issues, such as:

— the need for specific formulation, pharmaceutical form, strength or route of administration in relation to the chosen paediatric subsets/age groups and the benefit of the chosen formulation, pharmaceutical form, strength or route of administration;

— potential issues in relation to excipients and their (anticipated) exposure levels to be used in the paediatric population;

— administration of the medicine to paediatric subsets (e.g. acceptability, use of specific administration devices, ability to mix with food);

— precision of dose delivery and/or dose accuracy for any pharmaceutical form, with regard to the anticipated paediatric dose and indicated age range; and

— timeframe for the development of an age-appropriate formulation/pharmaceutical form, where required.

If it is not possible, based on scientific justifications, to develop a formulation/pharmaceutical form which is relevant and acceptable for paediatric use on an industrial scale, the applicant should state how it intends to facilitate the industry-verified or extemporaneous preparation of an individual ready-for-use paediatric formulation.

2.5.2.2. Summary of all planned and/or ongoing measures in the pharmaceutical development

The application should contain in tabular form a list of planned and/or ongoing measures and studies intended to address the issues discussed under point 2.5.2.1. This should consist of the proposed key elements, as relevant and in accordance with the annex to this guideline, and be submitted using the specific form published by the Agency.

If the strategy is to create age-appropriate pharmaceutical form, formulation, strength or new route of administration, the necessary pharmaceutical development studies may need to be more extensive. Proposed measures of particular relevance to the development of paediatric products include:

— compatibility with paediatric administration systems, e.g. medical devices; and

— taste-masking and acceptability (including palatability).

2.5.3. *Non-clinical studies*

2.5.3.1. General strategy

This section should discuss the strategy for the non-clinical development which is needed to support paediatric use in addition to classical non-clinical development or existing data. If human safety data and previous animal studies are considered insufficient for reassurance on the likely safety profile in the intended paediatric age group, juvenile animal studies should be considered on an individual basis.

Reference to guidelines on non-clinical development should be made as necessary when discussing non-clinical studies.

The standard non-clinical development should not be submitted or discussed unless it adds relevant information to the paediatric development and is not covered elsewhere (e.g. the annexed investigator's brochure).

The following aspects should be discussed, taking into consideration existing scientific guidance:

(a) pharmacology:

— the need for proof of concept for use in paediatric populations, e.g. using non-clinical *in vitro* and/or *in vivo* models;

— the need for pharmaco-dynamic studies (e.g. to establish a dose relationship for a pharmaco-dynamic endpoint, if there is a reliable animal model to justify the choice of the most relevant species for potential juvenile animal studies); and

— the need for any paediatric-relevant safety pharmacology data (studies using non-clinical *in vitro* and/or *in vivo* models to investigate specific functions of the physiological system);

(b) toxicology:

— the need for toxicity studies to address specific endpoints, e.g. neurotoxicity, immunotoxicity or nephrotoxicity at a particular developmental phase.

2.5.3.2. Summary of all planned and/or ongoing non-clinical studies

A tabular list should be provided, with the proposed non-clinical studies. This should consist of the proposed key elements for the non-clinical studies, as relevant and in accordance with the annex to this guideline, and should be submitted using the specific form published by the Agency.

2.5.4. *Paediatric clinical studies*

2.5.4.1. General strategy

This section should discuss and justify the strategy for the clinical paediatric development, in relation to the development in adults where applicable and in relation to existing data and the potential to extrapolate. This should include only critical aspects of study design and should present the strengths, advantages and disadvantages of the proposed clinical development. Where appropriate, the extension of adult trials to paediatric patients (e.g. adolescents) may be considered.

In this section, the application should also:

— discuss possible complete or partial extrapolation from adult data to paediatric patients and between paediatric subsets;

— explain the interrelation, in terms of common studies, data and timelines, between development in adults and paediatric populations;

— if extrapolation is a substantial component of the proposed development, describe a specific extrapolation study with a defined protocol in the list of measures; and

— where necessary, a discussion on how dosing in very young and young children is determined and verified.

Trials should be performed in the least vulnerable groups whenever possible (i.e. in adults rather than in children, in older rather than younger children). If results cannot be extrapolated to younger groups, this should be justified.

2.5.4.2. Paediatric pharmaco-kinetic/pharmaco-dynamic studies

The following aspects should be considered, where relevant:

(a) pharmaco-dynamic studies:

— pharmaco-dynamic differences between adult and paediatric populations (e.g. influence of maturation of receptors and/or systems);

— use of pharmaco-dynamic modelling and clinical trial simulations;

— discussion of any biomarkers for pharmaco-kinetics/pharmaco-dynamics; and

— use of the pharmaco-dynamic approach, particularly where pharmacokinetics cannot be measured; and

(b) pharmaco-kinetic studies:

— possibility of using sparse pharmaco-kinetic sampling;

— use of pharmaco-kinetic modelling and clinical trial simulations;

— use of population pharmaco-kinetics;

— discussion of age groups where more extensive studies are needed, e.g. due to expected high kinetic variability; and

— pharmacogenetics.

2.5.4.3. Clinical efficacy and safety studies

The following aspects should be discussed, where relevant:

— the need for specific dose-finding studies;

— the selected efficacy and/or safety endpoints (primary or secondary), in each of the relevant paediatric subsets;

— issues of relevance across the proposed studies, such as use of placebo or active control, age appropriateness of endpoints, use of surrogate markers, use of alternative study design and analysis, potential need for short-term and long-term safety studies and differential risks by age group;

— issues related to the feasibility of the proposed studies (e.g. recruitment capacity);

— any potential concern as to long-term safety or efficacy in the paediatric population; and

— specific measures proposed to protect the paediatric population involved in development, e.g. the use of less invasive methods.

2.5.4.4. Summary of all planned and/or ongoing paediatric clinical studies

A tabular list should be provided, with the proposed clinical studies. This should consist of the proposed key elements for clinical studies, as relevant and in accordance with the annex to this guideline, and be submitted using the specific form published by the Agency.

The table should propose timelines for the initiation and completion of each study, including either specific dates (month and year) or ranges of up to six months, and specify whether a deferral is being requested for the initiation and/or completion of each measure. Alternatively, timelines for initiation may be linked to the completion of a study in adults ('x months after completion of study y') or a measure in the PIP.

