**Applicable from 19 November 2020**
EMA/672643/2017 Rev. 3
Human Medicines Division

# Guidance on paediatric submissions

Via eSubmission Gateway and eSubmission Web Client

**Disclaimer:**

The following guidance outlines the main steps to take in preparation for submission and a list of documents required for the **main**[1] types of paediatric submissions.

This document should be read in conjunction with other relevant guidance on content available on the EMA website, such as the European Commission Guideline on the Format and Content of PIP applications; Paediatric Medicines; Paediatric investigation plans: questions and answers; and the Paediatric Regulation.

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[1] *If you need further guidance on any other procedure type/category not listed, please contact us via ASK EMA.*

# 1. Outline of paediatric submission steps[2]

1. **In advance** of your targeted submission deadline please ensure access to:

   - eSubmission Gateway or Web client (register if not yet done)

     *Important: Using one of these submission channels is required for all applicants and all types of paediatric submissions.*

   - Ensure access to EudraLink (instructions to open an EudraLink account)

   - Unless you already have it, you can request a Research Product Identifier (RPI) by submitting a "Request for Research Product" via IRIS (following these instructions).

     *Important: For paediatric submissions this is optional until further advance notice.*

2. For your submission, please use the latest versions of templates and forms, observing the drafting notes provided.

   The forms and templates should be downloaded first and only then completed, using for example "Save target as" function as illustrated on the following screenshot:


   Where established, please name your documents as per the paediatric submission naming convention.

3. Upon submission, please follow the instructions for the **Paediatric submission** to create an XML delivery file, selecting the relevant options[1].

   Submit all the required documents/ZIP files **in a single folder** (as paediatric submissions do not follow eCTD standards) via the eSubmission Gateway or the Web Client.

4. Following your submission, within 5 working days after the relevant submission deadline the latest, you will receive an acknowledgement of your submission via EudraLink that will contain a full paediatric procedure number to be used in any further correspondence about this procedure.

   *Important: If you have not received this EudraLink message from EMA, and it has been more than 5 working days since the submission deadline, please contact us via ASK EMA as your submission may have not reached us.*

[2] *A letter of intent to submit a paediatric application is no longer required or processed with an exception of submissions where an expedited review is foresean on the EMA website (e.g. Covid-19 related submissions).*

# 2. List of required documents by procedure type

## *2.1. Paediatric investigation plan (PIP) and product specific waiver submissions*

To contain:

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

  *Note on Part A:*

  *Part A must be submitted as an electronically-signed[3] **active** PDF form (containing active fields), i.e. **not** flattened, printed or a scanned PDF. If this technical requirement cannot be met, then two files are required:*

  - *one (unsigned) completed PDF form containing the active/live fields; and*
  - *one scanned copy of the completed PDF with wet signature.*

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

  *Note on KEF:*

  - *The key elements form should be used to propose key elements in short bullet-point style for all completed, ongoing and proposed future steps in the pharmaceutical development for children, including quality, non-clinical and clinical, modelling and simulation and extrapolation studies which are proposed for inclusion in the PDCO's opinion.*
  - *It must not include background information, explanations, justifications, legal requirements (e.g. consent) or additional detailed information (Scientific document, Parts B-F, is to be used for such information.*

- Template for scientific document (Parts B-F)

  *Note:*

  - *This document must be submitted in **Word** format. Cross-references and hyperlinks in the text should be avoided.*
  - *The `drafting notes in the template` and the European Commission Guideline on the Format and Content of PIP applications are intended to guide completion.*

- Copy of literature references, as a single zip file.
- Letter authorising the person appointed in Form Part A, section A.1, to communicate with EMA regarding this paediatric procedure on behalf of the applicant.
- Other supporting information (as listed in Form Part A, section A.10), as a single zip file, if applicable/available, e.g.:
  - scientific advice CHMP/NCA/third countries/FDA written requests;
  - risk management plan;
  - summary of product characteristics;
  - investigator's brochure;
  - copy of the Commission decision on Orphan designation.

