May 2013

Regulation on Clinical trials: Why do definitions matter

A factual 3-slide presentation with examples

Slides 1: **Why post-authorisation efficacy and safety studies (PAES) are clinical trials**

Slides 2 : **Why 'Low-intervention' trials are not necessarily 'low-risk' to patients**

Slide 3: **What you can do to protect participants and public health**

Post-authorisation efficacy and safety studies (PAES) should not fall into clinical trial definition? [FALSE]

The Facts:

- **Medicines are often authorised when there is not enough evidence about their efficacy and safety**
  (For instance, medicines approved under exceptional circumstances or granted conditional approval, as well as medicines targeting rare diseases).
- In these instances, **post-authorisation efficacy and safety studies (PAES) are required to complete the evaluation.**
- Pharmaceutical companies signaled their intentions to use PAES to obtain accelerated marketing approval: "***PAES could be used to underpin accelerated development and approval of products*** *(…) ; in such circumstances* ***PAES could be used to confirm the evidence on which the approval is based.*** *(…)*" (1)

That is why the 2010 pharmacovigilance legislation required **additional monitoring** for these medicines (to be duly identified with a black symbol).

PAES = clinical trials

1- European Federation of Pharmaceutical Industries and Associations (EFPIA)'s answer to the European Commission's consultation on PAES ; 18 February 2013 : 18 pages. http://ec.europa.eu/health/files/pharmacovigilance/2013_pc_paes/efpia.pdf

‘Low-intervention’ trials mean ‘low-risk’ to patients?

[FALSE]

- According to the European Commission and to the OECD classification, clinical trials could be **considered ‘low-intervention’ as long as medicines are tested in accordance with their marketing authorisation**

Consequences of ‘low-intervention’ trials:
- Trial sponsors are exempted from damage compensation;
- Regulatory authorities have less time for approval of trial applications;
- Reporting of adverse drug reactions is less demanding

The Facts:

- **Post-safety studies are conducted when there are serious safety concerns**

Examples: Even when tested in accordance with their marketing indication, **the REGULATE study [**aimed at substantiating *benfluorex*’s (Mediator°) adverse effects on heart valves**]** and **the VIGOR study [**aimed at substantiating *rofecoxib*’s (Vioxx°) cardiovascular adverse effects**] did put participants at increased risk of serious adverse reactions**, when compared to other

- Due to a lack of data at the time of marketing appproval, **medicines are increasingly authorised and subsequently withdrawn due to safety problems**

Example: Just recently (January 2013), several **combinations of *nicotinic acid* + *laropiprant* with centralised authorisations**, were **withdrawn from the European market for safety reasons thanks to the results of a long-term post-marketing randomised clinical trial** (2).

2- "European Medicines Agency confirms recommendation to suspend Tredaptive, Pelzont and Trevaclyn” www.ema.europa.e u 18/01/2013.

What you can do to protect public health

- **Reintroduce the comprehensive definition of a clinical trial as established in Directive 2001/20/EC** (vote **in favour of amendment 182 and 186**).

- Make sure the **clinical trial definition encompasses "*post-authorisation safety and post-authorisation efficacy trials on a medicinal product authorised within the last 10 years*"** (vote in favour of **amendment 185**; and vote **against amendment 84**).

These amendments are important to secure participants' protection by:

- **encouraging the conduct of good-quality post-authorisation studies, as the protocol will have to be approved** (i.e. conducting randomised clinical trials; protocols taking into account outcomes that are relevant to patients)
- **guaranteeing greater transparency on the clinical trial results.**