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Did Pfizer Fail to Perform Industry Standard Animal Testing Prior to Initiation of mRNA Clinical Trials?

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TrialSite has learned of material information regarding mRNA vaccine safety revealed by a freedom of information act (FOIA) request filed by a group of Canadian physicians. These doctors have become concerned about COVID-19 mRNA vaccine safety. This new safety information involves the Pfizer mRNA-based vaccine known as BNT162b2 or "Comirnaty."

The FOIA documents reveal animal study results demonstrating that the Pfizer mRNA-based vaccine does not remain at the injection site, but rather appears to spread widely after injection.

According to the documents, pre-clinical studies show that the active part of the vaccine (mRNA-lipid nanoparticles), which produce the spike protein, spreads throughout the body and is then concentrated in various organs, including the ovaries and spleen.

The FOIA-produced data sets are incomplete, so the full meaning of these data cannot be determined at this time. TrialSite has also learned via regulatory documents that apparently (at least in their European Medicines Agency submission), Pfizer did not follow industry-standard quality management practices during preclinical toxicology studies during vaccines, as key studies did not meet good laboratory practice (GLP). The full panel of industry-standard reproductive toxicity and genotoxicity studies were apparently also not performed. But does this matter in light of the risk-benefit analysis associated with regulatory emergency use authorization (EUA)?

Recently, there has been speculation regarding potential safety signals associated with COVID-19 mRNA vaccines. Many different unusual, prolonged, or delayed reactions have been reported, and often these are more pronounced after the second shot. Women have reported changes in menstruation after taking mRNA vaccines. Problems with blood clotting (coagulation) – which are also common during COVID-19 disease – are also reported.

Among the most critical tests, which must be performed prior to testing any drug or vaccines in a human being, is whether it can cause mutations in the DNA (genotoxicity), or whether it could cause problems with cells or tissues of the reproductive tract – including ovaries (reproductive toxicity). In the case of the Pfizer COVID mRNA vaccine, these newly

revealed documents raise additional questions about both the genotoxicity and reproductive toxicity risks of this product. Standard studies designed to assess these risks were not performed in compliance with accepted empirical research standards. Furthermore, in key studies designed to test whether the vaccine remains near the injection site or travels throughout the body, Pfizer did not even use the commercial vaccine (BNT162b2) but instead relied on a "surrogate" mRNA producing the luciferase protein.

These new disclosures seem to indicate that the U.S. and other governments are conducting a massive vaccination program with an incompletely characterized experimental vaccine.

It is certainly understandable why the vaccine was rushed into use as an experimental product under emergency use authority, but these new findings suggest that routine quality testing issues were overlooked in the rush to authorize use.

People are now receiving injections with an mRNA gene therapy-based vaccine, which produces the SARS-CoV-2 spike protein in their cells, and the vaccine may be also delivering the mRNA and producing spike protein in unintended organs and tissues (which may include ovaries). Unfortunately, there is no way to know if this is related to vaccine safety signals or reports of menstrual irregularities; the required studies were either not done or not done properly.

How mRNA Vaccines are Believed to Work

The current mRNA vaccines are theorized to act locally in draining lymphoid tissue. Formulated lipid nanoparticles that contain mRNA able to produce the spike protein are syringe injected into a muscle such as the deltoid (shoulder muscle). Once the injection occurs, the muscle cells near the injection site are impacted by the mRNA-based vaccine (e.g. the lipid nanoparticles), while much of the dose moves into the intracellular fluid surrounding the muscle cells and consequently drains to lymph nodes (see for example here).

According to this theory, a properly functioning mRNA-based vaccine is delivered into and drives production of the SARS-CoV-2 Spike protein in muscle and lymph node cells. The cells then produce the Spike protein, which is then moved to the surface of these cells where it becomes attached.

