Warp speed for COVID-19 drugs and vaccines - time to re-consider how we use the term 'children'

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Dear Editor,

Two recent papers in your journal recommend pediatric vaccination studies for COVID-19.[1,2] Both emphasize correctly that minors are also affected by COVID-19. Most minors have few clinical symptoms; however some become quite ill and have died. Both papers accept the chronological definition of "children" used inter alia by the American Academy of Pediatrics (AAP),[3] the US Food and Drug Administration (FDA), and the European Medicines Agency (EMA).[4] We would like to note that not all persons <21-years-old (AAP)[3] or <18-years-old (FDA/EMA)[4] are physiologically still children. Adolescents are physiologically mature regarding how they metabolize medications, and even prepubertal children are no longer as immature and vulnerable as preterm and term newborns.[5-7] Despite this fact, "pediatric drug development" demands "pediatric" studies in administratively defined "children" irrespective of the maturity of their body.[5,8] More recently, drug developers have used different age limits for COVID-19 vaccines and drug trials.[9] The Pfizer/BioNTech vaccine has been approved from the 16th birthday, and others from the 18th birthday on. In 94.5% of "pediatric" studies in adolescents the resulting dosing recommendations were identical to adults.[10]

The term "multiple inflammatory syndrome" (MIS) in children ("MIS-C"), anounced by the Centers for Disease Control and Prevention (CDC), has also been applied uncritically. MIS is a late systemic inflammatory response to COVID-19 that can occur at any age. Despite this, the CDC has used two terms for this disorder: one in children ("MIS-C"), and the other in adults ("MIS-A") which is clearly flawed.[9] We agree that vaccinations of minors should start as soon as possible. There is no valid medical reason to deny adolescents vaccination against COVID-19.[9] Additional "pediatric" vaccination studies in adolescents would only confirm the vaccines' efficacy, would be medically pointless, and would therefore be a breach of the declaration of Helsinki. They would also cause unnecessary delay and be a waste of time and resources.

The history of separate approval in administratively labeled "children" is long and complex.[5] In COVID-19, the best pragmatic approach would be to lower the age limit for all vaccines to 12 years, based on our present understanding of the developing human body,[6,7] and initiate vaccinations immediately. In prepubertal children, dose recommendations should be developed by pharmacokinetic calculation, to be confirmed in small post-approval "opportunistic" studies.[5,9] For remdesivir, the FDA recommends pediatric dosing based on body weight down to 3.5kg.[9] The EMA demands separate "pediatric" studies for COVID-19 drugs and vaccines in "pediatric investigation plans" (PIPs).[9] Institutional Review Boards (IRBs)/ ethics committees (ECs) should reject these unnecessary studies. It is time to differentiate between reasonable age classification for administrative purposes and the need to base medical treatment on the physiology of the body, not the legal status.[5,9]

Although this challenge is not limited to drugs and vaccines for COVID-19, the current pandemic might offer the chance to address the underlying challenges immediately.

Conflicts of Interest:

JMGK reports being a shareholder of VeraDermics Inc, outside of the submitted work (no resulting conflicts of interest with the contents of the submitted manuscript). KR reports personal fees from several pharmaceutical companies (consulting pharmaceutical companies on pediatric investigation plans (PIPs). None of these PIP consultations are directly related to the submitted manuscript), outside the submitted work; KR has worked for twenty years in pharmaceutical research & development, and consult since ten years pharmaceutical companies on pediatric aspects of drug development. KR has never received any payments from any pharmaceutical company for scientific publications. TO has worked since April 16, 2021 for Abbvie, outside the submitted work (no conflicts of interest with this publication). PS reports grants from Proveca and personal fees from Kolfarma, outside the submitted work.

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