Clinical studies are deemed to have been completed on the date of the last visit of the last subject in the study or at a later point in time as defined in the protocol. It is advisable that the dates proposed in the table take account of the time needed to complete, analyse and report the studies to the competent authorities.

2.5.4.5. Details of the planned and/or ongoing paediatric clinical studies

To facilitate the scrutiny of the proposed development programme, the applicant may, in addition to the proposed key elements, provide more detailed information, such as a synopsis of the study protocol (or the full protocol if available).

Further information, if available and as appropriate to the stage of product development, should be provided on the following:

— justification of type of study, study design and methodology;

— justification of the dose of the proposed product and its regimen, and of the type of control (e.g. placebo or active control, with dose to be used);

— description of the sample size/power calculation (as appropriate; with expected effect size in children) used to determine the proposed number of subjects (male/female). This discussion should include, where possible, a sensitivity analysis (a tabulation with varying assumptions and statistical parameters, and the resulting sample sizes);

— justification of the relevant age groups or subsets included in the study (and of staggered inclusion where applicable);

— justification of the proposed duration of treatment (and duration of post-treatment observation if included in the study);

— justification of main inclusion/exclusion criteria;

— justification of the choice of outcome parameters/endpoints (primary, secondary);

— justification and, if needed, a more detailed description of statistical methods than that contained in the key elements; and

— discussion of options in the event of recruitment issues.

2.5.5. *Other studies*

If extrapolation and/or modelling and simulation studies are part of the proposed PIP, a tabular list with the proposed studies should be provided. This should consist of the proposed key elements, as relevant and in accordance with the annex to this guideline, and be submitted using the form published by the Agency.

Those other studies are deemed to have been completed on completion of the relevant study report.

2.6. **Part E: Request for deferral**

Where it is not planned that a study or other measure in the PIP will be initiated or completed before the submission of the corresponding marketing authorisation application in adults, a deferral may be requested. Requests for deferral should be justified on scientific and technical grounds or on grounds related to public health.

In accordance with the Paediatric Regulation a deferral will be granted when:

— it is appropriate to conduct studies in adults prior to initiating studies in the paediatric population; or

— studies in the paediatric population will take longer to conduct than studies in adults.

With reference to the timelines in Part D, any request for deferral of the start or completion of studies or other measures should make clear to which study/measure the deferred timeline relates.

For timelines, either specific months and years should be given or a range of up to six months; timelines for initiation may also be expressed in relation to the development in adults.

Particular emphasis should be placed on the timing of the measures as compared with the development for adults, e.g. as expressed in the ICH guideline E11.

2.7. **Part F: Annexes**

The annexes to the application should include the following, if available:

— references (i.e. published literature);

— the investigator's brochure (latest version) and protocol of the listed studies;

— the latest approved summary of product characteristics and risk management plan for a product already authorised;

— the reference number or a copy of any scientific advice of relevance to paediatric development (pharmaceutical, nonclinical, and clinical) given by the Agency;

— a copy of any scientific advice of relevance to paediatric development (pharmaceutical, non-clinical and clinical) given by a competent national authority;

— a copy of any written request by the United States Food and Drug Administration and/or of any advice/opinion/decision relating to paediatric information given by a regulatory agency outside the EU;

— a copy of any Commission decision on orphan designation; and

— the reference number or a copy of any previous Agency decision on PIPs or a negative opinion of the Paediatric Committee on such plans.

2.8. **Modification of an agreed paediatric investigation plan**

Article 22 of the Paediatric Regulation provides for an agreed plan to be modified where necessary. Such modifications are required where key elements of the PIP are unworkable or no longer appropriate. A request for modification of an agreed PIP is not necessary if the modification affects only aspects of a study or a measure that are not reflected in any agreed key element.

Applicants should explain the lack of appropriateness or the feasibility issue underlying each key element for which modification is being requested and discuss whether this should be addressed by a modification, a deferral or a waiver. An assessment of the effect of both making and failing to make the proposed change should be provided.

Submission of an application to modify the PIP will be particularly important if new information may have an impact on the nature or timelines for completion of one of the key elements in the Agency decision on the PIP.

Applications for modification should follow the same structure as initial applications, but only sections relevant to the change should be completed. Applications should be accompanied by an application summary of no longer than 500 words.

3. **OPERATION OF THE COMPLIANCE CHECK**

In accordance with Articles 23 and 24 of the Paediatric Regulation, compliance with the agreed PIP is checked at various stages by the competent national authorities or the Agency:

— pursuant to Article 23, compliance may need to be checked as part of the validation of applications for marketing authorisation, their extensions or variations that fall under the obligations of Articles 7, 8 or 30. Non-compliance will lead to non-validation of the application;

— validation of application may not require a compliance check procedure if none of the studies or other measures in the agreed PIP have a timeline for completion that precedes the date of submission of the application; and

— pursuant to Article 24, detection of non-compliance during the scientific assessment of a valid application will result in non-inclusion in the marketing authorisation of the compliance statement referred to in Article 28(3); the medicinal product will not be eligible for the rewards and incentives provided for in Articles 36, 37 and 38.

The compliance check prior to or upon validation of a marketing authorisation application is of particular importance. Article 23 provides that the Paediatric Committee may on request issue an opinion on compliance and clarifies who can request such an opinion and when. For example, the Agency or the competent national authorities may request an opinion when validating an application. Under the second subparagraph of Article 23(3), Member States must take account of the opinion of the Paediatric Committee.

The compliance checks will determine whether:

— the documents submitted pursuant to Article 7(1) cover all subsets of the paediatric population;

— for applications falling within the scope of Article 8 of the Paediatric Regulation, the documents submitted pursuant to Article 7(1) cover the existing and the new indications, pharmaceutical forms and routes of administration; and

— all the measures in an agreed PIP have been carried out in accordance with the key elements specified in the decision approving the PIP.

The studies or other measures checked for compliance are those that are part of the condition covering an indication for which an application for marketing authorisation is made and that were to have been completed at the time of the submission. Where the scope of the application is exceptionally covered by more than one PIP, all concerned PIPs will be checked for compliance.

Any necessary modification of the PIP should take place before the submission of the application for marketing authorisation or variation.

