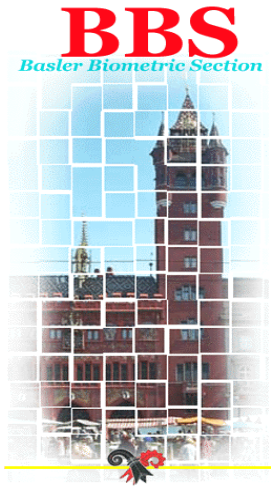
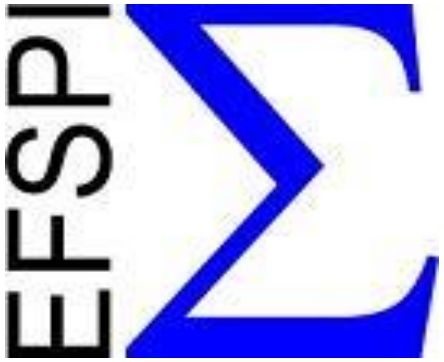




The application of the estimand framework: A Neuroscience perspective

Joint seminar of EFSPI and BBS

Outline of today

13:00-13:10 **Welcome. Introduction to the estimand framework**
Hans Ulrich Burger, BBS president

13:10-13:30 **Outline of an estimand strategy in MS**
Nikolaos Sfikas, Novartis

13:30-13:50 **Outline of an estimand proposal in migraine prevention and neuropathic pain**
Mette Krog Josiassen, Lundbeck and Peter Quarg, Novartis

13:50-14:10 **Using the Estimand Framework to address challenges in AD clinical trial with a closer look at the hypothetical strategy**
Paul Delmar, Hoffmann-La Roche AG

14:10-14:30 **Estimands in Huntington's disease**
Carrie Li, Hoffmann-La Roche AG

14:30-14:45 **Break**

14:45-15:05 **Impact of Covid-19 on studies in Neuroscience**
Andrew Hartley, PPDI

15:05-15:45 **Regulatory aspects of the estimand framework: Clinical and statistical perspectives**
Joel Raffel, MHRA and Khadija Rantell, MHRA

15:45-16:30 **Panel discussion including all speakers and Anja Schiel, Norwegian agency and Chair of Scientific advise working party SAWP**

