



## Questions and answers on the preparation of applications for a PIP and/or waiver

### 1) How and when should I submit a PIP Letter of intent?

The EMEA Secretariat should be formally notified of the intent to submit an application for paediatric investigation plan, and/or a request for waiver or deferral, using the published [Letter of Intent template](#).

The deadline for the Letter of Intent is normally 2 months before the planned submission date of the complete application.

The Letter of Intent should be sent to the following address: [paediatrics@emea.europa.eu](mailto:paediatrics@emea.europa.eu), using the EMEA secure email system, Eudralink. Should you not yet have a Eudralink account, please contact [eudralink@emea.europa.eu](mailto:eudralink@emea.europa.eu) in order to open an account. A referee contact person within EMEA is needed, when opening a Eudralink account. If you do not have a specific referee, please use “paediatric” as referee.

### 2) When should I submit the application for PIP and /or Waiver?

Applicants should submit their application for PIP and/or waiver according to the published deadlines for submission to the EMEA, which have been set according to the [Paediatric Committee](#) (PDCO) meetings.

The deadlines for submission are provided [here](#).

### 3) To whom should I submit the PIP/waiver application?

Applications for PIPs, waivers and deferrals should be sent to the European Medicines Agency to the attention of Dr. Agnès Saint Raymond, Head of Sector Scientific Advice, Paediatrics and Orphan Drugs.

Applicants will be informed of the names of the assigned Rapporteur, Peer-reviewer and the EMEA Paediatric Coordinator about a month before the proposed start date of the procedure. This will allow applicants to submit the applications to the EMEA, Rapporteur and Peer-reviewer in parallel. Please note that the EMEA Paediatric Coordinator is the contact person for the applicant.

Applicants will also be informed of the EMEA procedure number. This number should be clearly mentioned on the application and on all related correspondence.

### 4. How many copies should I submit for a PIP/waiver application?

Applications should be submitted to the EMEA as **one electronic copy on CD/DVD**, accompanied by a cover letter. The CD/DVD should include part A both as the original electronic PDF, and as a scan of the printed, signed document. For the check sum number, please refer to Q&A N. 5 (cover letter). The EMEA procedure number (PIP number), if available, should be indicated clearly on the cover letter and on the CD/DVD. Please note that the CD/DVD should reach the EMEA before or on the day of the published deadline; if this is not possible, the documents may be sent via Eudralink to [paediatrics@emea.europa.eu](mailto:paediatrics@emea.europa.eu), but the CD/DVD is still needed. Blu-ray discs are not acceptable.

In parallel to the submission to the EMEA, 1 CD/DVD of the application should be sent to the Rapporteur and Peer-reviewer.

In case of validation issues, you should provide the additional and modified files to the EMEA (please include a letter listing the changes) via Eudralink and CD/DVD, and to the Rapporteur and Peer-reviewer as amended full application, in a new CD/DVD.

On receipt of the EMEA validation letter confirming the start of the procedure, you should send immediately identical sets of the ‘final’ application as 1 CD/DVD to each of the other PDCO members and alternates (see contact details for the sending of applications on the web).

At this stage please send to the EMEA a confirmation that the application has been sent to all other PDCO members (email to: [paediatrics@emea.europa.eu](mailto:paediatrics@emea.europa.eu)).

Information on the contact details of PDCO members and alternates is provided on the EMEA website ([PDCO members](#)).

## **5. What information should be provided in the cover letter accompanying the application?**

You should clearly identify in the cover letter that it is an application for paediatric investigation plan, and/or requests for waiver / deferral, or request for modification of an agreed PIP, and you should mention the EMEA procedure number (PIP number). You should also declare that all electronic versions (Word and PDF) are identical.

Finally, the ‘checksum’ number received when the electronic application template form is saved should be mentioned in the cover letter.

## **6) What are the technical requirements for the electronic submission of PIP/waiver applications?**

The [application form](#) (part A) should be submitted as two PDF files: “one electronic” version (see question 7 below), which should then be printed, signed and scanned as a second PDF file. Annexes to the application form should be provided, as far as possible, as both PDF and Word files.

The scientific documentation (parts B to E, including the list of references) should be submitted both as a single PDF file and a single Word file (preferably Word 2000). See question 9 for more details on the scientific documentation (parts B to E).