To facilitate the work of the competent authorities and, where appropriate, the Paediatric Committee in reaching an opinion on compliance, applicants are encouraged to present a compliance report when submitting the application for marketing authorisation, extension or variation. Additionally, for nationally authorised products, applicants should submit the latest complete Agency decision (which includes the opinion with the key elements, and the summary report) to the competent national authorities concerned.

For medicinal products that fall under the scope of Articles 7 or 8, the compliance report should indicate in the form of a table how each subset of the paediatric population and, for applications falling under Article 8, how each of the existing and new indications, pharmaceutical forms and routes of administration have been covered by the documents referred to in Article 7(1).

A separate table should be included covering the applicant's position on compliance with the key elements and, where submitted with the marketing authorisation application, providing a cross-reference for each key element of the PIP to the location in the relevant module in the marketing authorisation application. If a PIP has been modified, the table should be based on the latest decision by the Agency.

It should be noted that:

— the relevant competent authority or the Agency will perform a detailed check on each key element of the agreed PIP against what has actually been submitted;

— applicants for marketing authorisation or variation will need to comply with each key element;

— minor deviations from key elements that have been requested by the competent authority that authorised the study should not affect compliance; and

— when conditional language such as 'could' or 'such as' is used in the Agency decision, compliance may be confirmed even if these measures were not followed as suggested.

When only some measures referred to in the Agency decision were to have been completed at the time of submission of the application, the Agency or the Paediatric Committee will provide the applicant with a letter confirming the compliance or otherwise of those measures. Where compliance is not confirmed, the grounds will be detailed in a report.

The compliance check under Article 23 is without prejudice to the possibility that the competent authority will conclude, when conducting the scientific assessment of a valid application, that the studies are in fact not in conformity with the agreed PIP.

The statement of compliance should be included in the marketing authorisation. This may be done by including it with other technical information forming part of the marketing authorisation ('technical dossier'), in which case the competent national authorities, or the Agency in the case of variations or extensions of centralised marketing authorisations, must confirm to the marketing authorisation holder that this has been done.

Where the measures in a PIP contain no study initiated before the entry into force of the Paediatric Regulation (i.e. 26 January 2007), the statement of compliance referred to in Article 28(3) will read as follows:

> 'The development of this product has complied with all measures in the agreed paediatric investigation plan [reference number]. All studies were conducted after the entry into force of Regulation (EC) No 1901/2006'.

Where the measures in a PIP contain some studies initiated before the entry into force of the Paediatric Regulation, the statement of compliance will read as follows:

> 'The development of this product has complied with all measures in the agreed paediatric investigation plan [reference number]. For the purpose of the application of Article 45(3) of Regulation (EC) No 1901/2006, significant studies in the agreed paediatric investigation plan were completed after the entry into force of that Regulation'.

4. CRITERIA FOR ASSESSING THE SIGNIFICANCE OF STUDIES PURSUANT TO ARTICLE 45(3) OF THE PAEDIATRIC REGULATION

4.1. Background

To qualify for the reward and incentives provided for in Articles 36, 37 and 38 of the Paediatric Regulation, PIPs which include studies initiated and/or completed before its entry into force must include 'significant' studies that were initiated and/or completed after that date (see Article 45(3)). The statement of compliance referred to in Article 28(3) of the Regulation will indicate whether the studies are considered 'significant' within the meaning of Article 45(3).

A study will be considered as having been completed after the entry into force of the Regulation if the date of the last visit of the last patient is after that date. Open extensions of studies consisting of treatment maintenance for patients will not be considered as continuing after the entry into force if this was not part of the protocol submitted to the relevant competent authorities.

4.2. Assessment criteria

In general, the significance of studies is determined by the clinical relevance of data generated for the paediatric population rather than by the number of studies. In exceptional cases, a set of non-significant studies might be considered significant if the results taken together are expected to provide important and clinically relevant information.

The Agency or the competent authorities will assess the significance of each study proposed in a PIP on a case-by-case basis. However, the examples below are provided as a guide to the assessment of the significance of studies.

The following study types will generally be considered as significant:

(a) comparative efficacy studies (randomised/active control or placebo);

(b) dose-finding studies;

(c) prospective clinical safety studies, if the results are expected to make a major contribution to the safe use of the medicinal product in the paediatric population (this includes studies on growth and development);

(d) studies to obtain a new age-appropriate formulation, if this is expected to be of clinical relevance for the safe and effective use of the medicinal product in the paediatric population; and

(e) pharmaco-kinetic/pharmaco-dynamic clinical studies that are likely to provide meaningful data that would preclude the need for a clinical efficacy study and therefore spare the numbers of children who may need to be enrolled in a larger trial.

In order to be considered significant, studies should normally cover several paediatric subsets, unless a waiver has been granted. However, studies conducted in a single subset of the paediatric population could be considered significant if:

— sufficiently extensive; or

— they make an important contribution to treatment of children; or

— they are carried out in a subset considered particularly difficult to study, e.g. neonates.

Where sufficient data for one or more of the paediatric subsets are already available, duplication of studies should be avoided and unnecessary studies will not be considered significant.

ANNEX

Key elements

1. Paediatric formulation development studies:

   (a) Pharmaceutical form, formulation, strength, route of administration for development for paediatric use

   (b) Timelines for completion

2. Non-clinical studies:

   (a) Type of study

   (b) Objective and outcome measure

   (c) Test system

   (d) Route of administration and doses

   (e) Duration of dosing

   (f) Timelines for completion

3. Paediatric clinical studies:

   (a) Type of study

   (b) Study design and control

   (c) Main objectives

   (d) Study population and paediatric subsets in which the study will be conducted (with key inclusion and exclusion criteria)

   (e) Minimum number of study participants

   (f) Paediatric formulation used in the study, dose ranges, treatment regimes, route of administration

   (g) Minimum study duration

   (h) Primary endpoint (and main secondary endpoints) and time of assessment

   (i) Statistical plan

   (j) Timelines for completion

4. Modelling and simulation studies:

   (a) Model objective and description

   (b) Data to be used to build model

   (c) Methodology and software

   (d) Co-variates

   (e) Model qualification

   (f) Timelines for completion

5. Extrapolation studies:

   (a) Type of study and design

   (b) Objective

   (c) Methodology

   (d) Study population and subsets

   (e) Minimum number of study participants

   (f) Timelines for completion

Key elements should not contain unnecessary details. Depending on the specificities of the application, not all key elements may need to be addressed in every measure/study. In duly justified cases, further key elements may be required. This may apply in particular to orphan-designated products, advanced therapy medicinal products, immunological medicinal products, radiopharmaceuticals and medicinal products based on human blood or plasma.

