EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 May 2018
EMA/672643/2017 Rev.1
Human Medicines Research and Development Support Division

Guidance on paediatric submissions

eSubmission Gateway and eSubmission web client

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1. Introduction

The first time an applicant submits a letter of intent to submit a paediatric investigation plan or a product specific waiver the Agency will assign a numerical code of six digits preceded by EMEA, for example *EMEA-123456.* Those six digits will identify the active substance/INN and should be used as reference in the initial and all follow up applications. It is also the number that applicants should use when creating a delivery file at the time of submission via eSubmission Gateway / Web Client. Please refer to the document User Guidance for submissions via eSubmission Gateway / Web Client using xml delivery files.

The following guidance is intended as a detailed, although non-exhaustive, list of documents required for each type of paediatric submissions. This document should be read in conjunction with the procedural guidance published on the EMA website: Paediatric Medicines and the European Commission Guideline on the Format and Content of PIP applications.

Documents should be named according to **the naming convention** at the end of this document. The templates for submission and submission deadlines can be found on the Paediatric investigation plans: Templates, forms and submission dates

Paediatric applications do not follow eCTD standards, all documents and zip files should be sent in a single folder.

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2. List of required documents by application type

2.1. Initial applications for requests of PIPs and product specific waivers

- Cover letter

Please clearly identify in the cover letter the following:

  - whether it is an application for a PIP, including a request for a waiver and/or deferral, or a request for a product specific waiver;
  - the product number (EMEA-xxxxxx)[1];
  - the UPI (Unified Product Identifier) number, if available;
  - the 'checksum' number generated when the electronic application template form is saved; and

- Letter of authorisation for the person authorised to communication on behalf of the applicant

The letter of authorisation can contain up to two people to communicate with the Agency during the procedure. The letter should be printed, signed and scanned as PDF.

- Electronic form for paediatric-investigation-plan application and request for waiver - (PED1) certified (also referred to as 'Part A')

The European Commission Guideline on the Format and Content of PIP applications offers a comprehensive guidance on how to fill it in.

Part A should be submitted as an electronically signed form; please refer to information on e-signature on http://esubmission.ema.europa.eu/eSignatures.html.

Alternatively, if you are unable to submit an electronically signed form, then two PDF files are required: one electronic version containing the live fields; and one printed, signed and scanned copy of the signature page. For more detailed technical guidance please see the procedural guidance in the Paediatric Medicines page of the EMA website.

- Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion

The key-elements form should be used to propose key elements for all completed, ongoing and proposed future steps in the pharmaceutical development for children, and for non-clinical and clinical studies which are intended to be included in the PIP opinion. This form should be used to list the key elements, as proposed by the applicant as a basis for the PDCO opinion, in short bullet-point style. This document must not include background, explanations, justifications, legal requirements (e.g. consent) or additional detailed information. This information should be included in the scientific document (see next bullet point).

- Template for scientific document (part B-F)

Please provide this document in Word only.

Use the *guidance on the template* and the European Commission Guideline on the Format and Content of PIP applications to complete this document. Please also submit the following as separate documents:

- Copy of literature references, as a single zip file;

[1] EMEA- followed by the six digit number is allocated at the time of submission of the letter of intent, e.g. EMEA-*123456*

- Other supporting information as listed in section A10 of the Electronic form (PED1) ('Part A'), as a single zip file:
  - scientific advice CHMP / NCA / 3dr countries / FDA written requests (if available);
  - risk management plan (if applicable/available);
  - summary of product characteristics (if applicable/available);
  - investigator brochure;
  - copy of the commission decision on Orphan designation (if applicable/available).

2.2. Answers to requests for modification (resubmission following clock-stop)

- Cover letter

Please clearly identify in the cover letter the following:

  - the product number (EMEA-xxxxxx);
  - the UPI (Unified Product Identifier) number, if available;
  - the 'checksum' number generated when the electronic application template form is saved, if changes to the application form are required; and

- Response document to request for modifications at Day 60, including a list of new references, in Word;
- Copy of additional references in a single zip file. Please do not include previously sent references;
- Additional supporting documents to support the responses not previously sent;
- Electronic form for paediatric-investigation-plan application and request for waiver - (PED1) certified, if changes to the form are required to address the request for modification at Day 60;
- Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion, if changes to the form are required to address the request for modification at Day 60.

Do **not** send the Template for scientific document (part B-F), even if modified. The answers to the request for modification should be address in the response document.

2.3. Modifications to an agreed PIP

- Cover letter

Please clearly identify in the cover letter

  - that it is an application for a request of modification to an agreed PIP including the full procedure number[2] to be modified;
  - UPI number if available;
  - the 'checksum' number generated when the electronic application template form is saved; and

- Letter of authorisation for the person authorised to communication on behalf of the applicant.

The letter of authorisation can contain up to two people to communicate with the Agency during the procedure. The letter should be printed, signed and scanned as PDF.

- Electronic form for paediatric-investigation-plan application and request for waiver - (PED1) certified. (also referred to as 'Part A')

A **new** form must be submitted containing a new checksum number, do not reuse the form sent with the initial application.