For part F, the published articles (referenced literature) should be submitted as separate PDF files (see item 8 below). The Investigator’s Brochure (if any) and the copy of the latest EU Risk Management Plan should be submitted both as single PDF files and single Word files (preferably Word 2000); if this is not possible, at least PDF files may be used, with text that can be copied.

All files should be included in the CD Rom.

The following requisites apply to the electronic version of the application:

1. The PDF file must be created in [PDF Reference third edition \(1.4\)](#) or later.
2. The PDF file must be created directly from the Office applications, using a PDF converter tool.
3. If a password (or other security settings) has been set up to protect the confidentiality of data in the Word and PDF files, this should be communicated to the EMEA and the PDCO delegates using Eudralink, so that it is possible to print, select the text and images, and copy them into another Office application.
4. Please ensure that the PDF/Word files created are compliant with full-text search engines.
5. Please **do not use hyperlinks** to references or tables/pictures, as they create problems when copying and pasting text in the summary report.
6. Scanning of physical documents or generation of PDF image file must be avoided as far as possible. When a document is only available in paper, please ensure that the scanned version is readable both on screen and when printed. The scan resolution should be set at 300 dots per inch (dpi), in black and white as it is good compromise between legibility and file size.

7. In the text of the application, references to the literature must be made using the Harvard Citation Style, e.g.: (Smith PH et al., 2004). Do not use footnotes or numbered items.
8. The reference list should be set in alphabetical order, by first Author's name.
9. The PDF files should be titled for ease of retrieval; for referenced publications, please use single files (one per reference), and name them as first author and year, such as in "Smith PH et al 2004.PDF".
10. All documents enclosed in the printed application should also be provided in electronic format, including the Investigator's Brochure(s) and the Risk Management Plan (if any).

## **7) How do I use the electronic template for PIP/waiver application (part A)?**

To submit an application, for part A please use the EMEA [application form](#), available on the [PIP webpage](#) of the EMEA website.

To download and save locally the [application form](#), right-click on the template link and select the option "Save Target As" (if you are using Internet Explorer) or "Save Link As" (if you are using FireFox). Please do not start to fill-in the template inside your Internet browser as you may not be able to save the content later. The local copy should be used instead.

The [application form](#) allows the EMEA to enter your data directly into a database. This is a new process and we apologise for this new process and any inconvenience caused.

For modifications of an agreed PIP, see answer to question 14.

The completed [application form](#) should be created and saved using the latest version of Adobe Reader® (at least version 8.0, available on the [Adobe website](#)); older versions of Adobe Reader or other PDF readers would not work, or may create difficulties (for example, they may swell the file to huge sizes).

The application form is a dynamic PDF form that allows possibility to interact with the form. For instance, some buttons are available to add or delete fields (e.g. "add substance", "delete substance"), some checkboxes are exclusive, the date fields propose a calendar, dropdown lists are used, etc.

When accessing the published [application form](#) template, only the first page is displayed. You must select either Article 7, or Article 8 or Article 30, as appropriate, in order to view the complete form. If the wrong article has been selected by mistake, a new form must be used, as there is no possibility to modify the initial selection. However, for all the other items of the application form you can correct the information if needed, without creating a new form.

Several versions of the application form can be saved, if needed, as you fill in the information required in the form. All sections of the application form must be filled in as far as possible. When saving the form, you will receive a 'checksum' number, but only if all fields highlighted in yellow have been filled in (see also below). This 'checksum' number is a representation of the information saved in the application form and is used to ensure consistency between the electronic and the paper versions.

When the application form has been finalised, you must print it, sign it and save it. The checksum number provided at this stage should be mentioned on the cover letter accompanying the PIP application.

The electronic template should be used for any type of applications (whether related to Article 7, Article 8 or Article 30 of the [Paediatric Regulation](#)). Further information is provided below (see Question 8) to guide you when filling in the application form.

The information filled into the application form can easily be used to fill another form, for example, in order to upgrade to the latest form available on the website, to create a different / related application, or to archive the information. To do this, open the electronic form in Adobe Reader, select from the menus "Document" – "Forms" – "Export data ..." and save it as an XML file. Conversely, in a fresh electronic form, chose "Document" – "Forms" – "Import data ..." to load it again.

## 8) What information should I include in the electronic template for PIP/waiver applications (Part A)?

The information provided in this section should be read in conjunction to the draft [EC guidance on format and content of applications for agreement or modification of a paediatric investigation plan and requests for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies](#). The draft EC guidance gives important additional information for the preparation of an application for a Paediatric Investigation Plan/waiver. Only practical information not covered in the EC guidance is listed below.

