PIPs: problems and solutions

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HIP

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PIPs problems and solutions: academia

Background to academic involvement in PIPs

1. Publically funded PIPs (e.g. FP7 projects mandated under Article 40)
2. Contribution to other PIPs (as supportive evidence or post hoc inclusion in PIPs
3. Advice about, and implementation of, PIPs

PIPs problems and solutions: academia

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Team A (neonatal)

- What is realistic is critically important. Many of the drugs we currently use have very little evidence to support their use. Very stringent requirements will mean that this will remain the case.
- The practice of providing D-30 feedback is very helpful. The request that a proposed modification be submitted informally a couple of months prior to its formal submission can add excessive cycle-time.
- The process to modify is relatively simple. The requirement that the modification justification be summarized in 250 words is very useful. However over time the Form B-F can be come unwieldy.
- A change of rapporteur, or other EMA staff can create the risk of misunderstood expectations. Where key EMA staff are reassigned, there should be a process where the incoming successor and the rapporteur is briefed on the history of the program to avoid repetitive questions etc.

Team B (paediatric)

- It is vital that all team members understand the overall PIP process, in particular what the key binding elements and measures mean (these must be met, otherwise you need to submit a request for modification).
- Be realistic about your clinical study design in terms of patient numbers and ages etc, as well as primary and secondary endpoints - are these achievable?
- Will your study enable you to generate the data required to support the use of the product in the intended population?
- In my experience the regulators might ask for more patients that you consider clinically necessary (and realistically able to recruit) and so it is important to have robust justification to support your proposals.

Team B (paediatric)

- In addition, I don't think the regulators fully appreciate the time, cost and effort required to open new study sites which is a huge challenge especially when budget and timelines are short.
- Open dialogue between the team and the regulators (Co-ordinator, Rapporteur and Peer Reviewer) is really valuable and should be maximised to avoid misunderstandings.
- Both "sides" should remember that we are working towards the same goal and be as open and honest as possible. As mentioned below, we had two "formal" telecons with the PDCO where we had the opportunity to get a better understanding of their perspectives and were able to share our views and experiences. This included feedback from some of our clinicians who gave a clear picture of the proposed patient population and routine clinical practice to help justify our position.
- We were also very fortunate that our Co-ordinator was happy to talk to me separately on the telephone when for example I needed clarity on some of the wording PDCO had proposed.

Team B (paediatric)

- I have to tell you that we had very good experiences with our PIP application and as well with a request for modification with the PDCO.
- My advice would be to explain more things around the application procedure, maybe to write down some real experiences, realistic time frame for preparation of the procedure - but I think the most important issue was that we had an excellent scientist
- What helped to get a smooth run through the PIP application?

1. Native and excellent scientist with experience in regulatory interaction
2. Early preparation! 6 months preparation phase for preparation of the PIP document
3. Talk to the PDCO and use TCs to understand the arguments and exchange arguments
4. Be patient: in total it took together with the preparation time 17 months!

Team B (paediatric)

APPLICATION for a REQUEST FOR MODIFICATION

1. Do not hesitate to request a modification: When it was apparent that the goals (PDCO requirements) negotiated could not be achieved due to the special patient population a request for modification procedure was started.

2. Prepare for this in a similar distinct way and show your data so that the PDCO can understand where the problems are: Preparation similar as with PIP application, also a TC was organized to have a discussion in which way the modification was possible on the basis of the already achieved patient recruitment status.

Team C (neonatal)

My concerns are

- There is no open communication between EMA and academic PIP leaders. If this could be established pre-submission it would save a lot of time and revisions.
- PDCO/expert advisors need to be more considerate about what is possible in real life:
  - what kind of studies will be acceptable to the international community e.g. clinicians and parents,
  - what studies can be realistically done in the time frame set by the funders;
  - which studies clinicians would engage

Team C (neonatal)

My concerns are

- what is the balance between getting the really necessary missing information on drugs which have been used off label for decades and what is possible to obtain in the clinical trials.
- If the processes remain so complicated not many neonatal drugs will make it to a PUMA.

Anon

“For me as a non-native English speaker the closed communication and the sometimes complicated “high formal English” are the biggest hurdles”

Solutions

- Trial preparedness
- Pre-submission briefing for academic projects
  - Or academic contributors to industry PIPs
  - Work with experienced consultants if expertise is not available in-house
- Better continuity within EMA Paediatric Team
- Version control for sections B – F
- Open communication
- Review extent of “Totality of evidence” required for legacy medicines
- More funding under Article 40