To: (10)(2e) (10)(2e) @sanofi.com]; (10)(2e) /FR[(10)(2e) @sanofi.com]; (10)(2e), (10)(2e) [(10)(2e) @umcutrecht.nl]; (10)(2e) [(10)(2e) @rivm.nl]; (10)(2e) @imperial.ac.uk'[(10)(2e) @imperial.ac.uk]; (10)(2e) @gsk.com'[(10)(2e) @gsk.com]
Cc: (10)(2e) [(10)(2e) @rivm.nl]; (10)(2e) [(10)(2e) @rivm.nl]; (10)(2e) [(10)(2e) @rivm.nl]; (10)(2e) [(10)(2e) @rivm.nl]; (10)(2e) [(10)(2e) @rivm.nl]
From: (10)(2e)
Sent: Fri 9/11/2020 8:02:48 AM
Subject: Re: PROMISE serology proposal and funding for RIVM
Received: Fri 9/11/2020 8:04:55 AM

Dear all,
I am not sure if everyone is aware of timelines but **there is an urgency to sorting out WP4 as we have just over two weeks to go until proposal submission**. A final draft of the full proposal will be shared with all partners on 18th and all changes therefore need to be finalised by 15th Sept. After 15th no major changes should be made. You will appreciate any changes in the proposal at this late stage is very likely to introduce errors as objectives and task descriptions are not merely limited to WP fiches but are referenced repeatedly throughout the proposal and puts the entire proposal we have all worked so hard on at risk.
So please can WP4 academic and EFPIA leads sort this out ASAP?
Thank you for your kind understanding.
(10)(2e)

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Usher Institute website: http://www.ed.ac.uk/usher

THE UNIVERSITY of EDINBURGH | usher institute

Athena SWAN Silver Award Edinburgh Infectious Diseases

Please excuse any inadvertent inconsistencies as speech recognition software has been used

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From: (10)(2e) (10)(2e) @sanofi.com>
Date: Friday, 11 September 2020 at 08:36
To: " (10)(2e) /FR" < (10)(2e) @sanofi.com>, " (10)(2e) " < (10)(2e) @umcutrecht.nl>, (10)(2e) < (10)(2e) @rivm.nl>, " (10)(2e) @imperial.ac.uk'" < (10)(2e) @imperial.ac.uk>, " (10)(2e) @gsk.com'" < (10)(2e) @gsk.com>

Cc: (10)(2e) < (10)(2e) @ed.ac.uk>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>
Subject: Re: PROMISE serology proposal and funding for RIVM

Dear all,

Thank you for sharing this proposal with me.
Our main interest is in section D of your proposal and I think it is the piece that fits the most our mandate to expand on RESCEU findings. I think pentaplex testing of samples from infants with known RSV infection status will allow to confirm your previous work and I'm glad you are interested in continuing the work.
On this point, I think the relevance of T4.3.1 hinges on the possibility of generating additional data (i.e., neutralizing Ab titers). Are sera samples still available for this purpose? Otherwise I would propose removing the modeling of Pienter data as I'm not convinced of the added value to the work you already did under RESCEU (JID paper in press). If you could get back to me on this by Monday so we can finalize the T4.3 piece, I would greatly appreciate it.

I understand section C may be of importance in the context of the PROMISE WP3 study but I think the interest for biomarker discovery/confirmation may be limited due to some specificities of the study design (i.e., sampling timepoints). I would suggest fitting it under WP3 activities – (10)(2e) does that make sense to you?

Finally, regarding sections A & B, while I fully agree the subject is relevant and the PiCo study even though not optimally designed for this purpose could start answering some questions, it would not fit under T4.3 objectives, but maybe would be better suited to an additional T4.4, budget permitting.

A few more technical comments:
(A) & (B) I'm not sure whether you are planning on testing ARI episodes for RSV, but I would strongly caution against relying on RSV serology alone to identify RSV (re)infections, especially in certain subpopulations. Indeed, we observed in the RESCEU older adult study that out of the 59 cases identified by PCR/POCT or serology (4 fold rise in preF and/or postF and/or neut titers), about one third (20) were identified solely by PCR following an ARI and didn't meet the serology criteria.
I agree with the risk you identified of COVID-19 protective measures impacting RSV incidence in the upcoming season, and we should keep in mind that this may make it impossible to collect enough observations to draw meaningful conclusions.

(C) Could you help me understand how you plan on contrasting the 2 timepoints? Would the acute sample be used as "pre" and convalescent as "post"? There are many potential caveats to this, some of which may be addressed by protocol design.

Apologies for the long email, but it is a rich proposal and I wanted to make sure I gave relevant feedback.

