To: 5.1.2e 5.1.2e

Cc: 5.1.2e 5.1.2e 6.1.2e @rivm.nl]

From: 5.1.2e 5.1.2e

Sent: Thur 1/14/2021 3:14:53 PM Subject: IIV protocol overview_@v4

Received: Thur 1/14/2021 3:14:54 PM

IIV protocol overview @v4.docx

Hi 5.1.2e and 5.1.2e

You both emailed me this week and I owe you both a reply, so I am combining this in one email .

As you know the IIV 'paraplu protocol' is underway but there are many questions still open. In today's kernteam / iMT meeting we proposed to have both an extra timepoint for innate sampling following the first dose of vaccination, as well as collect faeces for microbiome analyses – both would be in a subset of the participants.

However there are questions still unanswered to see if and how these fit best with this protocol or would best be answered in another study. Would you both be so kind as to join in next covid kernteam meeting this Monday? An invite will be sent to you by 5.1.2e / 5.1.2e

Important questions to be answered for feasibility are:

- · Optimal timepoint(s) for sampling and timewindow?
- Sample size required / power for meaningful analyses?
- Variation to be expected for different vaccine concepts (eg would an RNA vaccine require innate sampling at day 2 but vector based vaccines at day 5)?

If you are unable to join, you can send more info to me and I will do my best to voice your thoughts � However, since you are both the experts, it would be incredibly helpful if you could join this Monday.

In attachment a rough overview of the trial (you can see many open ends still) for your background information. Please let me know if anything is unclear!

Regards,