Finnish Medicines Agency

On changes to ongoing open-label clinical trials

19 August 2026 / John Aspegren

Disclaimer

The views expressed in this presentation are the presenter’s personal views and not necessarily the views of Fimea or EMA

Introduction

- Changes to **ongoing open-label** clinical trials are a pertinent topic in CHMP scientific advice and CTA/substantial modification assessment.
- Changes include, e.g.
  - change of sample size/event count for primary analysis,
  - introduction of a new interim analysis (IA),
  - deletion of an IA,
  - changes to timing of IA(s),
  - changes to success criteria of IA(s),
  - inclusion of sample size re-estimation, incl. so-called promising zone approach etc.
- In other words, changes to adaptive elements of a clinical trial.
- Changes are proposed also after a first IA has already taken place.
- Importantly, type 1 error is not controlled if changes are informed by accumulating data in the same trial.

Some messages from guidelines

- Pre-specify whenever possible. (ICH E9, EMA Missing Data GL)
- Finalise SAP before unblinding. (ICH E9)
- Document and justify all changes. (ICH E9, ICH E3)
- Clearly distinguish pre-planned from post hoc analyses. (ICH E9, ICH E3)

Questions to stimulate discussion

Question 1

a) In which circumstances/under which constrains do the industry panellists consider such changes acceptable and justified?

b) Is there a difference between open-label and double-blind trials?

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Question 3

Are we/you lacking regulatory guidance in this area?
To potentially push back on proposals from other functions?

Thank you

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