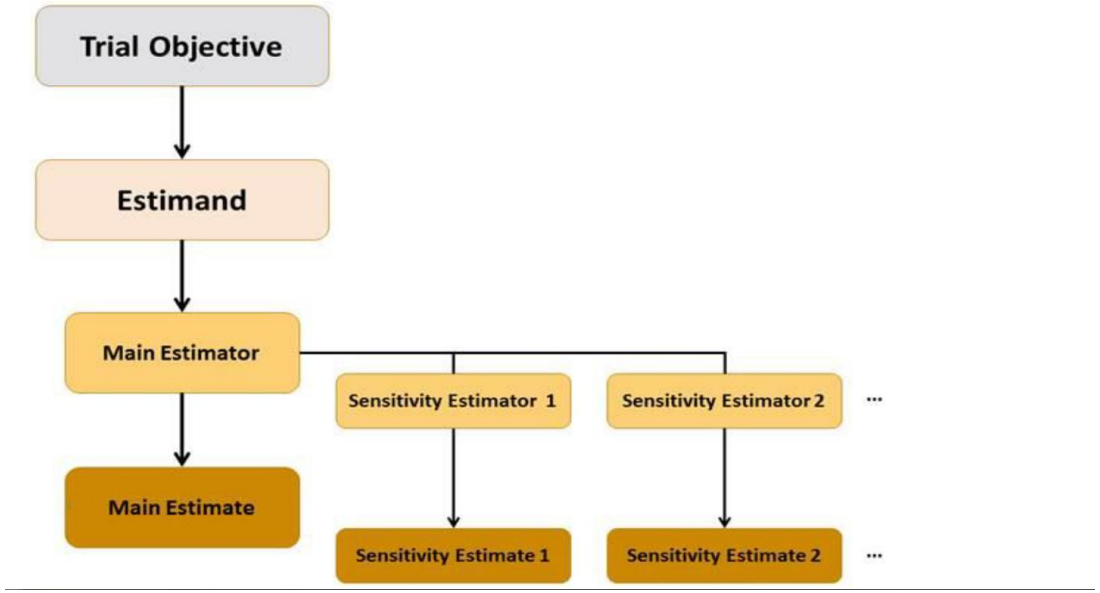
16:30 **End of the meeting**

ICH E9 (R1) addendum

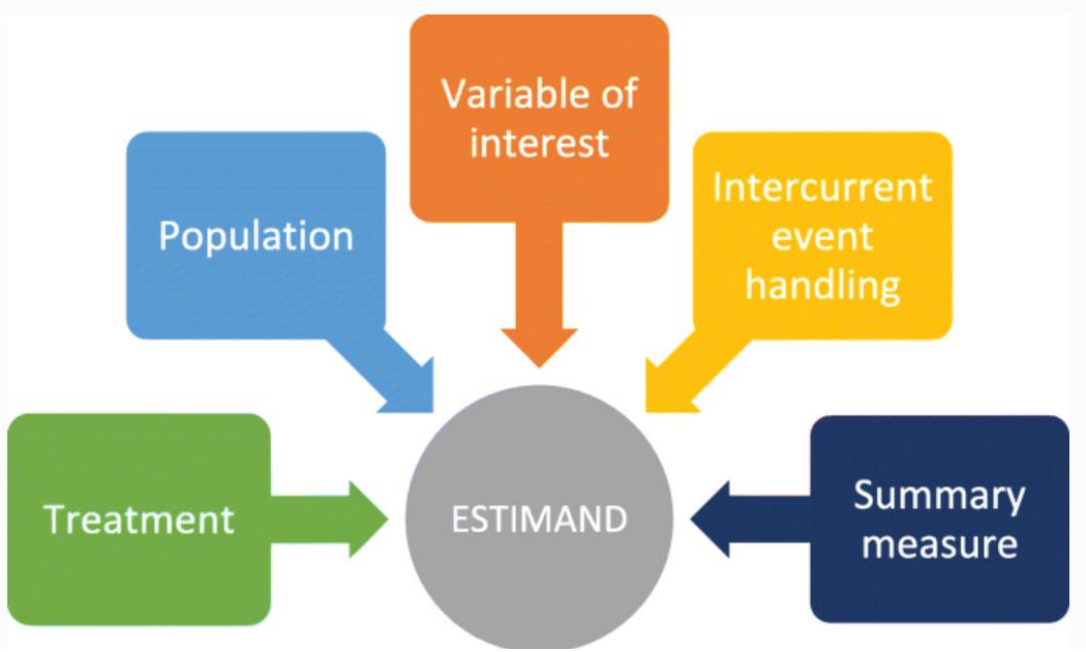
Estimand Framework

The estimand framework is a multidimensional concept used to align planning, design, conduct, analysis, and interpretation of a clinical trial

Principles of the framework



The estimand framework attributes



Always keep in mind the Scientific Questions of interest

Estimand attributes definitions

Population
Underlying study population suitable for the targeted question

Treatment
e.g. patients will be randomised to receive either test or placebo, plus any existing stable medication.

Variable or endpoint
The variable measured for each patient that is required to address the clinical question e.g. overall response, progression free survival

Intercurrent events
Events occurring after treatment initiation that affect the interpretation of measurements associated with the clinical question e.g. discontinuation from treatment due to adverse events, or death, use of rescue medication

Population summary measures
Provides the basis for comparison between treatment conditions, e.g. mean change from baseline, proportion of responders.