[3] *Further information on e-signatures: at http://esubmission.ema.europa.eu/eSignatures.html*

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

To contain:

- Response document to the PDCO request for modification, including a list of references used in the response, in Word format.
- Copies of additional references used in the response, in a single zip file (previously sent references should not be included).
- Additional relevant documents to support the response that were not previously sent.

**Only in case of changes to the previously submitted documents:**

- 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, see also Note on KEF.
- Electronic form for paediatric-investigation-plan application and request for waiver – (PED1) certified, see also Note on Part A.
- Letter authorising a new contact person appointed in updated Form Part A, section A.1, to communicate with EMA regarding this paediatric procedure on behalf of the applicant.

*Note:*

*An updated scientific document (Parts B-F) is **not** required and therefore should not be submitted. All answers including rationale must be provided in the response to the PDCO's request for modification document.*

## 2.3. Modification of an agreed PIP

To contain:

- Electronic form for paediatric-investigation-plan application and request for waiver – (PED1) certified

  *Note (*see also Note on Part A*):*

  *Avoid reusing the Form Part A submitted for the initial PIP procedure. Information provided in all sections must be up-to-date, including the current product's marketing authorisation status. Unless subject of this modification, pharmaceutical form, route of administration, condition and active substance (except if INN has been recommended meanwhile), should be in line with the EMA decision of the preceding procedure.*
- 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, as a single zip file.
- Other supporting documents, as a single zip file.
- Letter authorising the person appointed in Form Part A, section A.1 to communicate with EMA regarding this paediatric procedure on behalf of the applicant.
- Document "Decision with annexes" issued in the preceding procedure that is now being modified.
- Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion – **only for any new** study that is being proposed in this modification procedure. See also Note on KEF.

*Note:*

*An updated scientific document (Parts B-F) is **not** required and therefore should not be submitted. All proposed modifications to the agreed PIP and rationale/justification should be listed in the Request for modification of an agreed paediatric investigation plan template.*

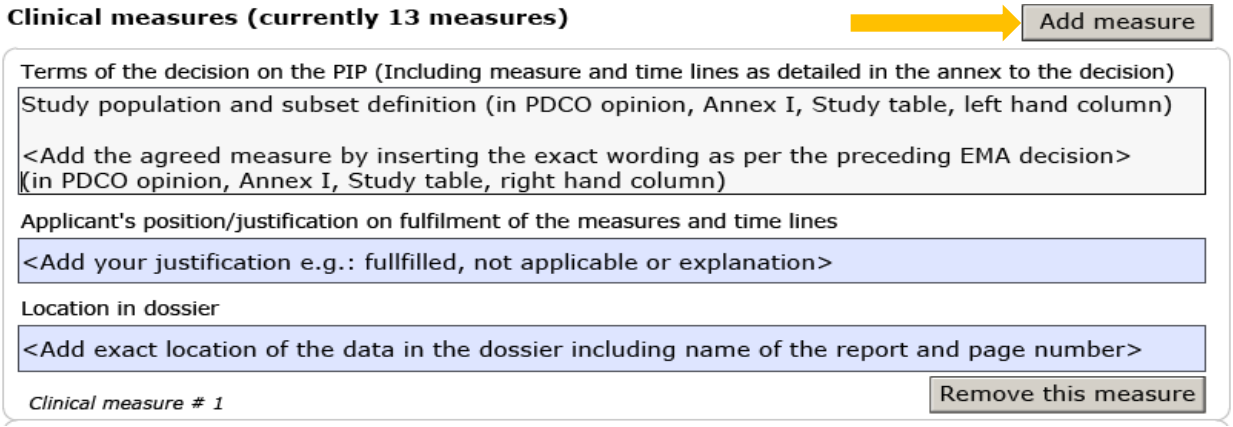
## 2.4. Compliance check request

To contain:

- Request for compliance check on an agreed paediatric-investigation-plan form – (PED3) certified.

