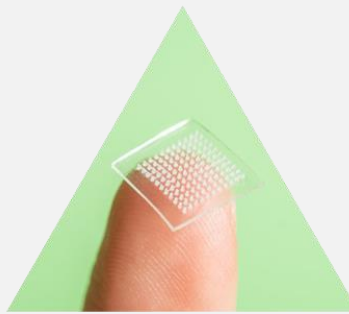
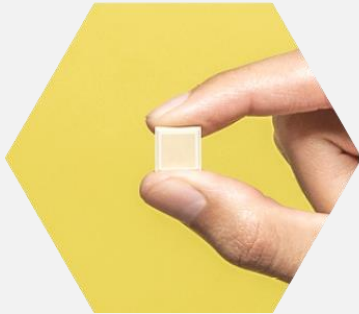


# Understanding user and program needs for the MAP technology



## Advancing the MAP technology platform

The PATH Center of Excellence for Microarray Patch (MAP) Technology was established to advance MAPs as a technology platform, address the need for improved presentations of vaccines and pharmaceuticals, and advance MAP development for high-priority needs in low- and middle-income countries (LMICs). Understanding, prioritizing, and evaluating global health use cases and value propositions is one of the strategic areas of work for the MAP Center of Excellence. This report provides an overview of the user and program needs activities that have been conducted, the results from this work, and some of the lessons learned that are relevant for the MAP platform as a whole.

## Understanding user and program needs

Building on previous user needs and stakeholder assessments conducted by PATH and others, including analyses focused on MAPs for vaccines such as measles-rubella and influenza as well as drugs such as antiretrovirals, antibiotics, and contraceptives, the MAP Center of Excellence user and program needs activities were designed to understand the global health use cases for a set of prioritized applications <sup>1,2,3,4,5,6,7</sup>. The focus was on the advantages and opportunities MAPs could provide for vaccines delivered outside of traditional well child visits through national immunization programs. These could include, for example, vaccines in which the target population is outside the age range of infant immunization programs (human papillomavirus [HPV]), postexposure prophylaxis (rabies), or for outbreak response (cholera, Ebola, pandemic flu, and yellow fever).

Gathering context-specific feedback from end users and stakeholders on new products is an important part of a human-centered design process, bringing real-world experiences, needs, and requirements into

the product development process. For each of the applications, stakeholder and end-user interviews were conducted to explore the potential benefits of MAPs for the target applications (see Figure 1). The goal was to obtain feedback on potential usability, acceptability, and programmatic fit; to determine key product attributes; to contribute to development of target product profiles; and to better understand opportunities and challenges related to the introduction of MAPs in these settings. As part of these interviews, an in-country evaluation was conducted in India about a potential rabies vaccine MAP. In-country evaluations are planned to collect feedback on MAPs for HPV.

### User and program needs—the perceived benefits of MAPs

Overall, there was strong interest and excitement about the potential benefits of the MAP technology platform for rabies, HPV, and outbreak response, particularly for addressing the barriers to access and delivery of vaccines.

#### Rabies vaccines

According to global and country stakeholders, a rabies vaccine MAP could address important barriers related to use of the rabies vaccine.

- **Access and availability:** In India, the availability of rabies vaccine in primary health centers needs to be increased. In addition, areas in India geographies are experiencing vaccine shortages. A rabies MAP with improved heat stability that would be easier to store could improve availability closer to people in need.
- **Adherence to the full dosing schedule:** Factors negatively impacting adherence include the direct cost of the vaccine (since patients often pay) as well as the indirect costs associated with transportation and loss of income. A rabies MAP that could increase access to rabies vaccines within local health centers or enable self-administration of subsequent doses could increase adherence.
- **Ease of use:** A MAP that could be applied by lower-level health care workers could make rabies vaccine more immediately available, for example, if clients arrived at a clinic after hours, or through self-administration of one or more doses.