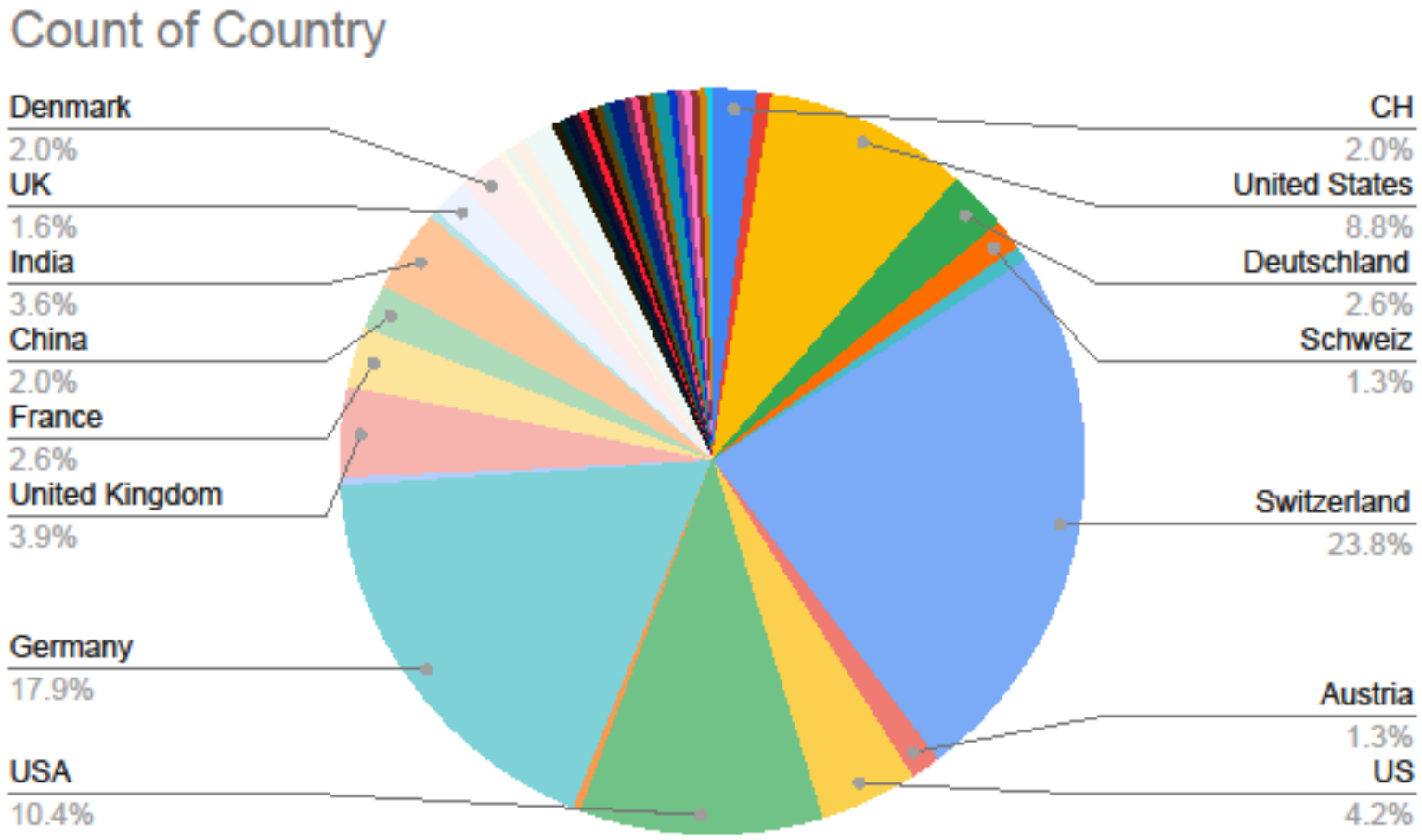
Strategies for handling post-randomisation events

Treatment policy strategy	*Hypothetical strategy*	*Composite variable strategy*	*While on treatment strategy*	*Principal stratum strategy*
The occurence of the intercurrent effect **is irrelevant** for the evaluation of the treatment effect and can be ignored	Evaluation of the treatment effect in the hypothetical scenario in which the **intercurrent event does not** occur	Intercurrent event in itself is **informative about patient's outcome** and is therefore incorporated into the definition of the variable	For this strategy, response to treatment **prior to the occurrence** of the intercurrent event is of interest	Target population to be the **"principal stratum"** in which an intercurrent event would (not) occur

