Don't shortchange public trust in science

The need to address COVID-19 is placing huge demands on biomedical research and regulatory processes. Under pressure, it is essential to uphold high bioethical principles and rigorous standards for the development and approval of medicines.

There is a lot to be said about cutting through red tape, especially when human lives are at risk. However, precisely because of the inherent danger for human life, shortcuts in the development, testing and regulatory approval process for medicines can be extremely risky and ethically questionable. The COVID-19 pandemic has highlighted this paradox more than any other medical crisis in recent memory, as the need for preventative and therapeutic medications continues to push against the cautious and strict procedures that regulate biomedical research and drug development. The pressure on science to speed up has been escalating over the course of the year, and understandably so — the caseload and death toll of COVID-19 is enormous, and the burden it poses on all facets of human life is unprecedented. Nine months into the pandemic, the world is in dire need of some good news on the therapy and vaccine fronts. However, the persistent focus on speed and the dangerous politicization of these biomedical efforts threaten to undercut scientific rigor and to erode public trust in science at a time when they are needed most. At this critical juncture, several recent regulatory approvals in different countries have been met with criticism and doubt.

In August, Russia announced that a vaccine, developed at the Gamaleya Research Institute in Moscow and imaginatively named 'Sputnik V', received domestic regulatory approval under a "conditional registration certificate." Rather than expressing excitement for the registration of the first vaccine against COVID-19, the international science world expressed skepticism and alarm. The urgency of the COVID-19 crisis has led stakeholders to attempt to condense the development and testing of vaccines — a process that typically takes years and necessitates large-scale testing of safety and efficacy — to a year or less. Accelerating the process should not involve bypassing critical steps that may ultimately jeopardize human life and health. However, although large-scale phase 3 clinical trials are reportedly planned for the Sputnik V vaccine, it received approval after undergoing only rapid and small-scale early-phase clinical trials. In fact, the first data on the safety profile and immune responses elicited by this vaccine were published at the time of this writing. This report included findings from two open, non-randomized phase 1/2 studies conducted at two hospitals with a total of 76 participants[1] and is already being scrutinized by the community.

On the heels of this news came the announcement that medical professionals and state employees who were deemed to be in high-risk professions in China had been receiving inoculations of an experimental vaccine developed by Sinopharm's China National Biotec Group Company since July, under an "urgent use" process. In this case also, phase 3 trials are underway, and scientific results about safety and efficacy are shrouded in secrecy. Earlier this summer, China had authorized a different experimental vaccine developed by the Beijing Institute of Biotechnology and CanSino Biologics specifically for military personnel under a "military specially-needed drug approval." Given the paucity of information on these vaccines, questions remain about the risks they might pose for the people receiving them.

In the USA, the Commissioner of the Food and Drug Administration (FDA) recently stated his agency's willingness to approve a vaccine before the completion of phase 3 trials, if benefits outweighed risks. Similar to the Russian "conditional registration certificate" and the "urgent use" protocol in China, the FDA can issue an "emergency use authorization" for medicines before clinical trials are complete, and such authorizations can be revoked if the medicines are deemed harmful or not beneficial. However, the possibility that the FDA might fast-track a vaccine approval came as an additional hit to its already shaken credibility after some key missteps this year. When an emergency use authorization of hydroxychloroquine and chloroquine was issued in March on the basis of limited data, it was welcomed as a major breakthrough by the administration and part of the media, only to be revoked in June when the lack of clinical benefit and serious safety concerns became clear. This was followed by another debacle in August, this time involving the emergency use authorization of convalescent plasma that was announced amid great fanfare at a White House press briefing and was hailed by the FDA as "another achievement in the administration's fight against the pandemic." The criticism by the scientific world, including the COVID-19 Treatment Guidelines Panel of the US National Institutes of Health, was sharp and swift. Critics noted the overall limited and inconclusive evidence to support this decision, the grossly misleading statements at the press briefing on the data in support of the clinical benefits of plasma for patients with COVID-19, and the highly political tone of the announcement. It should also be noted that such emergency measures in the absence of a solid scientific and clinical foundation can delay effective treatment evaluation in the long term, as they may undercut enrollment and completion of phase 3 trials, given that participants would face the possibility of receiving a placebo rather than an already authorized therapy. The FDA commissioner acknowledged through social media that the criticism about the description of convalescent plasma data was justified and has repeatedly defended his agency's decisions and dismissed concerns about political pressure. On the topic of COVID-19 vaccines, he stressed that decisions would be based on science, medicine and data, rather than politics, and committed to a transparent process, noting that an independent group of experts is tasked with advising the FDA after reviewing data on COVID-19 vaccines. Along the same lines, the chief executive officers of nine drug companies have issued a joint pledge to "stand with science" and to submit their candidate vaccines for approval or emergency use authorization only after safety and efficacy have been demonstrated through phase 3 clinical studies compliant with the requirements of expert regulatory authorities such as the FDA.

Such assurances are welcome, especially as vaccines are administered to healthy people as a preventative measure and thus should be held to higher standards with respect to potential risks and the rigor of the testing and approval process. Recent news that global trials of the AstraZeneca

Oxford vaccine — one of the nine vaccine candidates currently in phase 3 clinical studies — have been paused to investigate safety data in light of an unexplained illness in one participant further highlight the importance of conducting rigorous, large-scale studies. In contrast, episodes such as those described above do little to increase public confidence in science and the agencies set to regulate medicines and safeguard public health — confidence that unfortunately is already fragile, as far as vaccines are concerned. In a recent poll, only 49% of Americans surveyed said they would get a COVID-19 vaccine when it becomes available, with 31% saying they were not certain and 20% saying they would not get vaccinated. More reassuringly, a separate survey reported that 68% of respondents were confident that the FDA will approve a COVID-19 vaccine only if it is safe, with 67% saying that they would get a vaccine as soon as one is available. Nevertheless, in the same poll, 83% of those surveyed said they would worry about safety if a vaccine were approved quickly, and 78% thought that the approval process is being driven more by politics than by science. These numbers indicate that there is no room for further missteps.

Public trust in science is paramount during a public health crisis. Thus, it is essential to set aside political rhetoric touting the warp speed of efforts to develop vaccines and therapies, or likening them to the space race. Rather, we must stay the course of safeguarding scientific and bioethical standards through the integrity and dedication of researchers, clinicians and regulatory authorities. ❐

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