



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Status of PIP compliance check procedure

8th Industry Stakeholder Platform on Research and Development support

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H-EG-PME

An agency of the European Union





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Background

- This presentation has been prepared
 - taking the EMA-EC Paediatric Action Plan into account where simplification and streamlining of administrative procedures is one of the main objectives
 - in view of continued feedback received from various stakeholders, primarily pharmaceutical companies and trade associations (EFPIA letter to EC and EMA)



Duration of compliance checks (1)

- Over the years, EMA has taken several actions to improve, simplify and streamline the compliance check, e.g.:
 - Since 2017 our updated Standard Operating Procedure 3456 SOP provides the possibility of an EMA conclusion on partial checks without involving the PDCO
 - High flexibility with regards to submission deadlines by accepting compliance check requests outside of the published timetable
 - Ad hoc procedures to conduct the compliance check within 4 days for COVID-19 products
 - The default duration of the procedure is 60 days but the Agency systematically aims to conclude as early as possible, often using expedited timelines including consultation of the PDCO between plenary meetings and also in August when there is no plenary meeting



Duration of compliance checks (2)

- Since the Paediatric Regulation entered into force until 30 April 2022, 950 compliance checks (674 partial checks concluding in a report and 276 full or final checks concluding in a PDCO opinion) were performed by the Agency. The average number of days needed for conclusion was 33.
- These numbers include compliance checks performed before the 2017 SOP update; since then the average duration has further shortened.



Duration of compliance checks (3)

2017 – 2022 - partial

full/final

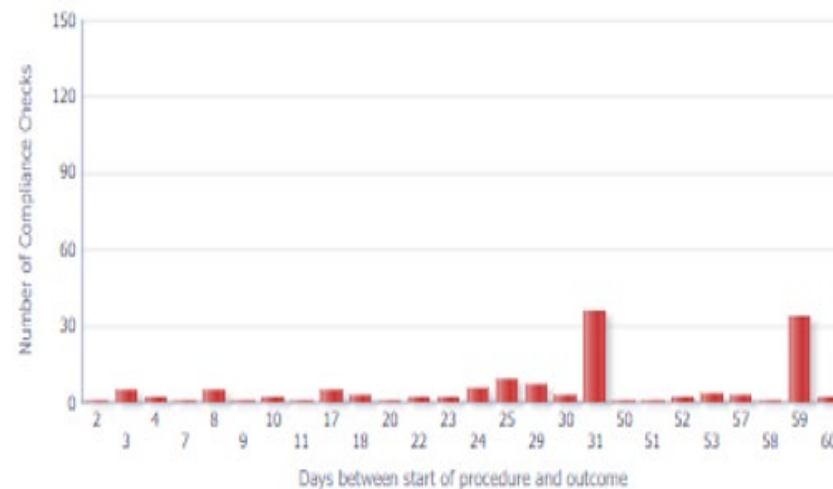
Event Name - Compare CC outcome

Duration of CC procedures



Event Name - Compare Opinion adopted

Duration of CC procedures



Status of PIP compliance check procedure - 11 July 2022



Duration of compliance checks (4)

- The current average time needed for conclusion since 01 January 2020 is 30 days
- The duration of compliance check procedures is systematically and significantly shorter than the 60-days legal timeframe
- Simplifications:
 - latest available draft report or a similar document accepted when CSR is not ready
 - Quality Module simplifications
 - Study initiation is usually “not determined by the PDCO”
 - See [Questions and answers on the procedure of PIP compliance verification at EMA, and on paediatric rewards \(europa.eu\)](#)



Industry suggestion 1: Checking only upon completion of all PIP measures (1)

- i.e. suggestion to abandon partial checking
- “an” application: every application
- compliance is a condition
- documents in points a)-d) are not mutually exclusive

Article 20

1. At the same time as the paediatric investigation plan is submitted under Article 16(1), a request may be made for deferral of the initiation or completion of some or all of the measures set out in that plan. Such deferral shall be justified on scientific and technical grounds or on grounds related to public health.

Article 7

1. An application for marketing authorisation under Article 6 of Directive 2001/83/EC in respect of a medicinal product for human use which is not authorised in the Community at the time of entry into force of this Regulation shall be regarded as valid only if it includes, in addition to the particulars and documents referred to in Article 8(3) of Directive 2001/83/EC, one of the following:

- (a) the results of all studies performed and details of all information collected in compliance with an agreed paediatric investigation plan;
- (b) a decision of the Agency granting a product-specific waiver;
- (c) a decision of the Agency granting a class waiver pursuant to Article 11;
- (d) a decision of the Agency granting a deferral.

For the purposes of point (a), the decision of the Agency agreeing the paediatric investigation plan concerned shall also be included in the application.

2. The documents submitted pursuant to paragraph 1 shall, cumulatively, cover all subsets of the paediatric population.



Industry suggestion 1: Checking only upon completion of all PIP measures (2)

EMA feedback

- Articles 7 and 8 aim to ensure that the evidence submitted to support a regulatory application is **generated in compliance with a PIP** and makes it a **condition for the successful validation of that application**.
- There is **no restriction and no exemption for initial applications before the full completion of the PIP**. This is why the compliance check of the results with the PIP is mandated.
- A **PIP is not deferred per se**, individual measures are. At MAA validation it is verified that all the non-deferred study reports are included in the submission.
- Therefore, performing only one compliance check upon completion of all PIP measures would **not be compatible** with the Paediatric Regulation.



Industry suggestion 2: No duplicative assessments by EMA/PDCO and CHMP

- Fully agreed and implemented
- EMA/PDCO check (compliance check): to determine that the evidence generated by a certain study is the same evidence as the one the PDCO requested in the PIP. This process does not include any assessment of the data.
- EMA check (validation): to verify that the documents are available in the submission and that they have been confirmed compliant (administrative check)
- CHMP: assessment of the data



Industry suggestion 3: No suspension of MAA validation because of missing compliance check

- Article 7 of Regulation (EC) No 1901/2006: an application is valid only if it includes (among others) the results of all studies performed and details of all information collected in compliance with an agreed paediatric investigation plan: *there is no validation without confirmed compliance*
- Article 23(2)(b) of Regulation (EC) No 1901/2006 allows EMA to request the opinion of the PDCO on compliance with the agreed PIP at the validation of the MAA.
 - We note that Article 23(2)(b) states that the PDCO opinion "may ... be requested" (not: shall be requested).
 - We further note that Article 23(2)(c) allows the CHMP or NCA to request the PDCO opinion when this has not yet been done prior to submitting the MAA or during validation.
- In order to avoid time constraints it is always recommended to complete the CC as soon as possible before submission of a regulatory procedure. However, to allow flexibility, there is the possibility to also request a CC during the validation phase.



Industry suggestion 4: Checks based on “essential” compliance

- Fully agreed and implemented
- Only the key elements stipulated in the PIP are checked for compliance
- Study results and data are never assessed at this stage
- Adequate alternative documentation is accepted when CSR is not ready
- No need for the Module 2 Quality Overall Summary



Further steps

- Previous continuous improvement activities have led to efficient and short compliance check procedures, which are sufficiently robust and prevent impact on the MAA review start if applied on time by the sponsor
- The Agency is committed to further optimising processes on paediatric activities
 - Ongoing initiative to streamline administrative procedures (part of the EC-EMA action plan)
 - Aim to improve information and communication to stakeholders
 - Work on the concept of an evolutionary PIP and key elements (Focus Groups)
 - Efforts to improve the administrative tools and requirements related to compliance checks, such as an update of the CC request form



Any questions?

Further information

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