Let me know how you would like to proceed,

(10)(2e)

From: "(10)(2e) /FR" < (10)(2e) @sanofi.com>
Date: Thursday, September 10, 2020 at 11:41 AM
To: "(10)(2e) ." < (10)(2e) @umcutrecht.nl>, (10)(2e) < (10)(2e) @rivm.nl>, "(10)(2e) @imperial.ac.uk'" < (10)(2e) @imperial.ac.uk>, "(10)(2e) @gsk.com'" < (10)(2e) @gsk.com>, (10)(2e) < (10)(2e) @sanofi.com>
Cc: (10)(2e) < (10)(2e) @ed.ac.uk>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>, (10)(2e) < (10)(2e) @rivm.nl>
Subject: RE: PROMISE serology proposal and funding for RIVM

Dear all,

Thank you very much for this information.
I copy here (10)(2e) as she is our expert on this field.

I support also the proposal discussion, that should be done in perspective with Task 4. 3 ongoing discussion as I think the task is not yet fully finalized.

Best regards
(10)(2e)

De : (10)(2e) . <(10)(2e)@umcutrecht.nl>
Envoyé : mercredi 9 septembre 2020 10:48
À : (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) @imperial.ac.uk' < (10)(2e) @imperial.ac.uk>; (10)(2e) @gsk.com' < (10)(2e) @gsk.com>
Cc : (10)(2e) < (10)(2e) @ed.ac.uk>; (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) /FR < (10)(2e) @sanofi.com>
Objet : [EXTERNAL] RE: PROMISE serology proposal and funding for RIVM

EXTERNAL : Real sender is (10)(2e)@umcutrecht.nl

Dear WP4 leaders, cc (10)(2e)

I support discussing the proposal within WP4 leadership as the objectives fit the PROMISE scope and these studies would further the use of the pentaplex. Of course, I also realize we have budget limitations, but I support a thorough evaluation of Rob's proposal.

Yours, (10)(2e)

Van: (10)(2e) < (10)(2e) @rivm.nl>
Verzonden: dinsdag 8 september 2020 16:37
Aan: (10)(2e) @imperial.ac.uk' < (10)(2e) @imperial.ac.uk>; (10)(2e) @gsk.com' < (10)(2e) @gsk.com>
CC: (10)(2e) . <(10)(2e)@umcutrecht.nl>; (10)(2e) < (10)(2e) @ed.ac.uk>; (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) < (10)(2e) @rivm.nl>; (10)(2e) < (10)(2e) @rivm.nl>
Onderwerp: PROMISE serology proposal and funding for RIVM

Dear (10)(2e)

Attached you will find a revision of a concept proposal for PROMISE.
Louis Bont has probably introduced this concept during a previous meeting with you.

Let me briefly introduce myself, I am a senior scientist at the RIVM vaccine and immunology department of RIVM, and the successor of (10)(2e), who, together with (10)(2e), has previously developed the RSV serology for RESCUE, but has just retired. I have been mostly involved in research on humoral and cellular responses on measles, mumps and influenza. Our recent achievement has been the development and publication of an accurate multiplex assay for COVID-19 based on RSV experience, which meets all requirements for population surosurveys and studies into the immunobiology of COVID- 19 and future evaluation of vaccine candidates.

Now I had to find my way in RSV and PROMISE. From (10)(2e) I got insight into the WP1/WP2 workpackages, but this is another trajectory than the one for RSV biomarkers and serology (WP3/4). Now Louis Bont previously gave me some guidance here, yet it is not clear whether we can become a true partner again in PROMISE. I understand that we cannot obtain budget from the WP1/2 programme as this has already been planned and cannot be downscaled anymore.

Now Charlotte Vernhes from Sanofi has shown great interest in our pentaplex assay, and wrote a proposal with a request to support their study. Louis Bont showed similar interest with respect to mucosal versus serum response. Now I understand the limitations of the PROMISE budget, but we need a basic project and funding to be able to also carry out investigations for PROMISE partners.

Therefore, I would like to discuss with you the concept of the project proposal, and see where we can meet. In case of conflicts of interest or scientific overlap, please let me know.
Also, I have changed the previous concept and budget request a little less ambitious, as we do feel there are risks involved in engaging a very large Pienter/Pico cohort for the study as outlined under A and B, as we cannot predict serodynamics of RSV infections on beforehand across different age groups, and possible changes in the RSV epidemiology related to COVID-19 distancing measures.
That's why we have restricted the survey to an analysis of the first 1000, as to provide serological proof of RSV (re-) infection first.
I hope this is sufficient basis to discuss the opportunities within your team as to support our research initiatives.

Hope to hear from you,

(10)(2e)
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