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?

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)

PAES = clinical trials

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

- 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

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 medicines.

- Due to a lack of data at the time of marketing approval, medicines are increasingly authorised and subsequently withdrawn due to safety problems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recently (January 2013), several combinations of nicotinic acid + laropiprant with centralised authorisations, were withdrawn from the European market for safety reasons thanks to the results of a long-term post-marketing randomised clinical trial (2).

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.