For a new product not authorised in the Community (Article 7), if at completion of the human pharmacokinetics in adults the applicant intends to develop simultaneously several indications, only one comprehensive PIP should be submitted.

For Article 8, the PIP application should cover all the existing and the new indication(s), pharmaceutical form(s) and routes of administration(s) (where relevant).

- *Proposed pharmaceutical form(s) in relation to the proposed paediatric development. (page 1)*

In this section, for Article 8, all existing pharmaceutical forms and new pharmaceutical forms under development for the proposed PIP should be listed, irrespective of whether you request a waiver, or a PIP with or without deferral. You should specify whether the pharmaceutical form is under development or is authorised.

For Article 30, only the pharmaceutical form(s) discussed in the PIP should be mentioned. You should also specify whether the pharmaceutical form is under development or is authorised.

‘Authorised’ means here authorised in (at least) one Member State of the Community.

- *Request for a waiver*

In this section, if there is more than one condition in your application, you should repeat the information for each condition/indication, by clicking on the button “add”. To delete a condition/indication, the button “delete” should be clicked.

You should select the appropriate age group where the waiver applies. You have the possibility to select specific age group(s), different from ICH classification, if this is more appropriate.

Please, tick the grounds for the waiver for each age group mentioned in this section. There is no possibility to add grounds for waivers not defined by the legislation.

For conditions included in the EMEA list of class waivers, see answers to question 10.

- *Name of the active substance*

You should select the appropriate nomenclature following the priority order. There is no need to select more than one nomenclature.

- *Details of the medicinal product*

The proposed pharmaceutical form mentioned in page 1 should be repeated here with the corresponding route of administration. If an additional formulation is under development (adult formulation for example), it should be listed here. Please use the list of standard terms from the [European Pharmacopoeia](#).

- *A6 Marketing authorisation application*

The button “Copy” gives you the possibility of repeating the information provided in one box, for one country, without re-typing it. After copying, if you wish to modify the information copied (e.g. country), it can be changed easily (e.g. another country can be selected from the list). This tool facilitates the entry of similar information in the table.

Similarly the “Add” or “delete” buttons allow you to either ADD or DELETE information.

- *Date of completion of human pharmacokinetic studies in adults/Planned submission of application*

The date must follow the format dd/mm/yyyy. If the exact date cannot be specified for a planned application for marketing authorisation (or a variation request), you should select the appropriate month of the appropriate year, and select the last day of the month by default. (e.g. 31/07/2010 for July 2010).

The same rules apply if you would like to select a trimester for example, please use the last month of the trimester. Please note that these dates are just for planning purpose and therefore are not binding on you.

- *Contact point for the applicant for public enquiries from interested parties.*

At the time of the publication of the Decisions on a PIP and/or waiver, on the [decision page](#) of the EMEA website, this contact will be made public. A generic (not personal) email address, telephone and fax is therefore preferable.

- *Checksum*

The text “Checksum: All yellow fields must be completed, in order to get a “checksum” code; this is displayed at the bottom of each page.

Example: before: Checksum: All yellow fields must be filled in to get a checksum

Example After: Checksum: d13f91951bbde7ce5f0b71dce3f348f9afc52d6b

This text will change to a series / combination of numbers and letters when a print or save action is performed. Please note that it will only change when all “yellow” fields have been filled. It prompts the user with a warning message.

The ability to Save or Print is still active, and users are still able to perform this function even if the checksum has not changed. However once the checksum has been activated, it tracks changes to the document, and the combination will change each time there is a change in the document. Below is an example before and after checksum changes

## **9) How should I present the scientific documentation (part B to E; references separate part F)?**

For the scientific part (Part B to E), if several conditions are submitted in the same application, you should address all parts related to one condition first (Part B to E) together, and then repeat the information for each subsequent condition. As a rule, parts B to E should be submitted as a single file (both in Word and PDF format) in the electronic version, with page numbers on each page. Separate files for each condition may be considered for convenience; in this case, please submit a single reference list as a separate file.

