Guidelines, Standard PIPs, Output on Expert Meetings at EMA/PDCO – Industry experience

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Example of diverging EMA and FDA-requirements and difficulties to resolve them

Dilemma:
- FDA and PDCO having different expectations to the paediatric program.
- Often solved by the EMA-FDA teleconferences – but not always..
PIP Case

- EU guideline requirement that paediatric trial may only start after a certain number of dosings in adults
- FDA and PMDA had provided viewpoints to Novo Nordisk that differed from those of PDCO.
- Novo Nordisk became unsure on how to act concerning planning of the trials in US and Japan

What happened?

- Novo Nordisk asked EMA during clockstop if the issue could be discussed at the monthly FDA-EMA TC.
- Not done initially.
What happened then?

- The issue was taken up at EMA-FDA TC later – after day 90
- NN was informed on outcome via the summary report

Moving forward…

- Important that the company gets timely feedback from the EMA-FDA teleconference if company’s PIP has been discussed.

- Can the company request an issue to be discussed at an EMA-FDA teleconference?
- Is feedback from TC always put into summary report?
- Could guidance be included in EMA Q&A document?
Hard to present US viewpoint of EU procedure

- EMA has done an outstanding job of transparency: requirements, obligations, cooperation, working toward the right goals.
  - Perhaps PDCO too 'enthusiastic' from feasibility view
  - Industry is a full partner

Industry interested in global pediatric programs

Guidelines are most helpful not only for companies and investigators but for other regulatory authorities to know what EU expecting
  - (jointly developed guidelines ideal but not likely feasible)

Standard PIPs
  - Have advantage of incorporating regulatory 'guidelines'
  - Have advantage of 'quick' approval
  - Have advantage of academic input
  - Common background information
  - FDA collaboration
  - Similar research plans can lead to easy comparison of data as well as meta-analyses
  - Tend to discourage innovation

Expert meetings need to include all experts and that means that pediatricians with expertise in the area who work in industry who can offer unique perspective

Enpr-EMA steering committee must include representatives from industry
Bristol-Myers Squibb Company, USA

- Issue is co-developing a pediatric plan between industry and both FDA-EMA
- Scientific differences are expected
- With timing of consideration askew, no opportunity to gain consensus
- Examples:
  - FDA first; EMA second. Occurred more in early days of EU pediatric regulation
  - EMA first; FDA second. Most common. FDA division dependent
  - Simultaneous consideration

Transparency: the next generation

- All initiatives to include industry, academia and regulatory agencies
- Sharing of pharmacometric data related to developmental changes in drug metabolism
- Disease registries, e.g. JIA CoRe, PRINTO
  - Regulatory approval for PMR
  - Data access and timely reporting
  - Data mining for hypothesis generation but not efficacy reporting
- Cooperative Programs in Pre-competitive space:
  - PRO, formulation development, palatability assessment
  - Biomarker/endpoint development and validation
- Public Private partnership for study to determine best therapy for given disease state
Current situation:

- Most often EMA guidelines combined adult and paediatric recommendations
  - RA and JIA guidelines are one of the exceptions
- Some standards PIPs are available
- Closed workshops are organised by PDCO

Any need for improvement?

Rheumatology as an example: 3 paediatric EMA WSs with academia experts were organised, the last one in Nov.10

- Meeting report provides useful information
- Several important actions identified ... without any timelines
  - To develop a standard PIP
  - To develop non clinical recommendations for NCEs in JIA
  - To analyse the role and limits of extrapolation of efficacy for implementation in the standard PIP where applicable
  - To elaborate a mechanism of implementation of safety concerns, and PV measures to be addressed within the PIP and post-authorisation - in co-operation between PDCO, CHMP, rheumatology working party and PVWP, and learned societies and paediatric networks such as PRES and PRINTO
Our expectations

• More transparency – why not inviting other stakeholders in workshops organised by PDCO
  – There are precedence’s, eg M&S in paediatrics, anti-infective WS...

• Reliable work plan and timelines to help streamlining our drug development

About procedures:
  – Procedures do run pretty well, the introduction of pre-submission meetings has added a new useful tool to clarify late details
  – A “collaborative” set between the Industry team and EMA coordinator takes shape
  – Some refinements seem still possible during the last phase of the evaluation/decision, some last minute issues could be anticipated
Next Steps: enhanced dialogue on content
- Attention to be shifted now on content. Considerable knowledge has been cumulated over these five years of PIP experience
- Interest of discussing reference based, therapeutic area approach
- How useful to have Standard PIPs?
- Balance with freedom of science in clinical development

Conclusions:
- Continue EMA FDA alignment efforts
- Opening regulatory science discussions to all stakeholders – streamlining guidance building process; participating (not interfering)
- Good administrative procedures and support
- EMA PdCo has now build a considerable base of knowledge in paediatric planning: good time for more discussion on contents