Ethical Challenges of Advances in Vaccine Delivery Technologies

by ARTHUR L. CAPLAN, KYLE FERGUSON, ANNE WILLIAMSON, and THE ETHICS AND POLICY WORKING GROUP ON NEW VACCINE DELIVERY TECHNOLOGIES

For many decades, the technologies used to administer vaccines have seen little improvement. Arguably, the greatest advances were the disposable syringe in the 1950s and the autodisposable syringe in the 1990s. In another development, bifurcated needles were introduced in the campaign to eliminate smallpox in the 1960s and 1970s, which allowed monitoring of who was vaccinated, as the needle left a small scar on the arm. Yet these advances are far fewer than those for many other medical technologies. A health worker from the 1970s would not be surprised by how vaccines are given today. Although the availability of so many new vaccines—mRNA vaccines; protein-based vaccines; combination vaccines; vaccines against the human papillomavirus, Ebola, and so on—might be a welcome surprise, the tools for delivering them would be familiar.

Yet the current tools for vaccine delivery pose many problems. People are often afraid of large needles and injection-related pain for themselves or their children, which lowers vaccine uptake.[1] Most current vaccines leave no marks or scars, so accurate recordkeeping and constant reminders are needed to establish vaccination status and to achieve completion of multidose regimens. In much of the world, recordkeeping is not reliable, leading to patients' receiving repeat doses that may not be necessary. This repetition increases worry and drives up costs. Meanwhile, there is no certainty that people who missed the first vaccination are identified and protected through subsequent campaigns.[2]

Recent technological advances can address some of these issues. Yet we live in a climate of distrust in science and public institutions,[3] significant disinformation about vaccine safety,[4] and a rise in vaccine hesitancy.[5] No single action will resolve all doubts people have about vaccines, but reviews of strategies to address misinformation and hesitancy about vaccines suggest the importance of introducing new vaccine delivery technologies with the utmost transparency, care, and community involvement.[6] Two emerging technologies, one a skin-patch vaccine and the other a dye, provide excellent examples of vaccine-delivery technologies for which such an approach should be developed and tailored to increase vaccine uptake in the interest of individual and public health.

Skin-patch vaccines consist of a "sticker" covered with microscopic needles. The sticker is pressed onto the skin, which is especially rich in immune cells, providing both painless and effective vaccination.[7] This microarray sticker technology is effective for measles and rubella immunizations.[8] The technology could overcome the anxiety many people have around the much larger needles now used. Other advantages of the technology are that it results in less medical waste, can be produced through 3D printing, and does not require cold-chain transportation and storage, which is a huge hindrance to vaccine access in many low- and middle-income countries (LMICs).[9]

A related new technology, developed by the Langer Lab at the Massachusetts Institute of Technology, is an infrared dye nanocrystal that shows that someone has received a vaccine.[10] The dye fades in about a year, is harmless, and is not visible to the human eye. A handheld infrared scanner or special cell phone can be used to examine people's arms to ascertain who has been vaccinated without the need for unreliable paper-based vaccine cards, external finger markings that easily wear off, or other inadequate means of tracking individual vaccination status.

From the ethical point of view, there are clear benefits to this dye technology. First, the dye does not pose any significant risk. It is made of fully biodegradable materials and is well tolerated by the body, with only a minimal local reaction in thorough testing on animal and human skin.[11] It also

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does not undermine the efficacy of the vaccine it accompanies: the immune response is the same with or without the dye. Second, the dye technology can support elimination of diseases that pose a huge health burden, from measles to cholera. As a sign of vaccination, the dye can be useful much as vaccine scars were in coordinating successful smallpox eradication efforts decades ago. Moreover, the scannable dye can supply even richer information than scars can—for instance, showing how many doses have been administered for multidose vaccines or the date of vaccination. This information can help solve recordkeeping problems and reduce the risk of superfluous, potentially harmful repetitious vaccination. Prime settings for deploying the dye technology are LMICs where measles or cholera outbreaks are frequent and where limited resources undermine vaccine tracking and delivery.