COMMUNICATION FROM THE COMMISSION

Updating of data used to calculate lump sum and penalty payments to be proposed by the Commission to the Court of Justice in infringement proceedings

(2014/C 338/02)

I. INTRODUCTION

The 2005 Commission communication on the application of Article 228 of the EC Treaty [1] (now Article 260(1) and (2) of the TFEU) established the basis on which the Commission calculates the amount of the financial sanctions (either lump sum or penalty payments) that it requests the Court of Justice to apply when the Commission brings a case before the Court under Article 260 TFEU, in the context of infringement proceedings against a Member State.

In a subsequent communication of 2010 [2] on the updating of the data used for this calculation, the Commission established that these macroeconomic data be subject to revision every year, in order to take into account inflation and GDP movements.

The yearly update provided in this Communication is based on developments in the inflation and GDP of each Member State [3]. The relevant rate of inflation and GDP statistics to be used are those established two years prior to the update ('n-2 rule'), as two years is the minimum period of time necessary for gathering relatively stable macroeconomic data. This Communication is therefore based on economic data for nominal GDP and the GDP deflator for 2012 [4] and the current weighting of Member State voting rights in the Council.

The Commission empowered its President, acting in agreement with the Member responsible for economic and monetary affairs, to adopt the above measures [5].

II. COMPONENTS OF THE UPDATE

The list of economic criteria to be revised is as follows:

— the standard flat-rate amount for the penalty payment [6], currently fixed at EUR 650 per day, to be revised in line with inflation,

— the standard flat-rate amount for the lump sum payment [7], currently fixed at EUR 220 per day, to be revised in line with inflation,

— the special 'n' factor [8], to be revised in line with the GDP of the Member State in question taking into account the number of voting rights it has in the Council; the 'n' factor is identical for the calculation of lump sum and daily penalty payments,

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[1] SEC(2005) 1658; OJ C 126, 7.6.2007, p. 15.

[2] SEC(2010) 923/3. This communication has been updated in 2011 (SEC(2011) 1024 final), in 2012 (C(2012) 6106 final) and in 2013 (C(2013) 8101 final), for the yearly adaptation of economic data.

[3] According to the general rules set out in the communications of 2005 and 2010.

[4] The GDP price deflator is used as a measure of inflation. The uniform amounts for lump sum and penalty payments are rounded to the nearest multiple of ten. The minimum lump sums are rounded to the nearest thousand. The 'n' factor is rounded to two decimal places.

[5] Empowerment of 13 December 2005 for the adoption of decisions updating certain data used to calculate lump sum and penalty payments under the Commission's policy regarding the application of Article 228 of the EC Treaty; SEC(2005) 1616.

[6] The standard or uniform flat-rate amount for daily penalty payments is defined as the fixed basic amount to which certain multiplier weightings are applied. The weightings are the coefficients for the seriousness and the duration of the infringement and the special factor 'n' corresponding to the Member State concerned that are to be applied for the calculation of a daily penalty payment.

[7] The flat-rate amount is to be applied when calculating the lump sum. As regards Article 260(2) TFEU, the lump sum will result from multiplying a daily (lump sum) amount (resulting from multiplying the flat-rate for lump sum payments by the coefficient for seriousness and the result of this calculation being multiplied by the special factor 'n') by the number of days the infringement persists between the date of the first judgment and the date that the infringement comes to an end or the date of delivery of the judgment under Article 260(2) TFEU. As regards Article 260(3) TFEU, according to point 28 of the Commission Communication on 'Implementation of Article 260(3) of the Treaty' (SEC(2010)1371 final; OJ C 12, 15.1.2011, p. 1), the lump sum will result from multiplying a daily (lump sum) amount (resulting from multiplying the flat-rate for lump sum payments by the coefficient for seriousness and the result of this calculation being multiplied by the special factor 'n') by the number of days from the day after the time limit for transposition set out in the directive expired until the first judgment under Articles 258 and 260(3) TFEU. The (daily) lump sum will be proposed by the Commission when the result of the abovementioned calculation exceeds the minimum fixed lump.

[8] The special factor 'n' takes into account the capacity of the Member States to pay (gross domestic product (GDP)) and the number of votes it has in the Council.

— minimum lump sum payments [1] to be revised in line with inflation.

III. **UPDATES**

The Commission will apply the following updated figures to calculate the amount of the financial sanctions (lump sum or penalty payments) when it brings a case to the Court of Justice under Article 260(2) and (3) TFEU:

(1) the standard flat-rate amount for calculating the penalty payment is fixed at **EUR 660** per day,

(2) the standard flat rate for the lump sum payment is fixed at **EUR 220** per day.

(3) The special 'n' factor and the minimum lump sum (in EUR) for the 28 EU Member States are set as follows:

	Special 'n' factor	Minimum lump sum (EUR 1 000)
Belgium	5,13	2 829
Bulgaria	1,53	844
Czech Republic	3,27	1 803
Denmark	3,16	1 743
Germany	21,22	11 703
Estonia	0,64	353
Ireland	2,59	1 428
Greece	3,68	2 030
Spain	12,72	7 015
France	18,53	10 219
Croatia	1,33	733
Italy	16,27	8 973
Cyprus	0,64	353
Latvia	0,72	397
Lithuania	1,16	640
Luxembourg	1,00	552
Hungary	2,60	1 434
Malta	0,35	193
Netherlands	6,74	3 717
Austria	4,23	2 333
Poland	7,75	4 274
Portugal	3,40	1 875

[1] The minimum fixed lump sum payment is determined for each Member State according to the special 'n' factor. The minimum fixed lump sum will be proposed to the Court when the summed up daily lump sum payments do not exceed the minimum fixed lump sum.

	Special 'n' factor	Minimum lump sum (EUR 1 000)
Romania	3,28	1 809
Slovenia	0,91	502
Slovakia	1,70	938
Finland	2,80	1 544
Sweden	4,87	2 686
United Kingdom	18,02	9 938

(4) The Commission will apply the updated figures to decisions it takes to bring a case before the Court of Justice under Article 260 TFEU as from the adoption of this Communication.