The European Commission Guideline on the Format and Content of PIP applications offers a comprehensive guidance on how to fill in this form.

The electronic form (Part A) should be submitted as an electronically signed form; please refer to information on e-signature on http://esubmission.ema.europa.eu/eSignatures.html.

Alternatively, if you are unable to submit an electronically signed form, then two PDF files are required: one electronic version containing the live fields, and one printed, signed and scanned copy of the signature page.

- Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion

The updated key-elements form should include both the studies as listed in the latest Decision of the agreed PIP, unchanged, and the proposed changed or new studies.

- Request for modification of an agreed paediatric investigation plan template.

Please submit this template in Word only.

- Copies of new literature references not previously submitted and other new supporting documents, as a single zip file

Do **not** send the Template for scientific document (part B-F). All requests for modification to the agreed PIP should be added to the Request for modification of an agreed paediatric investigation plan template.

[2] e.g.: EMEA-000001-PIP01-01

2.4. Compliance checks

- Cover letter

You should clearly identify in the cover letter that it is a request for an interim (partial), final or full compliance[3]. You should also mention the full procedure number (PIP number).

- Letter of authorisation for the person authorised to communication on behalf of the applicant.

The letter of authorisation can contain up to two people to communicate with the Agency during the procedure. The letter should be printed, signed and scanned as PDF

- Request for compliance check on an agreed paediatric-investigation-plan form - (PED3) certified.
- Study Reports, if available

Full (complete) study reports should be submitted for the compliance check. Otherwise, the latest available report or a similar document should be submitted, which must contain sufficient information to allow the check of compliance with the agreed key elements in the decision; in such cases it is recommended to discuss with the paediatric coordinator, prior to the submission of the compliance check, the suitability of the available report. Individual patient data listings (section 16.4) are not needed.

- Summary of product characteristics, if available
- Evidence of study initiation, if applicable

When initiation of a clinical study is not deferred, the applicant should submit a signed and dated declaration from the principal investigator certifying that at least one participant has been included in the study/trial (i.e. specifying the date of signature of the informed consent).

- Quality measures (e.g. age-appropriate formulation)

[3] A final compliance check is the last and final request after one of several interim compliance requests. A full compliance is a request in all studies/measures agreed in a PIP

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3. Naming Convention

Applicants are kindly asked to avoid sending documents inside folders and only bundled them in zip files as mentioned below.

Document code	Document type	Document format	Naming convention	Mandatory (M) / Not applicable (N/A) / if applicable (I/A)			
				Initial application	Answer to RfM (re-start)	Modification of an agreed PIP	Compliance check
00	Template for letter of intent to submit an application	PDF	00-Letter of intent	**N/A**	N/A	**N/A**	N/A
01	Cover letter	PDF	01xxxxxx CL†	**M**	**M**	M	M
02	Letter of authorisation for the person authorised to communication on behalf of the applicant	PDF	02-xxxxxx LoA	M	I/A	M	M

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				Initial application	Answer to RfM (re-start)	Modification of an agreed PIP	Compliance check
03	Electronic form for paediatric-investigation-plan application and request for waiver - (PED1) certified	PDF (active form and scanned copy if needed)	03-xxxxxx Application form 03-xxxxxx Application form signed(if needed)	M	I/A	M	**N/A**
04	Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion	PDF (active form)	04-xxxxxx KEF	I/A	I/A	I/A	N/A
05	Template for scientific document (part B-F)	Word	05-xxxxxx Scientific document	M	N/A	N/A	N/A
06	**Response document to request for modifications at Day 60**	**Word**	**06-Responses to D60**	**N/A**	**M**	**N/A**	**N/A**
07	Copies of literature references	ZIP**	07-xxxxxx Literature	M	I/A	M	N/A
07	Other supporting documents listed in part A.10 of the electronic application form (Part A)*	ZIP**	07-xxxxxx Supporting documents	M	I/A	I/A	N/A
07	Other references*	ZIP**	07-xxxxxx Other	**I/A**	I/A	I/A	N/A
08	Request for modification of an agreed PIP	Word	08-xxxxxx Request for modification.	N/A	N/A	M	N/A
09	Request for compliance check on an agreed paediatric-investigation-plan form - (PED3) certified	PDF (active form)	09-xxxxxx Request for compliance check	N/A	N/A	N/A	M

Document code	Document type	Document format	Naming convention	Mandatory (M)/ Not applicable (N/A)/ if applicable (I/A)			
				Initial application	Answer to RfM (re-start)	Modification of an agreed PIP	Compliance check
10	Study reports	ZIP**	10-xxxxxx study reports	N/A	N/A	N/A	M
11	Evidence of study initiation*	PDF	11-xxxxxx evidence of initiation	N/A	N/A	N/A	I/A
12	Quality measures*	ZIP**	12-xxxxxx quality measures	N/A	N/A	N/A	I/A

† xxxxxx refers to the EMEA number assigned after submission of the letter of intent, e.g. EMEA-*123456*
* When available/if applicable
** Ensure that the name of the Zip file does not contain any special characters such as brakets (), it will prevent successful submission.