**The scientific part of the application should be as concise / short as possible, but still explicit and readable as a self-standing document.** It is recommended to avoid repetitions, and to make use of cross references if possible (but avoid hyperlinks). The application should be particularly specific in part D. Although the documentation should be comprehensive, **please keep the total number of pages of your application (excluding references) below 50 per condition if possible.**

Any request for a deferral should include the proposal of the study(ies) and timelines to be deferred. In other words, it is not sufficient to simply ask for a deferral, without providing a complete PIP: a plan with timelines and proposed studies needs to be provided for every condition/indication for which a waiver is not sought.

If you require additional information or clarification when filling in the information, please refer to the draft [EC guidance on 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](#). This document gives important additional information for the preparation of an application for a Paediatric Investigation Plan/waiver. If still in doubt, please send a request to the following address: [paediatrics@emea.europa.eu](mailto:paediatrics@emea.europa.eu).

## 10) What shall I submit in case my product is developed for a condition listed in the EMEA decision on class waiver?

If you are developing a medicinal product intended to treat one or more conditions identified in the list of class waivers of conditions adopted by the EMEA, the need to produce data in all subsets of the paediatric population in compliance with an agreed paediatric investigation plan shall be waived. As a result, there is no requirement to submit an application for a waiver. However, please consult the following information.

### *Recommendation*

Even if you are developing a medicinal product intended to treat one or more conditions identified in the list of class waivers of conditions, this information is of high value and interest to the PDCO. Information on the medicinal product will help the PDCO to inform you as to whether this product could have a therapeutic interest and fulfil a therapeutic need of the paediatric population in another condition. This may allow you to benefit from the incentives of the Paediatric Regulation.

You are therefore encouraged to provide background information on the product (e.g., description, mechanism of action, etc.). This could be for instance in the form of an investigator brochure sent to the EMEA for submission to the PDCO. If an area of high interest for paediatric development is identified, this will be communicated to you. This would allow you to submit a formal application for a PIP to follow the normal procedure.

### *Confirmation of the applicability of the EMEA decision on class waivers*

If you are developing a product for a condition included in the list of class waivers, you may wish to request confirmation of whether the scope of the EMEA decision on a class waiver for a condition is applicable to your product. This may facilitate the future validation of your subsequent application for marketing authorisation or extension/variation. To this aim you should fill in the template for [Confirmation of the applicability of the EMEA decision on class waivers](#), and provide some background information on the product, for instance in the form of the investigator brochure. Upon review by the PDCO, you will receive an outcome letter confirming or not if your product is considered to fall under the scope of the EMEA Decision on class waivers.

If the PDCO considers that the class waiver is not applicable to your product, you will have to submit a formal application for a PIP and/or a product-specific waiver, which will follow the normal procedure.

For further information, please refer to the [EMEA decision on class waivers](#).

### *Applications covering both one (or more) condition included in the list of class waivers, and other conditions*

If a product is intended for one (or more) condition that is included in the list of [class waivers](#), but also for other conditions, you should submit an application for a Paediatric Investigation Plan or for a product-specific waiver for all the conditions not included in the list of class waivers. In addition, please inform the EMEA (using the application form) that the development will also be pursued in conditions included in the list of class waivers. If you require a confirmation that the scope of the EMEA decision on [class waivers](#) is applicable to your condition(s), as above, please specify it in the cover letter.

## 11) Should I submit a separate PIP/waiver application in case of multiple marketing authorisations/marketing authorisation applications?

In case of medicinal products having multiple marketing authorisations or ongoing marketing authorisation applications, separate PIP applications (and/or requests for waiver) should be submitted for each marketing authorisation of the medicinal product (regardless of the type of authorisation procedure, i.e. duplicate applications or informed consent). In the application form, you should duly complete the section on information on related applications.

## **12) How shall I answer the PDCO's Request for modification of a PIP and/or waiver?**

At day 60 of the procedure, the PDCO may request the applicant to propose modifications to the plan. In this case, the procedure will be suspended until such proposed modifications are submitted by the applicant. The request for modification of the plan is identified in the last section of the Summary Report. It is established on the basis of both the assessment of the application (Summary Report) and the PDCO discussions at day 30 and day 60.

You are expected to address each issue listed under the section Request for Modification in a specific "response document". The "response document to the request for modification" should include links to the revised section of the annexed modified paediatric investigation plan.

The modified PIP/waiver sections (part C and/or part D) should be submitted separately as modified PIP, highlighting all additions / modifications (or by using 'track changes'). Please also submit a "clean" version of the modified PIP (without highlighting or track changes) as a separate file. If the modifications also affect part A of the application (the PDF application file), or the new PDF module for the non-clinical and clinical studies, these too should be modified and submitted accordingly.