IV

(Notices)

NOTICES FROM EUROPEAN UNION INSTITUTIONS, BODIES, OFFICES AND AGENCIES

COUNCIL

COUNCIL DECISION

of 25 September 2014

appointing the members and alternate members of the Advisory Committee on Freedom of Movement for Workers

(2014/C 338/03)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EU) No 492/2011 of the European Parliament and of the Council of 5 April 2011 on freedom of movement for workers within the Union [1], and in particular Articles 23 and 24 thereof,

Having regard to the lists of candidates submitted to the Council by the Governments of the Member States,

Whereas:

(1) By its Decisions of 4 October 2012 [2] and 20 November 2012 [3], the Council appointed the members and alternate members of the Advisory Committee on Freedom of Movement for Workers (the 'Committee') for the period from 25 September 2012 to 24 September 2014.

(2) The members remain in office until they are replaced or reappointed.

(3) Members and alternate members of the Committee should be appointed for a period of two years,

HAS ADOPTED THIS DECISION:

Article 1

The following are hereby appointed as members and alternate members of the Advisory Committee on Freedom of Movement for Workers for the period from 25 September 2014 to 24 September 2016:

I. GOVERNMENT REPRESENTATIVES

Country	Members	Alternates
Belgium	Ms Gylvie GUELLUY Mr Jacques OUZIEL	Mr Thierry LHOIR
Bulgaria	Mr Hristo SIMEONOV Ms Tatiana GUEORGUIEVA	Ms Dimitrina KOSTADINOVA
Czech Republic	Ms Kateřina ŠTĚPÁNKOVÁ Ms Eva DIANIŠKOVÁ	Ms Eva NOVÁKOVÁ

[1] OJ L 141, 27.5.2011, p. 1.
[2] Council Decision of 4 October 2012 appointing the members and alternate members of the Advisory Committee on freedom of movement for workers (OJ C 302, 6.10.2012, p. 1).
[3] Council Decision of 20 November 2012 appointing the members and alternate members of the Advisory Committee on Freedom of Movement for Workers for Italy (OJ C 360, 22.11.2012, p. 4).

Country	Members	Alternates
Denmark	Mr Stig Hansen NØRGAARD Ms Rikke Mark SEERUP	Ms Simone HEINECKE
Germany	Ms Vera BADE Mr Johannes RASCHKA	Ms Anne Katrin LUTZ
Estonia	Ms Marit RAIST Ms Liis REITER	Ms Kristi SUUR
Ireland	Ms Mary Joan KEHOE Mr Anthony MORRISSEY	Ms Aedin DOYLE
Greece		
Croatia	Ms Marija KNEŽEVIĆ KAJARI Ms Ivana GUBEROVIĆ	Ms Aleksandra GAVRILOVIĆ
Spain	Ms Paloma MARTÍNEZ GAMO Mr Miguel COLINA ROBLEDO	Ms Rosalía SERRANO VELASCO
France	Ms Magali MARTIN Mr Albert MARTINO	Mr Laurent FRIBOULET
Italy		
Cyprus		
Latvia	Ms Ilze ZVĪDRIŅA Mr Kristaps ZIEDIŅŠ	Ms Linda PAUGA
Lithuania	Ms Rasa MALAIŠKIENĖ Ms Agnė PECIUKEVIČIENĖ	Ms Inga LIUBERTĖ
Luxembourg		
Hungary		
Malta	Mr Mario SCHEMBRI Mr Nicola CINI	Mr George CAMILLERI
Netherlands	Mr Onno BRINKMAN Ms Cristel van TILBURG	Mr Mark JACOBS
Austria	Mr Heinz KUTROWATZ Ms Martha ROJAS-PINEDA	Mr Günter STICKLER
Poland	Ms Magdalena SWEKLEJ Mr Marcin WIATRÓW	Ms Agnieszka ZDAK
Portugal		
Romania	Mr Auraş MARINESCU Ms Simona ŞTEFAN	Mr Bogdan-Tiberius PAŞCA
Slovenia	Ms Sonja MALEC Mr Grega MALEC	Ms Mateja GOLJA
Slovakia	Ms Zuzana KRCHŇAVÁ Mr Jaroslav KOVÁČ	
Finland	Ms Katri NISKANEN Mr Olli SORAINEN	Ms Elina HIRTTIÖ
Sweden	Ms Maria NORDIN SKULT Ms Madeleine ÖHBERG	Ms Kristina EKBERG
United Kingdom	Ms Janina CIECIORA Ms Deborah MORRISON	Mr Jonathan PIGGINS

II. TRADE UNION REPRESENTATIVES

Country	Members	Alternates
Belgium	Mr Koen MEESTERS Ms Hanne SANDERS	Mr Jean-François MACOURS
Bulgaria	Ms Atanaska TODOROVA Mr Daniel YANEV	
Czech Republic	Mr Vít SAMEK Mr Pavel JANÍČKO	Mr Petr ŠULC
Denmark	Mr Jørgen Rønnow BRUUN Ms Helle Hjort BENTZ	Ms Käthe Munk RYOM
Germany	Ms Alexandra KRAMER Ms Ina HINZER	Mr Thomas BEMMANN
Estonia	Ms Mare VIIES Ms Liina CARR	Ms Aija MAASIKAS
Ireland	Ms Esther LYNCH Mr John DOUGLAS	
Greece		
Croatia	Ms Ana KRANJAC JULARIĆ Mr David Jakov BABIĆ	Ms Ana MILIĆEVIĆ PEZELJ
Spain	Ms Ana María CORRAL JUAN Mr Francisco GONZÁLEZ MORENO	Mr Jose Antonio MORENO DÍAZ
France	Ms Francine BLANCHE Ms Corinne MARES	Mr Ommar BENFAID
Italy		
Cyprus		
Latvia	Ms Natalja MICKEVIČA Mr Kaspars RĀCENĀJS	Mr Mārtiņš SVIRSKIS
Lithuania	Ms Janina ŠVEDIENĖ Ms Janina MATUIZIENĖ	Mr Ričardas GARUOLIS
Luxembourg		
Hungary		
Malta	Mr Ian Mark ZAMMIT Mr Jeremy J CAMILLERI	Mr Paul PACE
Netherlands	Ms Caroline RIETBERGEN Mr Martijn HORDIJK	Mr Henk BOSSCHER
Austria	Mr Johannes PEYRL Mr Oliver RÖPKE	Ms Lena KARASZ
Poland	Mr Jakub KUS Ms Krystyna CIEMNIAK	Mr Bogdan OLSZEWSKI
Portugal		
Romania	Mr Corneliu CONSTANTINOAIA Mr Liviu APOSTOIU	Mr Dragos FRUMOSU
Slovenia	Mr Marko TANASIČ Mr Jakob POČIVAVŠEK	Ms Nadja GÖTZ

