Response to „Incorrect use of data..” by Prof. Dr. Eugène van Puijenbroek”

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We are grateful to Prof. van Puijenbroek for raising his concerns. This starts a long-overdue debate on how to gauge the safety of COVID-19 vaccines. We would like to remind Prof. van Puijenbroek and all readers: These vaccines have had an emergency approval *without* the *necessary* safety data. Although we would agree with Prof. van Puijenbroek that the self-reporting system of side-effects for vaccines and other drugs is far from foolproof, it is the only data we have. So why should it not be put to use?

It is interesting to note that Prof. Puijenbroek, in his concern, describes the Lareb-ADR data as “spontaneous reporting”. In a statement in Regulatory Science 2021 (https://www.regulatoryscience.nl/editions/2021/12/prof.-dr.-eugene-van-puijenbroek-on-the-nature-of-signals; accessed 29th June 2021) he says:

> “The Netherlands Pharmacovigilance Centre Lareb collected 34.000 reports of adverse drug reactions in 2019, of which 14.000 reports are submitted directly to Lareb by *healthcare professionals* and patients and more than 20.000 were forwarded by the *marketing authorisation holders*. These reports are assessed and analysed, which may lead to safety signals about adverse drug reactions. These are reported to and reviewed by the Medicines Evaluation Board (MEB), supporting the MEB in its decisions in pharmacovigilance in the Netherlands and Europe.” (typos and grammatical errors removed, else identical with webquote at the end of the article)

So, what is really true and what should we go by: Is it true that roughly 60% of the adverse drug reaction (ADR)-data come from market authorization holders, who, by law, are required to report, and is it true that the data are reviewed, as stated on the website and in this article, or are these informations only true in all other cases but not in the case of COVID-19 vaccines? It would be good to have clarity on this point. We assumed that what Lareb says about all other ADR reports is also true of COVID-19 ADR reports. If we were mistaken in this assumption, perhaps Lareb should clearly state: “ADR reports are reviewed and evaluated in all cases of ADR reports, but not with COVID-19 vaccines.” And, ideally, it should also give a reason, why this is so, if it is so.

Ideally the consequence of this debate is that someone sets up a systematic observational post-marketing surveillance study in a large number of vaccinated persons under public scrutiny to really document the side-effects that can be causally related to the vaccine. Currently we only have association, we agree, and we never said anything else. But the same is true with fatalities as consequences of SARS-CoV2-infections. The cases that are counted here as deaths are rarely vetted by autopsy or second opinion, but still counted as deaths due to COVID-19. And it is exactly this allegedly high number of COVID-19 related deaths that gave rise to an unprecedented sloppy regulation process

that allowed new types of vaccines using a mechanism never before tested in humans to be widely distributed in the population. Prof. Puijenbroek basically argues that the largest vaccination experiment in the history of medicine cannot be assessed for safety and unforeseeable toxicities, because we should not use the ADR data for such inferences. In contrast, we argue that it is mandatory that those data which are at hand are used to gauge the safety, and this is what we have done.

We are happy to admit that these data are far from perfect. But we repeat: they are the only ones that are available.

We quoted LAREB itself which states on its website at the time we checked the data: "*All reports received are checked for completeness and possible ambiguities. If necessary, additional information is requested from the reporting party and/or the treating doctor. If necessary, additional information is requested from the reporting party and/or the treating doctor. The report is entered into the database with all the necessary information. Side effects are coded according to the applicable (international) standards. Subsequently an individual assessment of the report is made. The reports are forwarded to the European database (Eudravigilance) and the database of the WHO Collaborating Centre for International Drug Monitoring in Uppsala. The registration holders are informed about the reports concerning their product*.").

We took this statement to mean that those reports that are obviously without any foundation are taken out such that the final data-base is at least reliable to some degree. Would it not be like that, why else would one want to collect these data and make them public in the first place?

We are happy to concede that the data we used – the large Israeli field study to gauge the number needed to vaccinate and the LAREB data to estimate side-effects and harms – are far from perfect, and we said so in our paper. But we did not use them incorrectly. We used imperfect data correctly. We are not responsible for the validity and correctness of the data, but for the correctness of the analysis. We contend that our analysis was correct. We agree with LAREB that their data is not good enough. But this is not our fault, nor can one deduce incorrect use of data or incorrect analysis.

And we hope that this stimulates governments or university consortia to collect valid data to prove us wrong. We would be the first to be happy about that. But the challenge is out: Prove that the vaccines are safe! No one has done so. We say they are not and we used the best data currently at hand. Our usage was correct. If the data were not, whose fault is this?