The proposed modified PIP/waiver application and the response document should be submitted to the EMEA electronically, including PDF files of previously unsubmitted bibliographical references, in a CD/DVD, accompanied by a cover letter with the PIP reference number. The files may additionally be submitted via Eudralink to comply with the resubmission deadlines (however, the CD/DVD is still needed).

Please submit both a PDF file and a Word/RTF file of the revised PIP and the the response document, (with the same modalities described in questions 6, 8 and 9).

At the same time, please send all documents in electronic format on a CD/DVD to the Rapporteur and Peer reviewer(s), and to all other PDCO members and alternates.

There is no need to resubmit unchanged documents that were already included in the original application, such as literature references, investigator's brochure(s), etc.; there is also no need of printed copies of the documents.

The submission of the proposed modified PIP/waiver is expected within 3 months of the request. This 3-month timeframe is only indicative, and it is acknowledged that in some cases you may need more time to propose modification of the application. In any case, you should submit it in accordance with the published dates for the restart of the procedure.

For the purpose of planning activities, please inform the EMEA of the intended date of submission of your proposal, at least one month prior to the submission, with an email to [paediatrics@emea.europa.eu](mailto:paediatrics@emea.europa.eu) and to the paediatric coordinator.

## **13) What is the procedure to request a re-examination of the PDCO opinion on my PIP/waiver application?**

Please consult the [separate guidance document](#) available on the website.

## **14) How do I apply for a modification of an agreed PIP?**

If you wish to submit a request for modification of an already agreed PIP, a procedure similar to the submission of the initial application for Paediatric Investigation Plan/waiver applies.

1. A letter of intent, normally to be sent 2 months before the planned submission date of the complete application for modification of an agreed PIP, should be sent as for an initial application. The letter of intent shall cite the original EMEA PIP number and the date and number of the latest EMEA decision. The scope of the proposed modification of the agreed PIP shall be briefly summarised.

2. Applicants will be informed of the names of the assigned Rapporteur, Peer Reviewer and the EMEA Paediatric Coordinator immediately after start of procedure, when they will also receive the EMEA number for the modification procedure. This number should then be clearly mentioned on all related correspondence. As far as possible, the PDCO will appoint the same Rapporteur and Peer Reviewer for the modification procedure as for the initial PIP application(s). The PDCO may involve, if necessary, additional experts. The paediatric co-ordinator will also remain the same, as far as possible.
3. Applicants should submit their application according to the published [deadlines](#) for submission, which have been set according to the Paediatric Committee (PDCO) meetings. Applicants should submit the application to the EMEA and to all PDCO members and alternates at the same time, in parallel. The requirements are analogous to those for the initial application.
4. The application should include the [request for modification of an agreed paediatric investigation plan](#), a new electronic [application form](#) (part A, as for initial PIP application), and the supporting scientific documentation. The scientific documentation should follow the same structure as for an initial paediatric investigation plan (parts B-E), but only the relevant sections supporting the change should be completed. The need / rationale for the modification of the agreed PIP should be clearly indicated in the [request for modification of an agreed paediatric investigation plan](#).
5. The draft Summary Report will be sent to the applicant for information after the first discussion (Day 30). The PDCO may invite the applicant for a teleconference, or for an oral explanation. The PDCO shall adopt an opinion at day 60, refusing or accepting the proposed changes. The updated annex of the PDCO Opinion will not simply address the agreed modifications, but it will list all the measures and timelines of the new agreed PIP: the unchanged ones and those newly modified (including timelines).
6. The EMEA will forward the opinion, including the summary report, to the applicant. The post-opinion phase and the decision making phase will follow the same procedures as for the initial PIP application. When publishing the decision on a modification of an agreed PIP, the original decision, being superseded, will be removed from the EMEA website.

## **15) When is my product considered “not authorised in the Community”?**

As of 26 July 2008, applications for a marketing authorisation in respect of a medicinal product for human use which is not authorised in the Community at the time of entry into force of Regulation (EC) No 1901/2006 shall comply with the requirements of Article 7 of Regulation (EC) No 1901/2006.

