Appendix One to Rebuttal of Health Feedback Review of Rosemary Frei and Patrick Corbett's July 2 *Off-Guardian* Article on Dr. Stoian Alexov's Bombshell Revelations

Rosemary Frei

Details supporting information in the section on Error #2. *Health Feedback* says it's false that no monoclonal antibodies for the novel coronavirus exist. They cite five references to back up that assertion.

In this appendix I show that none of those five papers describes monoclonal antibodies specific to SARS-CoV-2. Instead, the papers either use monoclonal or polyclonal antibodies to SARS-CoV (References 1, 2 and 10), make no mention of monoclonal antibodies at all (Reference 4), or do not provide evidence that the commercial antibody-based tests they used to detect SARS-CoV-2 either are specific for the novel coronavirus alone or are accurate (Reference 3).

Reference 1 – published in *Nature* on May 18, 2020 – Pinto D et al. Cross-neutralization of SARS-CoV-2 by a human monoclonal SARS-CoV antibody.
- Most of the paper's authors are with Vir Biotech, a company that develops monoclonal antibodies (mAbs).
Therefore it's likely that this study is just like all those funded by industry – in other words, it is highly unlikely to be credible. I know this because I was a journalist for medical trade publications for 22 years and finally quit in 2016 because I was really tired of being lied to every time I interviewed medical researchers and clinicians about their papers. They always assured me that their work was unbiased, but I always detected strong manipulation of the methods and results by the papers' funders.
- The paper doesn't have a section on funding/conflicts of interest
- This paper is about the use of SARS mAbs, which the authors claim is 'cross-neutralizing' of SARS-CoV-2. So it doesn't describe a mAb created from antibodies to the novel coronavirus. If anyone could create a novel-coronavirus-specific mAb (and I agree with Dr. Alexov that the evidence indicates it has not yet been created) it would by definition be specific to the novel coronavirus *and only to the novel coronavirus*.
- They write, 'Here we describe several monoclonal antibodies that target the S glycoprotein of SARS-CoV-2, which we identified from memory B cells of an individual who was infected with severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003.'
- And, 'Eight out of the twenty-five mAbs bound to CHO cells that express SARS-CoV-2 S glycoprotein or SARS-CoV S glycoprotein.' And, 'S309 bound the most to the novel coronavirus.' And 'Furthermore, S309 contact residues [i.e., the amino acids of the virus that are contacted /bound by the antibody] are highly conserved across human and animal isolates of clade 1, 2 and 3 sarbecoviruses[39] (Extended Data Fig. 7c).' Collectively, our data suggest that S309 could neutralize potentially all SARS-CoV-2 isolates known to be circulating to date, and possibly many other zoonotic sarbecoviruses.' So they're saying themselves that this mAb is not at all specific to the novel coronavirus.
- So this indicates the mAbs aren't specific to SARS-CoV-2.

Reference 2 – published in *Nature* on May 4, 2020 – Wang C et al. A human monoclonal antibody blocking SARS-CoV-2 infection.

- "Competing interests: A patent application has been filed on 12 March 2020 on monoclonal antibodies targeting SARS-CoV-2 (United Kingdom patent application no. 2003632.3; patent applicants: Utrecht University, Erasmus Medical Center and Harbour BioMed). F.G., D.D., and R.v.H. are non-substantial interest shareholders in Harbour Biomed and were part of the team that generated the mice."

- The paper describes mAbs derived from SARS patients' plasma. So they are cross-neutralizing mAbs – i.e., not specific to the novel coronavirus. This is shown by this sentence for example: "The human 47D11 antibody **binds to cells expressing the full-length spike proteins of SARS-CoV and SARS-CoV-2."**

