Report from EMA workshop

March 20th, 2018 I participated in an EMA workshop in London. Patrik Hassel had originally been invited, but he could not participate. I was his stand-in and held a presentation on behalf of PHA Europe.

The topic for the workshop was «*EMA/EC multi-stakeholder workshop to further improve the implementation of the Pediatric Regulation*». The workshop was divided into five topics:

Topic 1: Identification of pediatric medical needs - Methodology
Topic 2: International cooperation of regulators for pediatric medicines
Topic 3: Timely completion of pediatric investigation plans (PIPs)
Topic 4: Improving the handling of PIP applications
Topic 5: Transparency measures

My presentation was part of topic 1. I was asked to hold a short presentation highlighting the following two questions:

1. *Which ongoing initiatives to identify pediatric medical needs are you working on or aware of?*

2. *Which criteria and methodology would you suggest to prioritize diseases/conditions of unmet pediatric needs?*

Eight speakers had been invited to speak on this topic. EMA tried to get the perspectives from three different angels: from the academia and health care professionals' perspective, the industry's perspective and the patients' perspective.

During my presentation, I started to talk about the initiatives that I was aware of: A project that was started after PHA Europe (Gerry and Patrik) had a meeting in London the summer of 2017 with EMA, FDA and Health Canada. The meeting resulted in the following initiatives:

- To accept non-invasive endpoints (e.g. 6MWT, NT Pro-BNP, MRI, etc instead of right heart catherization) in pediatric studies
- To develop new PROs (Patient Reported Outcomes) in pediatric studies
- To involve patients and carers early in pediatric study designs
- To redesign and improve existing registries with regards to pediatric data
- To address the lack of existing pediatric cardiology networks

When it came to criteria and methodology, I suggested to prioritize diseases based on the seriousness (progression, morbidity, QoL) and diseases that had available adult medication. I had, of course, PAH in mind which is a very serious and debilitating disease specially for children. There are 12-13 medication approved for adults, but only one for children. This leads to much off-label use.

For methodology, I suggested to remember to include all stakeholders in this work. I specifically mentioned regulators, pharma, clinicians, researchers and last, but not the least, the patients and carers. I also suggested that registries could be very useful if they were improved and that pediatric networks also could help to develop criteria and methodology.

This was my first visit to EMA. It was both interesting and impressive. The meeting was much larger than what I had anticipated with 160 people attending. They all seemed to be important KOL (key opinion leaders) and the level of discussion was very high.

The workshop also helped me understand the problem of pediatric medication better. Pharma industry is hesitant to spend much money on research in rare diseases for children. It is difficult to find and recruit patients to participate as carers often don't want their children to be included in studies for various reasons. Once a medication is approved for adults and doctor's prescribe the medication to children as off-label use, this makes it even more difficult to run any studies.

EU is aware of these difficulties, and passed a regulation in 2006 that aimed at solving, or at least, improving this issue. The regulation sets up a system of obligations, rewards and incentives, and puts in place measures to ensure that medicines are regularly researched, developed and authorized to meet children's therapeutic needs. It is base on the simple idea that a company should be obliged to screen every product it develops for its potential use in children, thereby progressively increasing the number of products with pediatric indication.

The regulation passed has without doubt made a big impact and the number of pediatric medications have increased substantially lately. The workshop was a result of a ten year evaluation of the regulation and the outcome of the workshop will be a report and summary that will be published in May. An action plan will be made in mid 2018 and then there will be subsequent reporting on the progress made. The end result will hopefully be that we will see much more pediatric PAH drugs being approved by EMA in the years to come.

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