However, an ethical analysis is incomplete if it fails to consider people's attitudes and potential resistance toward skin-patch vaccines, traceable dyes, or both. These attitudes constitute the main challenges to this technology.

One conspiracy theory circulated by antivaccine groups on social media during the Covid-19 pandemic has been that the novel vaccines for the virus contain microchips that governments or others were using to track vaccine recipients.[12] Other sources of disinformation alleged that Covid-19 vaccines magnetized the body to permit tracing and interactions with 5G cell phone towers.[13] The new microarray patch and dye technology may be cast in a similarly inaccurate light and viewed with fear.

As wildly incorrect as these conspiracy claims are, they have set the stage for the kind of resistance that can emerge around vaccines. Using language inaccurately to describe stickers as "chips" could easily reinforce existing paranoia about vaccination. Using tiny amounts of injectable dye and handheld devices or smart phones to assess vaccination status may also trigger renewed fears about third-party monitoring for nefarious purposes. The very image, made visible by infrared scanners or special cell phones, of QR codes or other markings on human arms may elicit visceral reactions or associations with horrific historical episodes of arm tattoos. Clear and sensitive communication in advance is essential to minimize these responses. Otherwise, such fears risk undermining these recent advances that, if rolled out effectively, could contribute to eliminating persistent diseases and saving millions of lives. So, although what makes these technologies attractive is their potential to prevent some types of fear and distrust by eliminating the need for relatively large needles and invasive monitoring and registries, we must still address fear and distrust for the technologies to fulfill their promise.

The rollout of the next generation of improved vaccination technology must be accompanied by clear ethical standards to blunt disinformation and conspiracy mongering. At all times, communicators must use appropriate terminology, such as "microarray patches" or "stickers." Where the infrared dye is available, every adult receiving a patch should have the option to consent to or refuse the use of tiny amounts of it to track their vaccine status; likewise, parents should have this option concerning the use of dye on their children. As antivaccine activism increasingly pervades both high- and low-income countries,[14] national immunization programs should introduce dye-containing vaccine patches cautiously, with explicit governmental and ethics committee approval and with community consultation and education campaigns. This could include beginning through pilot programs to monitor vaccine uptake and acceptance before advancing to more ambitious immunization campaigns. It is essential that community members understand and consent to the level and types of information encoded in any dye-based markings and that governments solicit and promptly address privacy and confidentiality concerns.

Campaigns should also make clear from the start which organizations have funded the research that produced the improved delivery technology, what the benefits are for individual recipients and their communities, and what the penalties are for sharing information on vaccine status with third parties not legally entitled to receive such information. International organizations need to set conditions as to when any vaccine status information can be shared, by whom, and for what reasons.

Many people are afraid of needles, some so much so that they avoid having themselves or their children vaccinated. No one choosing to be vaccinated wants to receive doses insufficient to provide protection or more doses than are necessary to do so. The technology is at hand to address these challenges. Care must be taken to ensure that the fear, concern, and distrust created for many years by vaccine opponents are recognized and addressed.

The Ethics and Policy Working Group on New Vaccine Delivery Technologies

Gabriela Arguedas, Anna Bershteyn, Noel T. Brewer, Peter J. Hotez, Heidi J. Larson, Joseph Mfutso-Bengo, Jonathan

Moreno, David Oshinsky, Brendan Parent, Dorit Reiss, Joanna Różyńska, and Maxwell J. Smith

1. A. Taddio et al., "Prevalence of Pain and Fear as Barriers to Vaccination in Children—Systematic Review and Meta-Analysis," *Vaccine* 40 (2022): doi:10.1016/j.vaccine.2022.10.026.

2. O. Ezezika et al., "What Are the Barriers and Facilitators to Polio Vaccination and Eradication Programs? A Systematic Review," *PLOS Global Public Health* 2 (2022): doi:10.1371/journal.pgph.0001283.

3. L. A. Taylor, G. E. Kaebnick, and M. Z. Solomon, eds., "Time to Rebuild: Essays on Trust in Health Care and Science," special report, *Hastings Center Report* 53, no. S2 (2023): S1-S104.