In accordance with Article 8 of Regulation (EC) No 1901/2006, the requirements of Article 7 shall also be applicable, as of 26 January 2009, to the authorisation of new indications, new pharmaceutical forms and new routes of administration of authorised medicinal products which are protected by a supplementary protection certificate or by a patent which qualifies for the granting of a supplementary protection certificate.

Since Articles 7 and 8 refer respectively to ‘a medicinal product for human use which is not authorised in the Community’ and to an ‘authorised medicinal product’, at the time of submitting a new stand-alone application it is necessary to establish whether the product applied for is considered or not a ‘a medicinal product for human use which is not authorised in the Community’. In this context, the Global Marketing Authorisation concept, as defined in Article 6(1), 2nd subparagraph of Directive 2001/83/EC, as amended, applies.

The global marketing authorisation contains the initial authorisation and all variations and extensions thereof, as well as any additional strengths, pharmaceutical forms, administration routes or presentations authorised through separate procedures and under a different name, granted to the marketing authorisation holder of the initial authorisation. For further reference, see NTA, chapter 1, section 2.3.

Thus, the Global Marketing Authorisation concept applies to products belonging to the same marketing authorisation holder. According to the [Commission Communication](#) on the Community

marketing authorisation procedures for medicinal products (98/C 299/03), applicants belonging to the same mother company or group of company, or which are "licensees", have to be taken as one.

The global marketing authorisation concept covers both orphan and non-orphan marketing authorisations held by the same marketing authorisation holder.

In view of the above, applicants will be asked to identify marketing authorisations falling within the scope of the global marketing authorisation in order to determine whether their application has to comply with the requirements of Article 7 or 8 of Regulation (EC) No 1901/2006 (see Question 16). It is the responsibility of the applicant to provide a truthful declaration.

### **16) Does Article 7 or Article 8 of the Paediatric Regulation apply to my application, taking into account the Global Marketing Authorisation concept?**

The Global Marketing Authorisation (GMA) concept together with the notion of 'same marketing authorisation holder' will be used to determine whether an application concerns a 'medicinal product for human use which is authorised or not in the Community' and whether Article 7 or 8 applies i.e. :

- If the applicant does not hold any other marketing authorisation for that substance, the medicinal product subject of the application will not be considered as authorised, and consequently, the application will fall under Article 7.
- If the applicant holds (an)other marketing authorisation(s) for that substance, (independently of the procedure of authorisation), the medicinal product subject of the application, will be considered as 'already authorised', in keeping with the Global Marketing Authorisation concept. Consequently Article 7 will not apply. If the medicinal product is protected by a Supplementary Protection Certificate (SPC), or a patent which qualifies for a SPC, Article 8 shall apply to that application. In this case, the PIP/Waiver Decision shall cover the existing and any new indication, pharmaceutical form or route of administration of the medicinal product concerned by the Global Marketing Authorisation.

For instance:

Company A holds a marketing authorisation in indication A for a product containing substance x (still patented).

Company B (subsidiary of company A) intends to apply for a new stand-alone marketing authorisation for substance x in a new indication B.

--> the product will be considered as 'already authorised' based on the GMA concept, and company B will be required to cover also indication A in its PIP (i.e. Art 8 applies).

The Global Marketing Authorisation approach applies to PIP or Waiver applications as well as to variations, extension and new marketing authorisation applications falling under the requirements of Article 7 and 8. Where relevant, applicants should also consider whether any modification to an agreed or ongoing PIP/Waiver decision may be required in case the GMA concept had not been applied, in order to avoid difficulties at validation of the subsequent regulatory submission.

### **17) What is a new indication in the context of Article 8?**

'New indication' is not defined in the Community legislation. However both the 'Guideline [on the elements required to support the significant clinical benefit in comparison to existing therapies of a new therapeutic indication in order to benefit from an extended \(11-years\) marketing protection](#)', and the 'Guideline on [a new therapeutic indication for a well-established substance](#)' provide a definition of what is considered a new indication. For the purpose of the application of Article 8 the same definition applies.

## **18) Does Article 7 or Article 8 of the Paediatric Regulation apply to my informed consent application?**

Article 7 applies to 'informed consent' applications submitted after 26 July 2008 and which cross-refer to a medicinal product for which a marketing authorisation application was submitted after 26 July 2008.

Please refer to question 11 - [Should I submit a separate PIP/waiver application in case of duplicate marketing authorisations/marketing authorisation applications?](#) – with regard to the need to submit a separate PIP/waiver application (and/or requests for waiver) per marketing authorisation and to provide a separate PIP/waiver decision in the module 1 of the informed consent application.