  *Note:*

  - *All sections should be up-to-date and in line with the EMA decision of the procedure that is being checked for compliance, incl.: name of the active substance (unless INN has been recommended meanwhile), pharmaceutical form, route of administration and condition and measures and timelines* ***to be checked****.*
  - *Each key element of each study that is to be checked for a compliance is to be entered as a* ***separate*** *measure in the compliance check form using "Add measure", see arrow and drafting notes on the following* ***example****:*




- Letter authorising the person appointed in the Request for compliance check form to communicate with EMA regarding this paediatric procedure on behalf of the applicant.
- Document "<EMEA-xxxxxx-PIPxx-yy-<Mxx>> Decision with annexes" issued in the procedure that is being checked for compliance.
- Study report(s)

  *Note:*

  *Full (complete) study reports should be submitted for the compliance check. If not yet issued, the latest available report or a similar document may be submitted, which must contain sufficient information to allow the check of compliance against the agreed key elements in the decision. In such cases, discussion of the suitability of the available report with the paediatric coordinator is recommended prior to submission of the compliance check. Individual patient data listings (section 16.4) are not required.*

**Only if available / applicable:**

- Summary of product characteristics (SmPC).
- Evidence of study initiation.

  *Note:*

  *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. Naming Convention

*Note: Wherever the naming convention is **not** established in the following table, the document included in your submission should be named to reflect its content, starting with the procedure number (where available), and observing the usual rules on naming documents such as avoiding symbols.*

| Document type | Document format | Naming convention<br>*(substitute xxxxxx with the 6-digit procedure number if available)* | Mandatory (M)/ Not applicable (N/A)/ If applicable (I/A) | | | |
|---|---|---|---|---|---|---|
| | | | PIP and waiver submissions | Answer to RfM | Modification of an agreed PIP | Compliance check |
| Electronic form for paediatric-investigation- plan application and request for waiver - (PED1) certified (Part A) | PDF active form (and scanned copy if needed) | 01 xxxxxx Application form<br>01 xxxxxx Application form signed *(if needed)* | M | I/A[a] | M | N/A |
| Key elements form: Applicant's proposal for a paediatric-investigation-plan opinion | PDF active form | 02 xxxxxx KEF | M[b] | I/A[c] | I/A[d] | N/A |
| Template for scientific document (part B-F) | Word | 03 xxxxxx Scientific document | M | N/A | N/A | N/A |
| Response document to request for modifications at Day 60 | Word | 03 xxxxxx Responses to D60 | N/A | M | N/A | N/A |
| Copies of literature references | ZIP [e] | xxxxxx Literature | M | I/A | M | N/A |
| Letter authorising the person appointed in Part A to communicate with EMA regarding this paediatric procedure on behalf of the applicant | PDF | xxxxxx LoA | M | I/A[f] | M | M |
| Other supporting documents (e.g. listed in Form Part A, section A.10) | ZIP[e] | xxxxxx Supporting documents | I/A | I/A | I/A | N/A |

| | | | | | | |
|---|---|---|---|---|---|---|
| Request for modification of an agreed PIP | Word | 02 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) | 01 xxxxxx Request for compliance check | N/A | N/A | N/A | M |
| Study reports (or equivalent) | ZIP[e] | 03 xxxxxx Study reports | N/A | N/A | N/A | M |
| Evidence of study initiation | PDF | xxxxxx Evidence of initiation | N/A | N/A | N/A | I/A |
| Quality measures | ZIP[e] | xxxxxx Quality measures | N/A | N/A | N/A | I/A |
| "Decision with annexes" | PDF | 03 xxxxxx Decision with annexes | N/A | N/A | M | M |

[a] *Applicable if there is any change of the information provided in this form since the submission.*

[b] *N/A for product specific waiver submissions.*

[c] *Applicable only if required to facilitate the PDCO's request for modification.*

[d] *Applicable only if a new study is being proposed in this modification.*

[e] *Ensure that the zip file name does not contain any special characters e.g. brackets (), as this will prevent successful submission.*

[f] *Applicable only if the applicant's contact person is changing after clock-stop.*