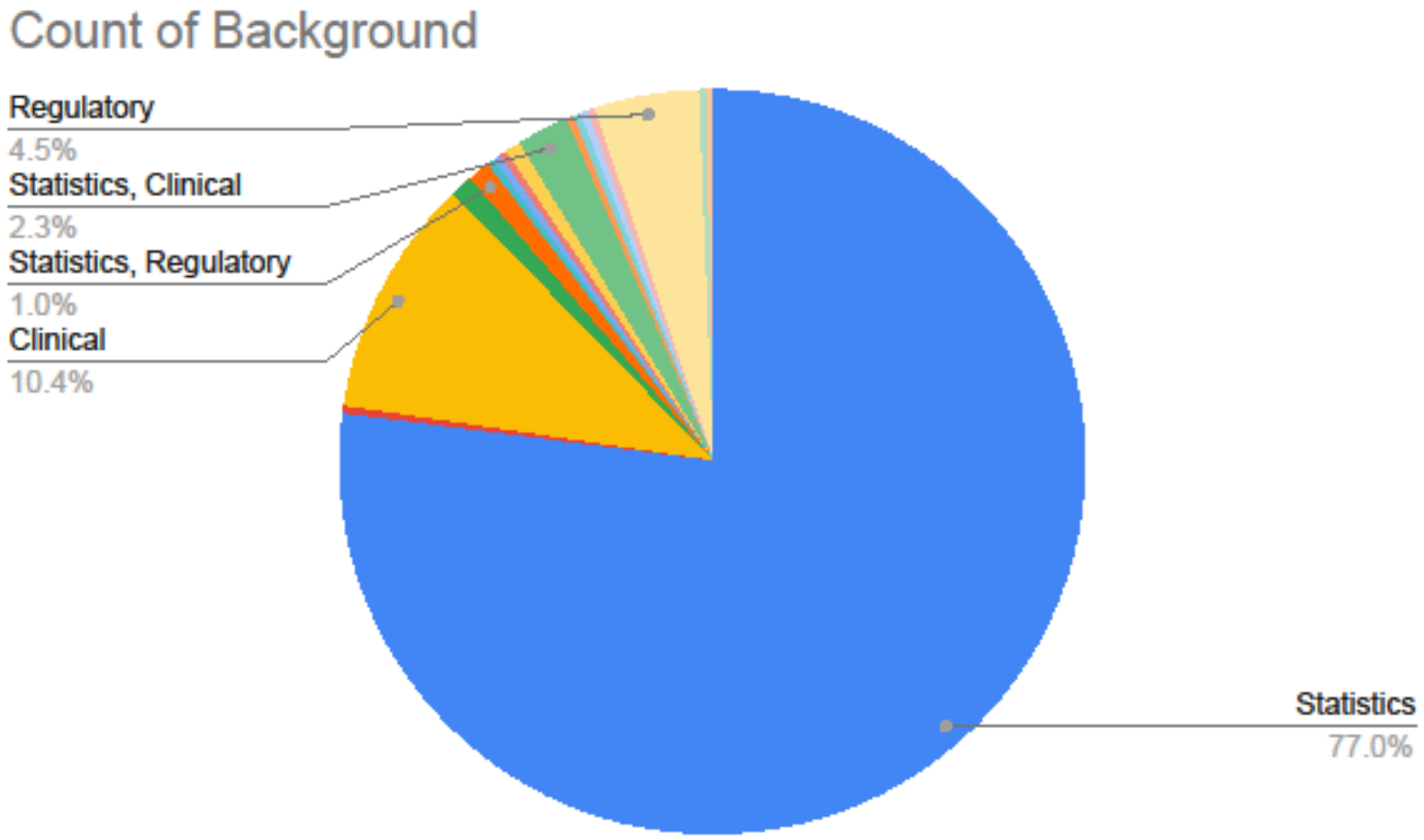
Some house keeping

- Keep yourself muted and do not switch on the camera to save bandwidth
- Use the Chat to pose questions
- There should be time for one questions for clarification after each talk. Content discussion should take place at the end in the panel discussion
- We have a 15 min break. For that we opened two more lines that we can meet in smaller chats. Speakers and panelist will also be available there
- How to do this?
  - Get out of this WebEx and join the one you like
  - Get out there after 15 min to join the plenum again
  - Hope this will be a more entertaining break
  - Of course you can also take a proper break

312 participants by country



Profession of participants



Institutional backgrounds of participants