However, Article 7 does not apply to 'informed consent' (MA) applications submitted after 26 July 2008 and which cross-refer to a medicinal product for which an application was submitted before 26 July 2008.

After authorisation of a medicinal product according to the 'informed consent' legal basis, Article 8 will apply as of 26 January 2009 if the conditions set out in this article are met.

## **19) Do the requirements of Article 7 of the Paediatric Regulation apply to fixed-combination products?**

Article 7 of the Paediatric Regulation applies to fixed-combination medicinal products, which are not authorised in the Community by 26 July 2008.

The GMA concept in relation to the combination concerned together with the notion of 'same marketing authorisation holder' (MAH) is used to determine whether an application for a fixed combination product concerns a medicinal product which is authorised or not as a fixed-combination in the Community, and therefore whether Article 7 or 8 applies (See **Question 16**).

Example 1. Fixed-combination medicinal product authorised: Substance A 5 mg / substance B 10 mg tablets.

The application concerns Substance A 5 mg / substance B 10 mg **capsules** (not tablets) by the same Marketing Authorisation Holder. This will be considered part of the GMA, therefore Article 8 applies (due to the change in the pharmaceutical form)

Example 2. Fixed-combination medicinal product authorised: same as above (Substance A 5 mg / substance B 10 mg tablets).

The application however concerns Substance A **10 mg** / substance B 10 mg tablets by the same Marketing Authorisation Holder. This is not a new medicinal product as the medicinal product is already authorised and this new strength falls within the same GMA; therefore, article 7 does not apply and neither does Article 8 as the conditions of this provision are not met (a change in strength does not trigger Article 8).

## **20) Is there a procedure to transfer the PIP/waiver decision to another applicant?**

The EMEA decision on a PIP and/or waiver is addressed to the applicant of the PIP/waiver application. The legislation does not foresee a procedure for "transfer" of the PIP/waiver decision to another applicant. However, the applicant for a marketing authorisation may be different from the PIP addressee on the understanding that there is a contractual agreement between the different parties.

In respect of compliance check, it has to be kept in mind that the full study reports have to be provided for this purpose. Any transfer of a PIP decision should take this into consideration.

## **21) Does Article 7 of the Paediatric Regulation apply to advanced therapy medicinal products (ATMPs) ?**

As of 30 December 2008, Article 7 of the Paediatric Regulation applies to advanced therapy medicinal products for which a first marketing authorisation application is submitted in accordance with Community pharmaceutical legislation.

### **Transitional period**

Advanced therapy medicinal products which were legally on the Community market on 30 December 2008 are subject to the transitional measures set out in Article 29 of Regulation (EC) No 1394/2007 on Advanced Therapy medicinal products.

According to this provision, a marketing authorisation application for an ATMP which is legally on the Community market on 30 December 2008 shall be submitted to the EMEA for evaluation within a defined period of time (30 December 2011 for ATMPs other than tissue engineered products; and 30 December 2012 for tissue engineered products).

In view of the above, and taking the application date of Article 7 into account, the requirements of Article 7 will apply to ATMPs as follows:

- ATMPs legally on the Community market on 30 December 2008 for which a marketing authorisation was granted before 26 July 2008 in accordance with Community pharmaceutical legislation:
  - Article 7 of the Paediatric Regulation does not apply as the medicinal product is already authorised;
- ATMPs legally on the Community market on 30 December 2008 for which a marketing authorisation was granted after 26 July 2008 in accordance with Community pharmaceutical legislation:
  - Article 7 of the Paediatric Regulation applies.
- ATMPs legally on the Community market on 30 December 2008 but for which no marketing authorisation has been granted to that date in accordance with Community pharmaceutical legislation:
  - Article 7 of the Paediatric Regulation applies.

Article 8 of the Paediatric Regulation applies when an application for a new indication, new pharmaceutical form or new route of administration is submitted as of 26 January 2009 in respect of an ATMP that is protected either by a Supplementary Protection Certificate (SPC) or by a patent which qualifies for the granting of the SPC.

Further information on Article 29 of Regulation (EC) 1394/2007 is available in the following document '[To manufacturers, companies and hospitals having advanced therapy medicinal products legally on the Community market in accordance with national or Community legislation](#)'.