The foreign virus Spike protein then triggers the immune system to recognize and attack any cell in the body that is either infected by SARS-CoV-2 or has Spike protein on its surface. The vaccine was designed so that the Spike protein is affixed via a transmembrane anchor region, so that it cannot circulate around the body via the bloodstream (see here). The same general scenario applies to all mRNA-based vaccines as well as recombinant adenoviral vectored vaccines (such as the J&J vaccine) designed to use gene-therapy technology to express Spike protein in cells and tissues. This general strategy is designed to reduce the risk that any residual vaccine dose that does somehow end up in the bloodstream (or organs and tissues) ends up not being a safety risk due to unintended biologic effects. Spike protein will remain affixed to cell surfaces, and therefore is not released into the blood where circulating Spike might cause problems by binding to its natural target, ACE-2 receptors. However, any cell that has Spike protein (or protein fragments) anchored on its membrane or displayed on MHC antigen-presenting molecules becomes a target for vaccine-activated immune cells and antibodies, which would then attack, damage or kill those cells in the same way that SARS-CoV-2 virus-infected cells would be attacked. In other

words, if very active mRNA delivery particles or recombinant adenoviral-vectored vaccines spread throughout the body, the resulting production of the vaccine antigen (Spike, in this case) will both stimulate immunity and also cause those same cells to be attacked by the immune system. If this actually happens, the resulting "vaccine reactogenicity" could resemble clinical symptoms seen with autoimmune syndromes.

EMA Pfizer/BioNTech Vaccine Distribution Studies

As standard practice, the European Medicines Agency (EMA) discloses their assessment of investigational new drug (IND) submissions. In the case of the Pfizer-BioNTech "Comirnaty" vaccine, the EMA assessment can be found on the Web here. This document includes a summary of EMAs evaluation of the non-clinical vaccine distribution studies reported to EMA by Pfizer-BioNTech. These studies were carried out using two methods: 1) use of mRNA producing the luciferase protein and 2) use of radioactive label to mark the mRNA (a more sensitive approach). These studies reveal that the majority of radioactivity initially remains near the injection site. However, within hours, a subset of the stabilized mRNA-containing particles become widely distributed throughout the bodies of test animals.

Upon inspection of the EMA summary document, *TrialSite* found evidence suggesting that the issue of biodistribution and pharmacokinetics of the "Comirnaty" BNT162b2 vaccine was not thoroughly examined in accordance with industry norms prior to the EMA review of the BNT162b2 IND/CTD. The reviewers share an explicit admission that "*No traditional pharmacokinetic or biodistribution studies have been performed with the vaccine candidate BNT162b2*." Rapporteur (Filip Josephson) and Co-Rapporteur (Jean-Michael Race) suggest, however, that Pfizer used "a qualified LC-MS/MS method to support quantitation of the two novel LNP excipients" and suggest that "the bioanalysis methods appear to be adequately characterized and validated for use in the GLP studies." However, the studies that were performed and submitted were non-GLP. Additionally, the EMA document states "Biodistribution: Several literature reports indicate that LNP-formulated RNAs can distribute rather nonspecifically to several organs such as spleen, heart, kidney, lung and brain. In line with this, results from the newly transmitted study 185350, indicate a broader biodistribution pattern." This EMA observation corresponds with what appears to be a growing number of adverse events and aligns with data *TrialSite* observed via the FOIA showing concentrations of LNP-formulated RNAs in the spleen, for example.

To obtain independent reviews of these EMA regulatory documents, *TrialSite* contacted both Dr. Robert W. Malone, MD, MS, and another expert that wished to remain anonymous, and provided them copies of the EMA analysis and the FOIA documents. Dr. Malone was the original inventor of the mRNA vaccine technology back in the late 1980s. He currently advises several companies in regulatory affairs and clinical development. One of TrialSite's other sources is a senior regulatory specialist who currently serves as the President of a prestigious European association. When asked to review and comment on the EMA assessment, Dr. Malone noted that normal pharmacokinetic and pharmaco-toxicology studies had not been performed before EUA authorization for the product. "I was particularly surprised that the dossier of regulatory documents indicates allowance for use in humans based on non-GLP PK and Tox studies relying on formulations which are significantly different from the final vaccine." After completing a review, *TrialSite's* other source noted the following:

> "A quick review the Toxicology Section (2.3.3) of *The European Medicines Agency (EMA)*

Assessment Report on Comirnaty (COVID-19 mRNA vaccine) issued on 19 February 2021, raises concerns about data applicability of preclinical study findings to clinical use:

> To determine the biodistribution of the LNP-formulated modified mRNA (modRNA), the applicant did study distribution of the modRNA in two different non-GLP studies, in mice and rats, and determined the biodistribution of a surrogate luciferase modRNA.
>
> Thus, one might question the validity and applicability of non-GLP studies conducted using a variant of the subject mRNA vaccine.
>
> In addition, no genotoxicity data were provided to EMA."

