EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Division

Guidance on paediatric submissions

eSubmission Gateway and eSubmission web client

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1. Introduction

A letter of intent to submit a paediatric investigation plan (PIP) or a product specific waiver is no longer required nor processed[i].

When creating a delivery file at the time of submission via eSubmission Gateway / Web Client, the following **six-digit** code is to be used:

- the **six digits** of the already assigned paediatric procedure number (e.g. 001234) - for any follow-up submissions, such as the second or further PIP/waiver submissions for identical active substances; for responses to PDCO requests for modifications; modifications on agreed PIPs, requests for compliance checks, re-examination grounds, withdrawal of procedure instructions, notifications of change; annual reports for deferrals; information on discontinuations;

  or if no procedure number was ever assigned:

- 000000 - for first-time PIP and product specific waiver applications, PIP unrelated requests for confirmation of class-waiver decision applicability, and pre-submission interaction requests **only**. A procedure number to use in any further correspondence will be communicated to the applicant when the first-time submission has been processed.

Detailed guidance on creating the delivery file is to be found in User Guidance for submissions via eSubmission Gateway / Web Client using xml delivery files. **All documents and zip files should be sent in a single folder as paediatric applications do not follow eCTD standards.**

The following guidance is intended as a detailed, although non-exhaustive, list of documents required for the main types 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.

Submitted documents should be named according to **the naming conventions listed** at the end of this document.

The templates for submission and submission deadlines can be found at: Paediatric investigation plans: Templates, forms and submission dates.

2. List of required documents by submission type

2.1. Paediatric investigation plan and product specific waiver submissions

- Letter authorising the person appointed in Part A (see next point) to communicate with EMA regarding this paediatric procedure on behalf of the applicant
- 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 comprehensive guidance. Part A should be submitted as an electronically-signed form; please refer to the information on e-signatures available at 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, including quality, non-clinical and clinical studies as well as modelling and simulation and extrapolation 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 - such 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 format.

  Use the *drafting notes in the template as guidance* and the European Commission Guideline on the Format and Content of PIP applications to complete this document.

  Using cross-references in the text should be avoided.

- Copy of literature references, as a single zip file.
- Other supporting information as listed in section A10 of the Electronic form (PED1) ('Part A'), as a single zip file:
  - scientific advice CHMP / NCA / third 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 PDCO requests for modification (resubmission following clock-stop)

- Letter authorising the person appointed in Part A (see next point) to communicate with EMA regarding this paediatric procedure on behalf of the applicant.
- Response document to the PDCO request for modifications, including a list of references used in the response, in Word format.
- Copy of additional references used in the response in a single zip file (previously sent references should not be included).
- Additional documents to support the response that were not previously sent.
- Electronic form for paediatric-investigation-plan application and request for waiver - (PED1) certified, in case of any changes.
- Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion, if changes to the form are required to address the PDCO's request for modification at Day 60.

NOTE: **No** updated scientific document (parts B-F) is required and therefore should not be submitted. All answers including rationale are to be provided in the response to the PDCO's request for modification document.

2.3. Modification of an agreed PIP

- Letter authorising the person appointed in Part A (see next point) to communicate with EMA regarding this paediatric procedure on behalf of the applicant.
- Electronic form for paediatric-investigation-plan application and request for waiver - (PED1) certified (also referred to as 'Part A')

  The product's authorisation information must reflect the current status, particularly if it has obtained marketing authorisation since the preceding procedure.

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

  The electronic form (Part A) should be submitted as an electronically-signed form; please refer to information on e-signatures at 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.
- Request for modification of an agreed paediatric investigation plan template, listing all requested changes, in Word format.
- Copies of literature references used in the request and other supporting documents, as a single zip file.
- Document "Decision with annexes" issued in the preceding procedure that is being modified.

NOTE: **No** updated scientific document (parts B-F) nor Key Elements Form are required and therefore should not be submitted. All proposed modifications to the agreed PIP and rationale/justification need to be listed in the Request for modification of an agreed paediatric investigation plan template.

2.4. Compliance check request

- Letter authorising the person appointed in Part A (see next point) to communicate with EMA regarding this paediatric procedure on behalf of the applicant.
- 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 discussing the suitability of the available report with the paediatric coordinator prior to submission of the compliance check. Individual patient data listings (section 16.4) are not needed.
- Summary of product characteristics (SmPC), 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).
- Document "Decision with annexes" issued in the procedure that is being checked for compliance.

3. Naming Conventions

Applicants are kindly requested to avoid sending documents inside regular folders - please only bundle them in zip files as mentioned below.

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
Letter authorising the person appointed in Part A (see next point) to communicate with EMA regarding this paediatric procedure on behalf of the applicant	PDF	01-xxxxxx LoA	M	I/A	M	M
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
Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion	PDF (active form)	04-xxxxxx KEF	M[1]	I/A	I/A	N/A
Template for scientific document (part B-F)	Word	05-xxxxxx Scientific document	M	N/A	N/A	N/A
Response document to request for modifications at Day 60	Word	06-Responses to D60	N/A	M	N/A	N/A
Copies of literature references	ZIP[ii]	07-xxxxxx Literature	M	I/A	M	N/A

[1] N/A for product specific waiver submissions.

Other supporting documents listed in part A.10 of the electronic application form (Part A)*	ZIP	08-xxxxxx Supporting documents	I/A	I/A	I/A	N/A
Other references*	ZIP	09-xxxxxx Other	I/A	I/A	I/A	N/A
Request for modification of an agreed PIP	Word	03-xxxxxx Request for modification	N/A	N/A	M	N/A
Request for compliance check on an agreed paediatric-investigation-plan form - (PED3) certified	PDF (active form)	02-xxxxxx Request for compliance check	N/A	N/A	N/A	M
Study reports	ZIP	03-xxxxxx Study reports	N/A	N/A	N/A	M
Evidence of study initiation*	PDF	03-xxxxxx Evidence of initiation	N/A	N/A	N/A	I/A
Quality measures*	ZIP	03-xxxxxx Quality measures	N/A	N/A	N/A	I/A
"Decision with annexes"	PDF	04-xxxxxx Decision with annexes	N/A	N/A	M	M

[i] Do not send letter of intent unless a pre-submission interaction is required.

[ii] Ensure that the Zip file name does not contain any special characters e.g. brackets () as it will prevent successful submission.