4. J. Knudsen et al., "Combating Misinformation as a Core Function of Public Health," *NEJM Catalyst* 4, no. 2 (2023): doi:10.1056/CAT.22.019.

5. P. J. Hotez, *The Deadly Rise of Anti-science: A Scientist's Warning* (Baltimore MD: Johns Hopkins University Press, 2023); M. C. Navin and K. Atwell, *America's New Vaccine Wars: California and the Politics of Mandates* (New York: Oxford University Press, 2023); M. J. Goldenberg, *Vaccine Hesitancy: Public Trust, Expertise, and the War on Science* (Pittsburgh, PA: University of Pittsburgh Press, 2021); H. J. Larson, *Stuck: How Vaccine Rumors Start—and Why They Don't Go Away* (New York: Oxford University Press, 2020).

6. E. Dubé et al., "Strategies Intended to Address Vaccine Hesitancy: Review of Published Reviews," *Vaccine* 33, no. 34 (2015): doi:10.1016/j.vaccine.2015.04.041; H. Whitehead et al., "A Systematic Review of Communication Interventions for Countering Vaccine Misinformation," *Vaccine* 41, no. 5 (2023): doi:10.1016/j.vaccine.2022.12.059.

7. K. J. McHugh et al., "Fabrication of Fillable Microparticles and Other Complex 3D Microstructures," *Science* 357 (2017): doi:10.1126/science.aaf7447.

8. F. Kritz, "Virtually Ouch-Free: Promising Early Data on a Measles Vaccine Delivered via Sticker," *Goats and Soda* (NPR blog), May 26, 2023.

9. L. C. Richardson and W. J. Moss, "Measles and Rubella Microarray Patches to Increase Vaccination Coverage and Achieve Measles and Rubella Elimination in Africa," *Pan African Medical Journal* 35, no. 3 (2020): doi:10.11604/pamj.supp.2020.35.1.19753; M. Hasso-Agopsowicz et al., "Accelerating the Development of Measles and Rubella Microarray Patches to Eliminate Measles and Rubella: Recent Progress, Remaining Challenges," *Frontiers in Public Health* 10 (2022): doi:10.3389/fpubh.2022.809675.

10. K. J. McHugh et al., "Biocompatible Near-Infrared Quantum Dots Delivered to the Skin by Microneedle Patches Record Vaccination," *Science Translational Medicine* 11 (2019): doi:10.1126/scitranslmed.aay7162.

11. Ibid.

12. E. Black and K. Tarasov, "Why the COVID Vaccines Can't Contain a Tracking Microchip or Make You Magnetic," CNBC, October 1, 2021.

13. J. Schwarcz, "Can Vaccines Make Our Body Magnetic?," *McGill Office for Science and Society*, June 11, 2021, https://www.mcgill.ca/oss/article/covid-19/can-vaccines-make-our-body-magnetic.

14. P. J. Hotez, "Will Anti-vaccine Activism in the USA Reverse Global Goals?," *Nature Reviews Immunology* 22 (2022): doi:10.1038/s41577-022-00770-9.

Hidden Ethical Challenges in Health Data Infrastructure

by NICOLE CONTAXIS

On January 25, 2023, the National Institutes of Health implemented a data-sharing and -management requirement for all research on human subjects conducted at or funded by the NIH.[1] In August 2022, the White House Office of Science and Technology Policy released a memorandum calling for increased public access to federally funded research.[2] Both the NIH policy and the OSTP memorandum demonstrate a larger evolution in the roles of data sharing, reuse, and open science, and both call for maximizing data sharing within accepted legal and ethical limits. There is a large literature on these ethical limits, particularly related to human subjects' data and the requirements of informed consent for data sharing and deidentification. However, data infrastructure remains largely out of view in that literature.

Nonetheless, data infrastructure, including the bureaucratic, technical, and social mechanisms that assist in data management and sharing, presents its own ethical considerations, outside of the actions (such as data sharing and data

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