Country	Members	Alternates
Slovakia	Ms Vlasta SZABOVÁ Ms Zdena DVORANOVÁ	Ms Mária SVOREŇOVÁ
Finland	Ms Eve KYNTÄJÄ Mr Heikki TAULU	Mr Ralf SUND
Sweden	Mr Thord INGESSON Ms Josefin EDSTRÖM	Ms Sofia RÅSMAR
United Kingdom	Ms Rosa CRAWFORD Mr Mohammed TAJ	Mr Wilf SULLIVAN

III. EMPLOYERS' ASSOCIATIONS REPRESENTATIVES

Country	Members	Alternates
Belgium	Ms Michèle CLAUS Ms Hilde THYS	Ms Monica DE JONGHE
Bulgaria	Mr Ivan ZAHARIEV Mr Martin STOYANOV	Ms Daniela SIMIDCHIEVA
Czech Republic	Ms Vladimíra DRBALOVÁ Ms Marie ZVOLSKÁ	Ms Jitka HLAVÁČKOVÁ
Denmark	Mr Henning GADE Mr Flemming DREESEN	Ms Karen ROIY
Germany	Mr Alexander WILHELM Ms Christina BREIT	Ms Carmen Eugenia BÂRSAN
Estonia	Ms Piia SIMMERMANN Ms Katrin TRUVE	Ms Mare HIIESALU
Ireland	Mr Tony DONOHOE Ms Kara McGANN	
Greece		
Croatia	Ms Milica JOVANOVIĆ Ms Milka KOSANOVIĆ	Ms Nataša NOVAKOVIĆ
Spain	Ms Helena MORALES DE LABRA Ms Patricia CIREZ MIQUELEIZ	Mr Luis MÉNDEZ LÓPEZ
France	Ms Garance PINEAU Ms Natacha MARQUET	Ms Pascale DESSEN
Italy		
Cyprus		
Latvia	Ms Anita LĪCE Ms Ilona KIUKUCĀNE	Ms Jolanta VJAKSE
Lithuania	Mr Justinas USONIS Mr Aidas VAIČIULIS	Ms Dovilė BAŠKYTĖ
Luxembourg		
Hungary		
Malta	Mr Lawrence MIZZI Mr Michael GALEA	Mr John HUBER

Country	Members	Alternates
Netherlands	Mr Rob SLAGMOLEN Mr A.P.M.G. SCHOENMAECKERS	Mr G.A.M. Gerard VAN DER GRIND
Austria	Ms Margit KREUZHUBER Ms Julia ENZELSBERGER	Ms Kornelia LIENHART
Poland	Ms Monika GŁADOCH Mr Grzegorz BACZEWSKI	Mr Andrzej STĘPNIKOWSKI
Portugal		
Romania	Ms Roxana PRODAN Mr Florian STAMATE	Mr Liviu ROGOJINARU
Slovenia	Mr Igor ANTAUER Ms Polona FINK RUŽIČ	Ms Maja SKORUPAN
Slovakia	Mr Radovan MAXIN Mr Peter MOLNÁR	Mr Martin HOŠTÁK
Finland	Mr Mikko RÄSÄNEN Ms Jenni RUOKONEN	Mr Simopekka KOIVU
Sweden	Ms Karin EKENGER Ms Carin RENGER	Mr Patrik KARLSSON
United Kingdom	Ms Sinead LAWRENCE Mr Rob WALL	Mr Tom SALLIS

Article 2

The members not yet nominated will be appointed by the Council at a later date.

Article 3

This Decision shall enter into force on the date of its adoption.

Done at Brussels, 25 September 2014.

For the Council

The President

F. GUIDI

COUNCIL DECISION

of 25 September 2014

appointing and replacing members of the Governing Board of the European Centre for the Development of Vocational Training

(2014/C 338/04)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to Council Regulation (EEC) No 337/75 of 10 February 1975 establishing the European Centre for the Development of Vocational Training ([1]), and in particular Article 4 thereof,

Having regard to the nomination submitted to the Council by the Commission in the category of Employees' representatives,

Whereas:

(1) By its Decision of 16 July 2012 ([2]), the Council appointed the members of the Governing Board of the European Centre for the Development of Vocational Training for the period from 18 September 2012 to 17 September 2015.

(2) A member's seat is available for Poland on the Governing Board of the Centre in the category of Employees' representatives,

HAS DECIDED AS FOLLOWS:

Sole Article

The following person is hereby appointed as a member of the Governing Board of the European Centre for the Development of Vocational Training for the remainder of the term of office, which runs until 17 September 2015:

REPRESENTATIVES OF EMPLOYEES' ORGANISATIONS:

POLAND	Ms Dagmara IWANCIW

Done at Brussels, 25 September 2014.

For the Council

The President

F. GUIDI

([1]) OJ L 39, 13.2.1975, p. 1.
([2]) OJ C 228, 31.7.2012, p. 3.

EUROPEAN COMMISSION

Euro exchange rates [1]

26 September 2014

(2014/C 338/05)

1 euro =

	Currency	Exchange rate		Currency	Exchange rate
USD	US dollar	1,2732	CAD	Canadian dollar	1,4148
JPY	Japanese yen	138,93	HKD	Hong Kong dollar	9,8772
DKK	Danish krone	7,4432	NZD	New Zealand dollar	1,6110
GBP	Pound sterling	0,78070	SGD	Singapore dollar	1,6189
SEK	Swedish krona	9,2132	KRW	South Korean won	1 330,36
CHF	Swiss franc	1,2071	ZAR	South African rand	14,2343
ISK	Iceland króna		CNY	Chinese yuan renminbi	7,7991
NOK	Norwegian krone	8,1675	HRK	Croatian kuna	7,6290
BGN	Bulgarian lev	1,9558	IDR	Indonesian rupiah	15 343,94
CZK	Czech koruna	27,534	MYR	Malaysian ringgit	4,1518
HUF	Hungarian forint	311,51	PHP	Philippine peso	57,134
LTL	Lithuanian litas	3,4528	RUB	Russian rouble	49,6730
PLN	Polish zloty	4,1805	THB	Thai baht	41,133
RON	Romanian leu	4,4027	BRL	Brazilian real	3,0850
TRY	Turkish lira	2,8736	MXN	Mexican peso	17,0351
AUD	Australian dollar	1,4483	INR	Indian rupee	77,9841

[1] *Source*: reference exchange rate published by the ECB.

