Should FDA, and other authorities, approve the SARS-CoV-2/COVID-19 vaccines?
– A scientific perspective

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COVID-19 is a recently labeled infectious disease which is presumably caused by a novel coronavirus labeled as SARS-CoV-2.

It is important to note that COVID-19 is not based on any defined and specific symptoms but common and general flu-like potentially treatable with antibiotic regimens [1]. However, medical experts and regulatory authorities, in particular FDA, have adopted an official position that illness is because of a viral infection caused by SARS-CoV-2. Being a viral disease led to a policy decision that a vaccine is needed for its treatment that is to be developed. The pharmaceutical industry has made great efforts in collaboration with the authorities to develop vaccines quickly. There have been media reports that some vaccines are at a late development stage and ready to be submitted to the FDA for marketing approval.

In general, the FDA approves medicinal products (medicines or drugs) under the mandate of evaluating them for safety, efficacy, and quality. These characteristics are generally assessed based on clinical trials. A clinical trial assesses drugs (including therapeutics and vaccines) in humans to demonstrate their efficacy without having any significant safety or toxicity concerns [2]. For efficacy assessment, a clinical trial's primary goal is to show that a drug is effective (has efficacy) to treat the illness. It means that the clinical trial would require a clearly defined and measurable efficacy (or disease) endpoint. What would be the endpoint in the case of vaccine development for COVID-19? The answer requires a short explanation.

It is a very well-known fact that, at present, the virus which is presumed to be causing the COVID-19 has never been isolated or positively identified. Therefore it cannot be used as an endpoint, i.e., if something is not shown to exist, how it could be killed or removed. Similarly, as the virus is not identified, it cannot be linked to the illness; hence, its specific symptom cannot be used as an endpoint. So, how could a pertinent clinical trial be conducted? And this is the fundamental weakness of modern drug development practices under the current regulatory system. As a result, under the current system, authorities and experts collectively develop some agreed-upon arbitrary criteria which could be used to monitor the illness. The success or failure of clinical trials, hence the development of drugs, is usually based on such "accepted" arbitrary criteria. The development of treatment or vaccine for COVID-19 is following the same path.

It appears that the chosen endpoint for the vaccines' development is the absence of flu-like symptoms supported by PCR tests. Both PCR tests and flu-like symptoms are non-specific and non-quantitative. Therefore, it is unlikely that the suggested endpoints will provide relevant and measurable monitoring of the illness, i.e., COVID-19.

However, authorities/FDA, in collaboration with the pharmaceutical industry, have developed "guidance or standards" for the industry to follow. It must be clear that these guidances and standards lack a link to the actual underlying (analytical) science/chemistry because of the

reasons mentioned above, but are only the FDA's suggested "compliance" criteria. For example, if no flu-like symptoms or negative PCR tests are to be observed in a "vaccine" treated group of volunteers than those of untreated (placebo), then the "vaccine" would be considered efficacious or effective. By way of an analogy, people with no or smaller amount of cash in their wallets would be regarded as low-income workers; in contrast, people with larger money would be viewed as higher-income workers.

Media reports regarding successful vaccine development are based on such criteria, i.e., lower flu-like symptoms and negative PCR test results with vaccine treatment. It could be argued that media reports may be a feeler to get a public reaction, i.e., to see if the public, including medics, to buy into the "developed vaccines" news to proceed with the regulatory approval process. Considering media reports, although they do quip about the subject to regulatory approval, the industry is expecting and planning for certain and swift regulatory approval. In practical terms, the industry's assumptions of vaccines' approval may be correct and valid because they most likely have done the studies following FDA acceptable guidance and criteria.

The next step still, however, would be submitting the clinical studies data to the FDA for formal approval. It is important to note that FDA and other regulatory authorities, as commonly presumed, usually do not have command in scientific expertise of drug development and manufacturing aspects [3]. FDA plays a role of a judge, to make a judgment or declaration, without having practical experience of the situation (science) but by listening to the industry and experts (often assumed independent and unbiased). There is a serious misunderstanding about the scientific capability of the authorities to monitor the scientific aspect. However, to maintain the impression and promotion of its public-safety watchdog status, neutrality, and authority on the subject matter, the FDA occasionally punishes the applicants, including industry, with denial of approvals and/or legal retributions. The authorities protect their authority often with extreme force and persuasive publicity.

Considering this background, let us see the potential outcome scenario of the vaccine approval exercise. From the perspective of meeting the study evaluation and the standards, it is highly unlikely that authorities would have any objection at present. The reasons being: (1) they would have limited, at least internally, expertise to independently and critically evaluate the studies; (2) most likely, the clinical trials would have followed the agreed-upon protocol and endpoints.

However, the safety aspect is usually the primary cause of concern for the authorities, and this is the sledgehammer authorities generally use to maintain and implement their authority. In this regard, developed vaccines may have considerable weakness because of the rush and lack of appropriate (animal and long-term human) studies, i.e., poor safety and toxicity assessment. Lack of such studies typically would be considered criminal negligence. Approving the vaccine at this stage could be a problematic undertaking of risk on the authorities' side, which authorities would be and should be unwilling to take, in my view. Therefore, authorities may seek some clear and measurable evidence of safety assurance. Also, there is a better understanding now that the virus, and its testing, are not as reliable as previously believed. It should make the authorities extremely cautious in approving the vaccines for a low-risk

illness with the potential of high-risk safety concerns. FDA is or will be in a very tough situation. The way out of this situation would be to resist the approval or delay it by seeking further clarifications and studies.

The delay could be justified with rationales such as; non-specificity of flu-like symptoms as an endpoint; availability of new information on irrelevancy and weakness of the PCR test; non-availability of the actual virus reference standard; lack of appropriate safety/toxicity monitoring, in particular, long term; significantly low death rate than predicted.

So, to the question, "Should FDA, and other authorities, approve the SARS-CoV-2/COVID-19 vaccines?" the answer is a no. It is hoped that the FDA will take this route, avoiding potentially severe detrimental impact on its credibility as a science-based regulatory authority.

On the other hand, as a side note, there is an urgent need to audit scientific expertise and capacity at the authorities, including the FDA, for drug approval practices. It is quite clear that isolation and identification of the virus and the associated disease have not been handled in a scientifically valid manner, which has led to the false declaration of the pandemic. Arguably, there appears to be no need, at least on an urgent basis, for developing a vaccine or any other new therapies for the illness showing mild flu-like symptoms, which could be handled with already developed and available medications. Clinical trials have been conducted without scientifically valid study designs based on vague endpoints, and invalid analytical (PCR) tests that ought to produce useless conclusions and products.

As a suggestion, responding to a currently under review Citizen Petition to FDA [4] would provide an excellent example for critically assessing product evaluation practices at the FDA and authorities worldwide.

References:

[1] http://www.drug-dissolution-testing.com/?p=3548

[2] http://www.drug-dissolution-testing.com/?p=3471

[3] http://www.drug-dissolution-testing.com/?p=3069

[4] http://www.drug-dissolution-testing.com/?p=3113