# 4. Paediatric submission – xml delivery files options

(See also: User Guidance for submissions via eSubmission Gateway / Web Client using xml delivery files)

| Choose from drop-down list a category relevant to your paediatric submission | | | | Complete applicable fields to identify the content of your submission | | | |
|---|---|---|---|---|---|---|---|
| **Submission type** | **Procedure Type** | **Submission-Unit** | **Submission description** | **Procedure number[g]** | **Active substance[h]** | **RPI[i]** | **Contact person's e-mail address** |
| **Paediatric submissions** (Regulation (EC) No 1901/2006) | **Paediatric Investigation Plan** *(Art 16(1) with or without Art 20 and Art 13)* | Pre-submission interaction *(see relevant Q&A)* | N/A | Complete only if already issued (e.g. 2nd submission for the same Active substance) in format EMEA-xxxxxx (otherwise leave blank) | Complete as instructed | Complete if available | N/A |
| | | Submission (application) *(Art 15)* | N/A | Complete only if already issued (e.g. 2nd submission for the same active substance or if Pre-submission interaction occurred) in format EMEA-xxxxxx (otherwise leave blank) | Complete as instructed | Complete if available | N/A |
| | | Validation response *(Art 16.3)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Request for clarification interaction *(Art 17.2)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Answer to PDCO's request for modification *(Art 17.2)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Additional information *(if invited by the PDCO)* | Response to Day 30 PDCO discussion | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | | Response to Day 90 PDCO discussion | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Re-examination *(Art 25)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Withdrawal *(of a procedure)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Notification of change *(see relevant Q&A)* | Applicant change due to take-over by new legal entity[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | Complete e-mail address of the person to contact if the Notification cannot be processed. |
| | | | Applicant particulars' change (legal entity unchanged)[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | |
| | | | Authorised contact person change[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | |
| | | | Public enquiry contact change[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | |
| | **Waiver** *(Art 13)* | Pre-submission interaction *(see relevant Q&A)* | N/A | Complete only if already issued (e.g. 2nd submission for the same active substance) in format EMEA-xxxxxx (otherwise leave blank) | Complete as instructed | Complete if available | N/A |
| | | Submission (application) *(Art 13.1)* | N/A | Complete only if already issued (e.g. 2nd submission for the same active substance or if Pre-submission interaction occurred) in format EMEA-xxxxxx (otherwise leave blank) | Complete as instructed | Complete if available | N/A |

[4] *If more than one description applies, select the first relevant description listed.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Validation response *(Art 16.3)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Answer to PDCO's request for information *(Art 13.2)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Additional information *(if invited by the PDCO)* | Response to Day 30 PDCO discussion | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Re-examination *(Art 25)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Withdrawal *(of a procedure)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | | Notification of change *(see relevant Q&A)* | Applicant change due to take-over by new legal entity[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | Complete e-mail address of the person to contact if the Notification cannot be processed. |
| | | | Applicant particulars' change (legal entity unchanged)[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | |
| | | | Authorised contact person change[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | |
| | | | Public enquiry contact change[4] | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | |
| | | Revocation *(Art 14)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy | Complete as instructed | Complete if available | N/A |
| | **Modification of an agreed PIP** *(Art 22)* | Pre-submission interaction *(see relevant Q&A)* | N/A | Complete in format EMEA-xxxxxx (as per initial PIP procedure) | Complete as instructed | Complete if available | N/A |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Submission (application) | N/A | Complete in format EMEA-xxxxxx (as per initial PIP procedure) | Complete as instructed | Complete if available | N/A |
| | | Additional information *(if invited by the PDCO)* | Response to Day 30 PDCO discussion | Complete in format EMEA-xxxxxx-PIPxx-yy-Mxx | Complete as instructed | Complete if available | N/A |
| | | Re-examination *(Art 25)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy-Mxx | Complete as instructed | Complete if available | N/A |
| | | Withdrawal *(of a procedure)* | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy-Mxx | Complete as instructed | Complete if available | N/A |
| | | Notification of change *(see relevant Q&A)* | Applicant change due to take-over by new legal entity[4] | Complete in format EMEA-xxxxxx-PIPxx-yy-Mxx | Complete as instructed | Complete if available | Complete e-mail address of the person to contact if the Notification cannot be processed. |
| | | | Applicant particulars' change (legal entity unchanged)[4] | Complete in format EMEA-xxxxxx-PIPxx-yy-Mxx | Complete as instructed | Complete if available | |
| | | | Authorised contact person change[4] | Complete in format EMEA-xxxxxx-PIPxx-yy-Mxx | Complete as instructed | Complete if available | |
| | | | Public enquiry contact change[4] | Complete in format EMEA-xxxxxx-PIPxx-yy-Mxx | Complete as instructed | Complete if available | |
| | **Compliance check** *(Art 23)* | Submission (application) | N/A | Complete in format EMEA-xxxxxx (as per initial PIP/modification procedure) | Complete as instructed | Complete if available | N/A |
| | | Additional information *(if invited by the PDCO)* | Response to Day 30 PDCO discussion | Complete in format EMEA-C<x>-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | N/A |
| | | Withdrawal *(of a procedure)* | N/A | Complete in format EMEA-C<x>-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | N/A |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Notification of change *(see relevant Q&A)* | Applicant change due to take-over by new legal entity[4] | Complete in format EMEA-C<x>-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | Complete e-mail address of the person to contact if the Notification cannot be processed. |
| | | | Applicant particulars' change (legal entity unchanged)[4] | Complete in format EMEA-C<x>-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | |
| | | | Authorised contact person change[4] | Complete in format EMEA-C<x>-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | |
| | | | Public enquiry contact change[4] | Complete in format EMEA-C<x>-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | |
| | **Annual report**[5] *(use for Art 34 and Art 33)* | Submission (application) | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | N/A |
| | **Discontinuation** *(use for Art 35, see relevant Q&A)* | Submission (application) | N/A | Complete in format EMEA-xxxxxx-PIPxx-yy<-Mxx> | Complete as instructed | Complete if available | N/A |
| | **Class-waiver confirmation request** *(see relevant Q&A)* | Submission (application) | N/A | N/A | Complete as instructed | Complete if available | N/A |
| | **Condition/ indication confirmation request** *(see relevant Q&A)* | Submission (application) | N/A | N/A | Complete as instructed | Complete if available | N/A |