Commission notice on current State aid recovery interest rates and reference/discount rates for 28 Member States applicable as from 1 October 2014

(Published in accordance with Article 10 of Commission Regulation (EC) No 794/2004 of 21 April 2004 (OJ L 140, 30.4.2004, p. 1))

(2014/C 338/06)

Base rates calculated in accordance with the Communication from the Commission on the revision of the method for setting the reference and discount rates (OJ C 14, 19.1.2008, p. 6). Depending on the use of the reference rate, the appropriate margins have still to be added as defined in this communication. For the discount rate this means that a margin of 100 basispoints has to be added. The Commission Regulation (EC) No 271/2008 of 30 January 2008 amending Regulation (EC) No 794/2004 foresees that, unless otherwise provided for in a specific decision, the recovery rate will also be calculated by adding 100 basispoints to the base rate.

Modified rates are indicated in bold.

Previous table published in OJ C 281, 23.8.2014, p. 3.

From	To	AT	BE	BG	CY	CZ	DE	DK	EE	EL	ES	FI	FR	HR	HU	IE	IT	LT	LU	LV	MT	NL	PL	PT	RO	SE	SI	SK	UK
1.10.2014	…	0,53	0,53	**2,46**	0,53	0,58	0,53	0,78	0,53	0,53	0,53	0,53	0,53	1,54	**2,38**	0,53	0,53	0,69	0,53	0,53	0,53	0,53	2,75	0,53	2,97	**0,68**	0,53	0,53	**1,04**
1.9.2014	30.9.2014	0,53	0,53	2,96	0,53	0,58	0,53	0,78	0,53	0,53	0,53	0,53	0,53	1,54	2,92	0,53	0,53	0,69	0,53	0,53	0,53	0,53	2,75	0,53	**2,97**	**0,81**	0,53	0,53	0,88
1.5.2014	31.8.2014	0,53	0,53	2,96	0,53	0,58	0,53	0,78	0,53	0,53	0,53	0,53	0,53	**1,54**	2,92	0,53	0,53	0,69	0,53	0,53	0,53	0,53	2,75	0,53	3,72	1,06	0,53	0,53	0,88
1.4.2014	30.4.2014	0,53	0,53	2,96	0,53	**0,58**	0,53	0,78	0,53	0,53	0,53	0,53	0,53	1,83	**2,92**	0,53	0,53	0,69	0,53	0,53	0,53	0,53	2,75	0,53	3,72	**1,06**	0,53	0,53	0,88
1.3.2014	31.3.2014	0,53	0,53	2,96	0,53	0,71	0,53	0,78	0,53	0,53	0,53	0,53	0,53	**1,83**	3,45	0,53	0,53	0,69	0,53	0,53	0,53	0,53	2,75	0,53	3,72	1,29	0,53	0,53	0,88
1.1.2014	28.2.2014	**0,53**	**0,53**	**2,96**	**0,53**	**0,71**	**0,53**	**0,78**	**0,53**	**0,53**	**0,53**	**0,53**	**0,53**	**2,35**	**3,45**	**0,53**	**0,53**	**0,69**	**0,53**	**0,53**	**0,53**	**0,53**	**2,75**	**0,53**	**3,72**	**1,29**	**0,53**	**0,53**	**0,88**

NOTICES FROM MEMBER STATES

Information communicated by Member States regarding closure of fisheries

(2014/C 338/07)

In accordance with Article 35(3) of Council Regulation (EC) No 1224/2009 of 20 November 2009 establishing a Community control system for ensuring compliance with the rules of the common fisheries policy [1], a decision has been taken to close the fishery as set down in the following table:

Date and time of closure	28.8.2014
Duration	28.8.2014-31.12.2014
Member State	Ireland
Stock or Group of stocks	RNG/8X14-
Species	Roundnose grenadier (*Coryphaenoides rupestris*)
Zone	EU and international waters of VIII, IX, X, XII and XIV
Type(s) of fishing vessels	—
Reference number	36/DSS

[1] OJ L 343, 22.12.2009, p. 1.

Information communicated by Member States regarding closure of fisheries

(2014/C 338/08)

In accordance with Article 35(3) of Council Regulation (EC) No 1224/2009 of 20 November 2009 establishing a Community control system for ensuring compliance with the rules of the common fisheries policy [1], a decision has been taken to close the fishery as set down in the following table:

Date and time of closure	28.8.2014
Duration	28.8.2014-31.12.2014
Member State	Ireland
Stock or group of stocks	BSF/56712-
Species	Black scabbardfish (*Aphanopus carbo*)
Zone	EU and international waters of V, VI, VII and XII
Type(s) of fishing vessels	—
Reference number	35/DSS

[1] OJ L 343, 22.12.2009, p. 1.

Information communicated by Member States regarding closure of fisheries

(2014/C 338/09)

In accordance with Article 35(3) of Council Regulation (EC) No 1224/2009 of 20 November 2009 establishing a Community control system for ensuring compliance with the rules of the common fisheries policy [1], a decision has been taken to close the fishery as set down in the following table:

Date and time of closure	28.8.2014
Duration	28.8.2014-31.12.2014
Member State	Ireland
Stock or Group of stocks	SBR/678-
Species	Red seabream (*Pagellus bogaraveo*)
Zone	EU and international waters of VI, VII and VIII
Type(s) of fishing vessels	—
Reference number	37/DSS

[1] OJ L 343, 22.12.2009, p. 1.

