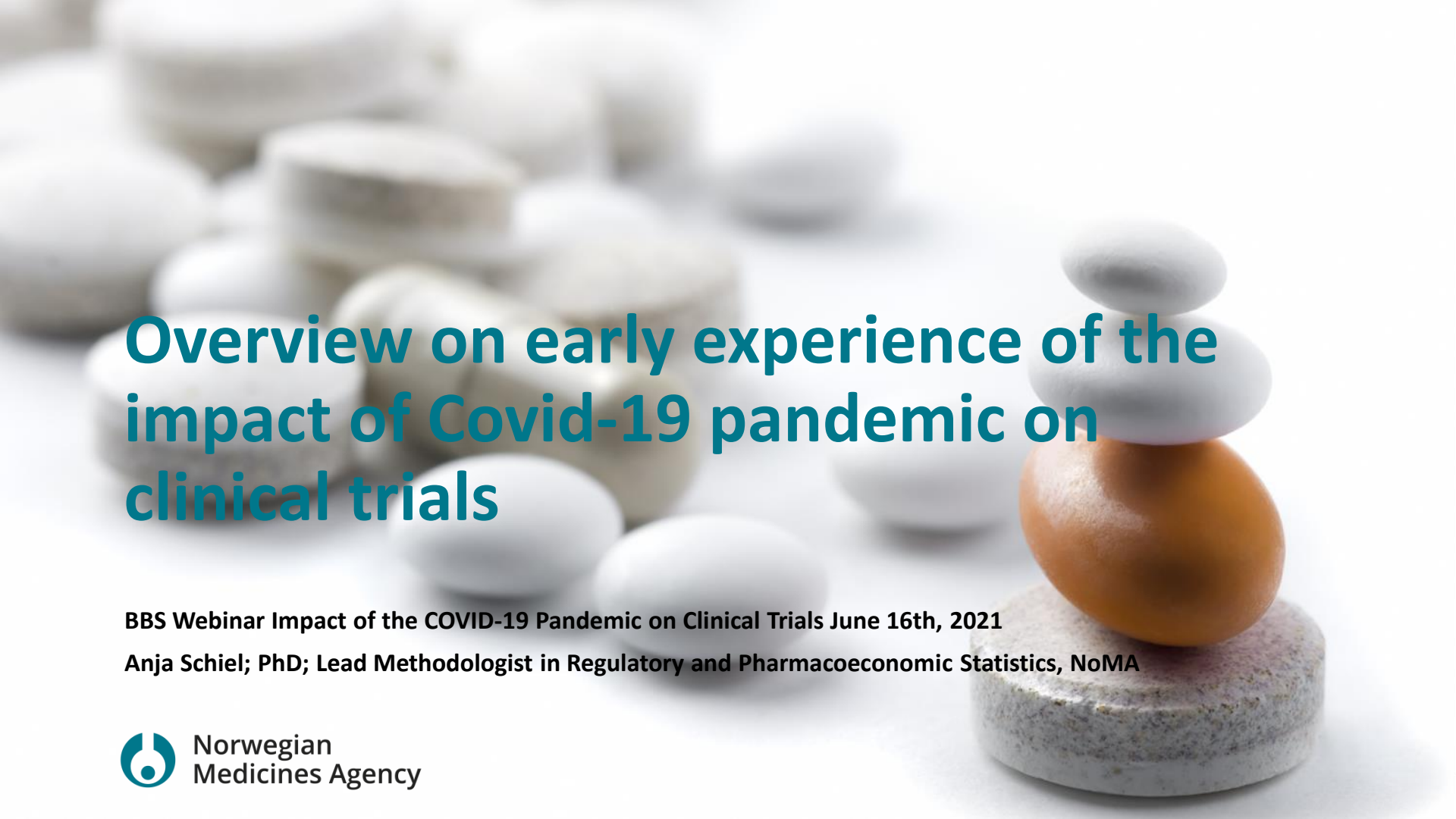

Overview on early experience of the impact of Covid-19 pandemic on clinical trials

BBS Webinar Impact of the COVID-19 Pandemic on Clinical Trials June 16th, 2021

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Norwegian Medicines Agency

- The views expressed in this presentation are personal views and may not be understood or quoted as being made on behalf of or reflecting the position of NoMA or EMA.

Two core documents to consider

EUROPEAN MEDICINES AGENCY
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HMA
Heads of Medicines Agencies

GUIDANCE ON THE MANAGEMENT OF CLINICAL TRIALS DURING THE COVID-19 (CORONAVIRUS) PANDEMIC

Version 4

04/02/2021

Points to consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials

Draft agreed by Biostatistics Working Party	March 2020
Adopted by CHMP for release for consultation	25 March 2020
Start of public consultation	25 March 2020
End of consultation (deadline for comments)	25 April 2020
Update agreed by Biostatistics Working Party	11 June 2020
Adopted by CHMP	26 June 2020

Keywords	COVID-19, ongoing clinical trials, protocol deviations, data collection, trial integrity, interpretability, DMC, Scientific Advice

Roughly three types of requests

- Never waste a good pandemic
  - Termination of studies (just because…)
  - Premature enrolment stopping (impact ignored/unclear)
  - Bring final analysis forward in time -> sometimes substantial reduction in amount of data and maturity
  - Major changes to the design of ongoing studies (with insufficient justification)

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  - Termination of studies (just because…)
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➢ In most cases neither the options described in the ‘Management of trials during COVID’ have sufficiently reflected nor the clear Statement in the BSWP document: *Beyond this, it is an ethical mandate to proceed with a trial that has been started so that the efforts taken by study participants and physicians can benefit drug development and inform patient care.*

➢ What is also missing is an assessment of the probability that the trial still can generate meaningful evidence that would allow assessment of the B/R.

Roughly three types of requests

- Limited changes, often in the direction of remote actions
  - Switch from F2F to remote interview, remote monitoring or remote assessments
  - Exchange of assessment method(s)
  - Potential changes to the statistical analysis plan (case by case)
  - Minor adjustments to ongoing studies (case by case)

Roughly three types of requests

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  - ➢ Elements of remote trial designs are tested due to necessity (not a bad thing)
  - ➢ Mostly covered by the two main documents, still a steep learning curve

Roughly three types of requests

- The Estimand discussion

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 June 2020
EMA/318376/2020
Human Medicines Division

Draft responses to stakeholder comments on the Points to consider on the impact of COVID-19 on methodological aspects of ongoing clinical trials

Very limited experience at SAWP

- Maybe 5 submissions until now that tried to address the issue
- Only one in which we started a true discussion on the role of the Estimand (or more precisely a potential change in the estimand)

➢ *It is not possible to provide detailed advice on how to handle COVID-19 related impact on methodological aspects (e.g. on endpoints, analysis method, handling of missing values, intercurrent events and strategies to handle them) as this will be different for each trial. However, Sponsors are encouraged to carefully reflect how certain COVID-19 might impact their trial and should seek advice to discuss the need for potential changes to the protocol or analysis plan. The estimand framework might prove helpful to discuss the implications of COVID-19 measures on ongoing trials.*

The 5 attributes

- Population
  - Impact of COVID is probably very indication dependent
- Treatment
  - Can be affected, more prominent in infected participants, but not only
- Variable
  - Endpoints might simply not be collectable, but mostly just more difficult
- ICE’s
  - As always, the most complex issue of them all
- Summary measure
  - Maybe not the biggest problem?

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