Coronavirus pandemic: Public/patients deserve better!

Saeed A. Qureshi, Ph.D. (principal@pharmacomechanics.com)

People should not be surprised to know what has been highlighted for many years. The current regulatory system for product quality assessment practices and the associated facility inspections are neither relevant nor scientifically valid [1-4]. In this regard, the regulatory requirements and practices are the main and biggest hindrance in the availability of pharmaceutical products to patients in a timely manner. The Coronavirus situation has not only highlighted but confirmed the irrelevancy and weakness of the current regulatory system [5]. For example, it has been reported that the FDA has granted permission to a manufacturer of hydroxychloroquine (a suggested treatment for Coronavirus aliment) from an Indian facility which is supposed to be banned from manufacturing and exporting the products to the USA as per US FDA inspection assessment [6]. The US President Trump requested Indian Prime Minister Mr. Modi to facilitate providing needed medicine [7]. In general, regulatory authorities in the USA, along with their external "experts/consultants," maintain a strong judgment against Indians and other nationals regarding the lack of manufacturing of "quality" pharmaceutical products [8].

It is hard to believe and accept that the USA president would allow or request products for its nation while knowingly that the products could be of substandard quality manufactured at substandard facilities. The only logical conclusion is that the FDA practices and facility assessment approaches have been considered weak or false and require reconsideration [9]. On the scientific ground, as has been described in the literature, the regulatory requirements not only do not make logical sense but are also scientifically irrelevant and invalid [10]. This is causing significant difficulties for the manufacturing of pharmaceutical products locally and internationally. Manufacturing could be made relatively easier and straight forward for pharmaceutical products, particularly tablet and capsule, leading to cost-effectiveness and ease of accessibility to the consumers and patients worldwide if they were based on well-established scientific principles. Some suggestions in this regard are: (1) pharmaceutical products should be described and assessed as chemical compounds and their composites; (2) quality of the pharmaceutical products should clearly be defined as their ability to release the drug from the products and established using valid scientific/analytical methods; (3) The methods currently used and required for the assessment of products (such as bioequivalence assessments and drug dissolution testing using USP apparatuses) should immediately be stopped. These methods have never been validated for their intended use (i.e., non-GMP) and provide false assurance about the quality and manufacturing of the products. Simple and scientifically valid available alternatives should be considered on an urgent basis.

Concerning the clinical aspect, denying and restricting access to small molecule product treatment assumes that only vaccines could cure this ailment. Hence wait ("social distancing") is necessary - perhaps the most tragic view or policy and certainly a misunderstood and misguided use of pharmaceutical development science. There are examples of treating viral infections with small

molecule-medicines such as HIV (where no vaccine is available) with small molecule medicine known as AZT (Zidovudine). Waiting for a vaccine could be highly risky, and a vaccine may not be developed in a timely manner or at all, as in the case of HIV [11]. Therefore, small molecule or "regular" drug treatment could provide a potential solution.

One should also keep in mind the clinical studies/trials that, although promoted as scientific or controlled, are often based on trial and error approaches with questionable end point monitoring. It is often impossible to generate sufficient and valid scientific data relating to an ailment, especially on short notice considering uncontrollable patient population variations and their physiological divergence. The suggestion that a vaccine could be developed within 12 to 18 months, with an acceptable long-term safety and efficacy profile, maybe an unreasonable expectation. For example, a bioequivalence assessment is a clinical study required and conducted to establish pharmaceutical products' quality. However, this study or test is based on statistical evaluations requiring some underlying assumptions not fulfilled by the studies' experimental (clinical) part. Therefore, conclusions drawn from such assessments have to be invalid and false. It is to be noted that all generic and innovators' products marketed and approved are based on this flawed (clinical) assessment [12]. Presumably, the test (bioequivalence assessment) has been adopted in haste and has been causing serious delays and exuberant costs, creating a shortage of critical and urgently needed medicines.

Suggesting that hydroxychloroquine, has not gone through "proper clinical trials" specifically for COVID-19 treatment, hence its use is irrational and invalid. With their clinical expertise and experiences, physicians are suggesting this treatment, not some street "snake oil vendors" [13]. Let us consider an analogy to explain the current situation. Suppose some people/physicians feel that drinking green tea provides people with energy, better sleep, and an improved immune system, avoiding seasonal flu episodes. In a current regulatory system, such claims would be treated as illegal because here, a medical claim has been made, i.e., linking green tea with the treatment of an ailment ("flu") without "proper clinical trials" support. Hence, no one, including physicians, would be allowed to suggest or prescribed green tea to anyone for "flu treatment" [14].

On the other hand, considering the acceptable safety profile of green tea as it has been in everyday use for many years, suggesting to patients will automatically become a valid scientific and clinical assessment/study. Indeed, other types of drugs or treatments for addressing flu should continue in parallel as well. Similarly, downplaying or limiting the clinical trial/assessment (in this case, with hydroxychloroquine with a long history of its safe use) does not appear to be based on scientific rationale but some other unexplained reasons.

In short, the unfortunate situation created by this Coronavirus pandemic is providing a serious opportunity for reassessing the current regulatory approaches for pharmaceutical product development as well as their manufacturing. So that in the future, such irrelevant discussion can be avoided, and patients can have access to modern and multiple options to treat ailments. Hopefully, in the future, patients will be treated with well-established products rather than products developed on the fly or with the use of

disposable gowns, masks, washing hands and/or staying home policy. They certainly are not the treatments. Patients expect and deserve something better from us as scientists, physicians, and regulators.

Reference:

1. Qureshi, S., and Sabnum. J. Eur J Pharm Sci. 2001 Jan;12(3):271-6.
2. Baxter, J.L., Kukura, J. & Muzzio, F.J. AAPS J. 2006 Jan 3;7(4)
3. Qureshi, S.A. and McGilvery, I.J. Drug Dev Ind Pharm. 1998, 24(11), 995-1005.
4. Healy AM, McCarthy LG, Gallagher KM and Corrigan OI. J Pharm Pharmacol. 2002, 54(3):441-4.
5. FDA Citizen Petition https://www.regulations.gov/searchResults?rpp=25&po=0&s=(FDA-2018-P-3742)&fp=true&ns=true
6. https://www.pharmacompass.com/radio-compass-blog/hydroxychloroquine-hype-versus-reality
7. Coronavirus task force briefing at the White House, Saturday, April 4, 2020, in Washington, DC @4:00:12 https://www.youtube.com/watch?v=p65Po-G-yBw
8. https://www.npr.org/sections/health-shots/2019/05/16/723545864/the-generic-drugs-youre-taking-may-not-be-as-safe-or-effective-as-you-think
9. http://www.drug-dissolution-testing.com/?p=3069
10. http://www.drug-dissolution-testing.com/?p=3368
11. https://en.wikipedia.org/wiki/Zidovudine
12. http://www.drug-dissolution-testing.com/?p=3037
13. https://www.youtube.com/watch?v=KlmAHSCRIns&feature=youtu.be
14. https://www.lifeextension.com/magazine/2011/8/fda-says-walnuts-are-illegal-drugs