Publication of an update to the list of national standardisation bodies pursuant to Article 27 of Regulation (EU) No 1025/2012 of the European Parliament and of the Council on European standardisation

(2014/C 338/10)

1. **BELGIUM**

NBN

Bureau de normalisation

Bureau voor Normalisatie

CEB/BEC

Comité électrotechnique belge

Belgisch Elektrotechnisch Comité

2. **BULGARIA**

БИС

Български институт за стандартизация

3. **CZECH REPUBLIC**

ÚNMZ

Úřad pro technickou normalizaci, metrologii a státní zkušebnictví

4. **DENMARK**

DS

Fonden Dansk Standard

5. **GERMANY**

DIN

Deutsches Institut für Normung e.V.

DKE

Deutsche Kommission Elektrotechnik Elektronik Informationstechnik im DIN und VDE

6. **ESTONIA**

EVS

Eesti Standardikeskus

TJA

Tehnilise Järelevalve Amet

7. **IRELAND**

NSAI

National Standards Authority of Ireland

8. **GREECE**

ΕΣΥΠ / ΕΛΟΤ

ΕΘΝΙΚΟ ΣΥΣΤΗΜΑ ΥΠΟΔΟΜΩΝ ΠΟΙΟΤΗΤΑΣ / Αυτοτελής Λειτουργική Μονάδα Τυποποίησης ΕΛΟΤ

9. **SPAIN**

AENOR

Asociación Española de Normalización y Certificación

10. **FRANCE**

AFNOR

Association française de normalisation

11. **CROATIA**

HZN

Hrvatski zavod za norme

12. **ITALY**

UNI

Ente nazionale italiano di unificazione

CEI

Comitato elettrotecnico italiano

13. **CYPRUS**

CYS

Κυπριακός Οργανισμός Τυποποίησης (Cyprus Organisation for Standardisation)

14. **LATVIA**

LVS

Latvijas standarts

15. **LITHUANIA**

LST

Lietuvos standartizacijos departamentas

16. **LUXEMBOURG**

ILNAS

Institut luxembourgeois de normalisation, de l'accréditation, de la sécurité et qualité des produits et services

17. **HUNGARY**

MSZT

Magyar Szabványügyi Testület

18. **MALTA**

MCCAA

L-Awtorità ta' Malta għall-Kompetizzjoni u għall-Affarijiet tal-Konsumatur

19. **NETHERLANDS**

NEN

Stichting Nederlands Normalisatieinstituut

NEC

Stichting Nederlands Elektrotechnisch Comité

20. **AUSTRIA**

ASI

Austrian Standards Institute (Österreichisches Normungsinstitut)

OVE

Österreichischer Verband für Elektrotechnik

21. **POLAND**

PKN

Polski Komitet Normalizacyjny

22. **PORTUGAL**

IPQ

Instituto Português da Qualidade

23. **ROMANIA**

ASRO

Asociația de Standardizare din România

24. **SLOVENIA**

SIST

Slovenski inštitut za standardizacijo

25. **SLOVAKIA**

ÚNMS

Úrad pre normalizáciu, metrológiu a skúšobníctvo Slovenskej republiky

26. **FINLAND**

SFS

Suomen Standardisoimisliitto SFS ry

Finlands Standardiseringsförbund SFS rf

FICORA

Viestintävirasto

Kommunikationsverket

SESKO

Suomen Sähköteknillinen Standardisoimisyhdistys SESKO ry

Finlands Elektrotekniska Standardiseringsförening SESKO rf

27. **SWEDEN**

SIS

Swedish Standards Institute

SEK

Svensk Elstandard

ITS

Informationstekniska standardiseringen

28. **UNITED KINGDOM**

BSI

British Standards Institution

29. **ICELAND**

IST

Staðlaráð Íslands

30. **NORWAY**

SN

Standard Norge

NEK

Norsk Elektroteknisk Komité

PT

Post- og teletilsynet

31. **SWITZERLAND**

SNV

Schweizerische Normenvereinigung

V

(Announcements)

PROCEDURES RELATING TO THE IMPLEMENTATION OF COMPETITION POLICY

EUROPEAN COMMISSION

Prior notification of a concentration

(Case M.7390 — OFI InfraVia/GDF SUEZ/PensionDanmark/NGT)

Candidate case for simplified procedure

(Text with EEA relevance)

(2014/C 338/11)

1. On 18 September 2014, the Commission received a notification of a proposed concentration pursuant to Article 4 of Council Regulation (EC) No 139/2004 [1] by which GDF SUEZ S.A. ('GDF SUEZ', France), PensionDanmark Holding A/S. ('PensionDanmark', Denmark) and InfraVia European Fund II ('InfraVia', France), owned by OFI InfraVia S.A.S. ('OFI InfraVia', France) and ultimately controlled by the Macif Group ('Macif', France), acquire within the meaning of Article 3(1)(b) of the Merger Regulation joint control of Noordgastransport B.V. ('NGT', the Netherlands), by way of purchase of shares. NGT is currently jointly controlled by GDF SUEZ and PensionDanmark.

2. The business activities of the undertakings concerned are:

— for OFI InfraVia: active in the infrastructure fund management across sectors including transportation, environment, energy and social infrastructure,

— for GDF SUEZ: energy group with global presence throughout the entire energy value chain in electricity and natural gas,

— for PensionDanmark: a Danish not-for-profit, labour-market-related, life-insurance limited company,

— for NGT: owner and operator of a subsea transportation system for natural gas in the Netherlands.

3. On preliminary examination, the Commission finds that the notified transaction could fall within the scope of the Merger Regulation. However, the final decision on this point is reserved. Pursuant to the Commission Notice on a simplified procedure for treatment of certain concentrations under the Council Regulation (EC) No 139/2004 [2] it should be noted that this case is a candidate for treatment under the procedure set out in the Notice.

4. The Commission invites interested third parties to submit their possible observations on the proposed operation to the Commission.

Observations must reach the Commission not later than 10 days following the date of this publication. Observations can be sent to the Commission by fax (+32 22964301), by e-mail to COMP-MERGER-REGISTRY@ec.europa.eu or by post, under reference number M.7390 — OFI InfraVia/GDF SUEZ/PensionDanmark/NGT to the following address:

European Commission
Directorate-General for Competition
Merger Registry
1049 Bruxelles/Brussel
BELGIQUE/BELGIË

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[1] OJ L 24, 29.1.2004, p. 1 (the 'Merger Regulation').
[2] OJ C 366, 14.12.2013, p. 5.

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