Reference 3 – published in *The Lancet* July 6, 2020 – Pollán M et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study.
- It's a study of the presence of antibodies in 61,075 people living in Spain using two tests.
- Here's the paper's description of one of the tests: "The point-of-care test (Orient Gene Biotech COVID-19 IgG/IgM Rapid Test Cassette; Zhejiang Orient Gene Biotech, Zhejiang, China; reference GCCOV-402a) was a lateral-flow immunochromatographic assay for qualitative differentiation between IgG and IgM against the receptor binding domain of SARS-CoV-2 spike (S) protein, 17"
- These are the detailed instructions for using this antibody test. Here's the part the instructions that describes how it works: "The burgundy colored conjugate pad contains colloidal gold conjugated to recombinant COVID-19 antigens (SARS-CoV-2 Spike S1 antigen. When a specimen followed by assay buffer is added to the sample well, IgM &/or IgG antibodies if present, will bind to COVID-19 conjugates making an antigen antibodies complex."
- That's it. There's no information or evidence showing whether this Spike S1 antigen is unique to SARS-CoV-2 and whether, if IgM or IgG antibodies in subjects' blood bind to the SARS-CoV-2 Spike 1 antigen, they are specific only to SARS-CoV-2.
- Note also that the instructions come with this warning: "**False positive results for COVID-19 IgG/IgM Rapid Test Cassette (Whole Blood/Serum/Plasma) may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Due to the risk of false positive results, confirmation of positive results should be considered using second, different IgG or IgM assay.**" That's not exactly reassuring that this test actually does what it's supposed to.
- The second test used in the paper is a chemiluminescent microparticle immunoassay for qualitative detection of IgG against SARS-CoV-2 nucleoprotein (SARS-CoV-2 IgG for use with ARCHITECT; Abbott Laboratories, Abbott Park, IL, USA; reference 06R8620). **The information about the test on the Abbott website doesn't include how the test was developed and therefore whether it is based on antibodies specific to the novel coronavirus or just antibodies specific to all SARS viruses, or even to all coronaviruses.**
- The product insert (https://www.fda.gov/media/137383/download) doesn't show any tests for cross-reactivity by the mAbs to SARS-CoV (see page 6 of the product insert).
- There's also no information on determination of the tests' sensitivity and specificity. Plus none of the information about the two tests appears to have been independently verified.

Reference 4 – posted on MedRxiv.org ('The preprint server for health sciences') on July 1, 2020 -- Mulligan MJ et al. Phase 1/2 Study to Describe the Safety and Immunogenicity of a COVID-19 RNA Vaccine Candidate (BNT162b1) in Adults 18 to 55 Years of Age: Interim Report.
- The full paper is here.
At the top of the paper it says that it has not been peer-reviewed

The paper doesn't mention monoclonal antibodies even once.

I could stop right there, but I thought I'd have fun by showing you how Swiss-cheesy this paper is.

- "**Competing Interest Statement: Competing interests NK, JA, AG, SL, RB, KS, PL, KK, WK, DC, KT, PRD, WG, and KUJ are employees of Pfizer and may hold stock options. US and ÖT are stock owners, management board members, and employees at BioNTech SE (Mainz, Germany) and are inventors on patents and patent applications related to RNA technology. MJM, KL, KN, EW, AF, RF, and VR received compensation from Pfizer for their role as study investigators. CFG and PYS received compensation from Pfizer to perform the neutralization assay.**"
- "Funding Statement: Role of the funding source: **BioNTech is the Sponsor of the study. Pfizer was responsible for the design, data collection, data analysis, data interpretation, and writing of the report.** The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit the data for publication. All study data were available to all authors."
- The mRNA vaccine that they were testing encodes trimerized SARS-CoV-2 spike glycoprotein receptor-binding domain (RBD). **That's it. There's no information or evidence showing whether this spike antigen is unique to SARS-CoV-2.**

While I'm at it, I'll note that there's also nothing in this paper indicating that novel-coronavirus-specific antibodies or monoclonal antibodies exist. The paper hinges on the binding to the spike glycoprotein receptor-binding domain of antibodies from subjects' blood that are specific to that domain.

- Here's the nub of the paper relating to that (it's on page 12 of the full paper): "In the RBD-binding IgG assay, a recombinant SARS-CoV-2 RBD containing a C-terminal AvitagTM (Acro Biosystems) was bound to streptavidin-coated Luminex microspheres. Bound human anti-RBD antibodies were detected with a R-Phycoerythrin-conjugated goat anti-human polyclonal secondary antibody (Jackson Labs)."
- **But it says nothing about how they verified that these "bound human anti-RBD antibodies" were specific for the novel coronavirus. Information about this is absolutely necessary for anyone to be able to objectively evaluate this paper.**

Reference 10 -- published in *JCI Insight* on May 7, 2020 – Liu J et al. Molecular detection of SARS-CoV-2 in formalin-fixed, paraffin-embedded specimens. Cross-neutralization of SARS-CoV-2 by a human monoclonal SARS-CoV antibody.

The authors write that they used a rabbit anti-SARS-CoV spike-protein antibody and a mouse monoclonal anti-SARS-CoV nucleocapsid protein antibody for cross-detection of the respective SARS-CoV-2 proteins by immunohistochemistry and immunofluorescence. Therefore they did not use monoclonal antibodies specific to SARS-CoV-2 and only specific to SARS-CoV-2.