Based on the FOIA documents, the biodistribution results (which are not disclosed in the public EMA summary document) suggest that the delivery technology results in mRNA delivery and significant concentration of the delivery lipids in ovaries, spleen, and other tissues and organs.

Urgent Emergency?

The discovery and review of the biodistribution and pharmacokinetics data obtained by the FOIA request underscores the reservations disclosed in the public EMA assessment. Although not performed to industry GLP standards, these results seem to indicate that lipid/mRNA nanoparticles, which code for the Spike protein, circulate throughout the body and then collect in a variety of organs and tissues, including the spleen and ovaries. This means that the vaccine is not remaining localized near the injection site and draining lymph nodes, but rather is also circulating in both blood and lymph and is subsequently concentrating in important organs. If this results in Spike protein being produced in unintended places including the brain, ovaries, and spleen, it may also be causing the immune system to attack these organs and tissues.

What's the Risk?

According to official government accounts, minimal risk is associated with this vaccine when compared to the risks of COVID-19 infection. That's why the U.S. FDA approved the Emergency Use Authorization (EUA) based on a risk-benefit analysis. *TrialSite*, a vaccine proponent, only raises the issue to ensure full disclosure of any material safety implications to our readership, including clinicians, clinical research safety committees, and public health professionals.

While, according to the CDC's VAERS database, over 4,000 deaths have been entered in association with all the vaccines, the US government argues that none of these deaths are formally linked to the jabs. About 291 million people have been vaccinated to date, hence overall reported adverse event risk is low. While it is true that many people are completely unscathed, the discovery of these documents and associated information may alter the risk-benefit assessment underlying the EUA decision.

TrialSite is aware that one must be particularly cautious about publishing or communicating speculations that might raise skepticism about vaccine use. Should researchers handle findings differently when there is a chance they might frighten the public? Perhaps small, inconclusive, worrying studies should not be published because they could do more harm than good. Dr. Paul Offit, Director of the Vaccine Education Center at the Children's Hospital

of Philadelphia, states: *"Knowing that you're going to scare people, I think you have to have far more data."*

One could argue that even an inconclusive paper can be important, as it can spur the larger, more definitive studies that are needed. It should be "*put out there for the scientific community, to look at it, see it, know about it, refine study design and go and look again*," says Gregory Poland, a renowned Mayo Clinic vaccinologist and the Editor-in-Chief of *Vaccine*. It is crucial, though, for researchers to carefully explain such results in their papers and regulatory filings to prevent misinterpretation or misunderstandings.

Other Relevant New Data

A recent study led by researchers at Brigham and Women's Hospital and the Harvard Medical School measured longitudinal plasma samples collected from 13 recipients of the Moderna vaccine. The manuscript has been accepted for publication by "Clinical Infectious Diseases" and the pre-print is available here. Out of these individuals, 11 revealed detectable levels of SARS-CoV-2 protein as early as day one right after first vaccine injection. The authors considered that to be normal clearance.

Clearance of detectable SARS-CoV-2 protein correlated with production of IgG and IgA. Measured mean S1 peak levels were 68 pg/mL ±21 pg/mL, and mean spike peak level was 62 pg/mL ± 13 pg/mL. Assuming an average adult blood volume of approximately 5 liters, this corresponds to peak levels of approximately 0.3 micrograms of circulating free antigen for a vaccine designed to only express membrane-anchored antigen. For comparison purposes, most influenza vaccines administer a total of about 15 micrograms of HA antigen per influenza strain. Total levels of antigen expressed by the experimental SARS-CoV-2 mRNA vaccines currently administered to patients are not known.

Root Cause Analysis Suggested

A root cause assessment is suggested to better understand if any of this information adjusts or modifies the EUA risk-benefit analysis. *TrialSite* suggests that regulators and pharma manufacturers at least review and assess the risk that foreign mRNA-based spike protein delivery and expression in tissues and organs distal to the actual injection site may be contributing to the unusual reactogenicity and adverse event profile associated with these products. The uptake in vaccination rates has slowed in the United States in part due to vaccine hesitancy. However, such a phenomenon can be overcome with acknowledgment, transparency, and continuous commitment to risk mitigation.

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