[5] *This category is to be used also for informing the EMA about placing a product on the market in the relevant Member State(s) after completion of an agreed PIP (for the Art 33 Register).*

**Explanatory notes on paediatric XML delivery file fields completion:**

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[g] ***Paediatric procedure number*** *is assigned by EMA upon receipt of your paediatric (pre-)submission, and communicated to you in an acknowledgement email via EudraLink. The number is also to be found on all procedural documents (EMA decision, PDCO opinion, Summary report) and formal communications sent to the applicant via EudraLink in one of the following formats ("x" denotes a number, "yy" denotes PIP/waiver year of submission):*

- *EMEA-xxxxxx – a temporary core number – use if available when the complete paediatric procedure number has not yet been issued by EMA, i.e. for Submission-Units: "Pre-submission interaction" and "Submission (application)" unless there was a Pre-submission interaction.*

  *The 6-digits "xxxxxx" will be identical for any of your subsequent submissions for the same active substance, e.g. 2nd PIP/waiver, modification of an agreed PIP, compliance check.*

*Complete paediatric number - use in all other Submission-Units, in a format relevant to the Procedure Type:*

- *EMEA-xxxxxx-PIPxx-yy for PIP and waiver*
- *EMEA-xxxxxx-PIPxx-yy-Mxx for modification of an agreed PIP*
- *EMEA-C<x>-xxxxxx-PIPxx-yy<-Mxx> for full or partial/interim compliance check.*

[h] ***Active substance*** *is a mandatory field, to be completed consistently throughout your submission as either:*

- *Recommended INN,*
- *EU Pharmacopoeia name,*
- *common name, or*
- *the exact scientific/chemical name,*

*in this descending order of preference.*

*For accelerated procedures foreseen on the EMA website add in front of the Active substance the reason, such us "Covid-19".*

*In any subsequent submissions (e.g. modification of an agreed PIP and compliance check) it should match the active substance in the preceding EMA decision unless e.g. an INN has since been recommended.*

[i] ***RPI*** *(i.e. Research Product Identifier, available via IRIS) is an optional field, to be completed if the number is already available at the time of the submission (leave empty if not).*