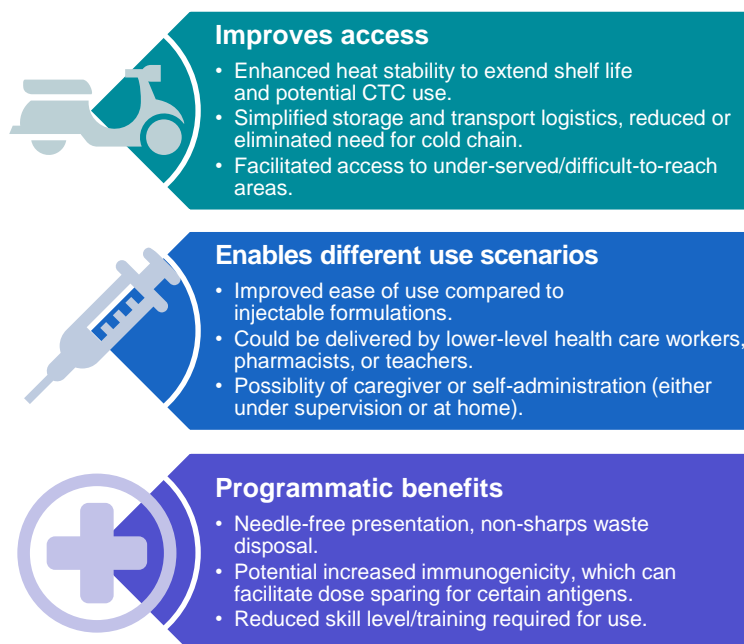
A rabies MAP  
“could help millions  
of patients.”  
—Indian medical provider

#### Vaccines for outbreak response

For outbreak response, the ability to rapidly deploy vaccines is critical. MAPs were seen as having several potential interrelated benefits.

- **Heat stability:** As an example, the logistics and resources required for storing or stockpiling Merck’s ERVEBO® Ebola Zaire vaccine, which requires storage at –80°C, are difficult. A MAP with improved heat stability would help alleviate some of these challenges and allow for expanded delivery scenarios.

Figure 1. Value proposition for microarray patch technology.



Abbreviation: CTC, controlled temperature chain.

- **Expanded scenarios of use:** Fixed-immunization sites were described as a limiting factor. A MAP that could be delivered by lower-level health workers and outside of clinic settings could support a flexible response and enable alternative delivery scenarios, such as house-to-house delivery, self- or assisted administration, or a mail delivery model.
- **Ease of use:** Time and ease were described as the “name of the game.” A small, easy-to-deliver MAP has the potential to reduce clinic throughput times and increase the number of people that could be vaccinated in a single session.

## HPV vaccine

Stakeholder interviews identified several ways an HPV MAP could address some of the programmatic barriers and improve the logistics for HPV campaigns. Additional in-country interviews are planned and will be shared in a future report.

- **Improve access and ease of use:** An HPV MAP that is easy to use and requires limited training would potentially remove the need for trained health care workers and reduce logistical and opportunity costs related to sending trained providers to schools. The pool of vaccine administrators could be expanded to include community health workers, pharmacists, school nurses, and school staff.
- **Heat stability:** The ability to store vaccines at a school for up to a week would improve the logistics for school-based immunization programs and could decrease the need for cold chain space at the point of administration.
- **Acceptability:** HPV is noted to cause injection site pain, which impacts acceptability and adherence to the second dose. A delivery method that causes less pain may improve uptake and community acceptance.

## Potential challenges and lessons learned

While each of the activities explored a specific vaccine, several important themes emerged from these discussions with stakeholders that are relevant for MAP development in general. These include opportunities and barriers related to (1) the overall status of the MAP platform and **the introduction of novel technologies**, (2) **technical feasibility** of optimal/desired product characteristics, (3) **contextual factors** related to specific vaccines and/or use cases, and (4) **critical assumptions** made by stakeholders regarding expected product attributes.

### New technology introduction and stakeholder acceptability

As a novel technology platform, MAPs for vaccine administration will need to contend with challenges that come along with the introduction of any new technology. Therefore, different stakeholder perspectives as well as attributes of certain vaccine programs will be important to consider.

The first vaccine MAPs will face larger hurdles, since this will be the first time questions about the technology, for example, from regulators and providers, will be answered. In addition to data on safety and efficacy of a particular MAP product, being able to demonstrate the applicability of MAPs to other vaccines will enhance the acceptability of the MAP platform as a whole as well as the acceptability of a specific vaccine MAP. Since, as stakeholders noted, providers are comfortable with what they know, adoption of new technologies takes time. Therefore, as the MAP platform matures, the timeline for approvals and uptake will decrease.

While feedback on MAP acceptability among potential clients and caregivers has been positive, with benefits including perceptions of reduced pain, reduced risk of contamination, and reduced hesitancy (related to anxiety around needles), the acceptability of and potential concerns around different delivery

methods and dosing schedules for a single vaccine need to be considered. Community perceptions around the effectiveness of different delivery methods will need to be addressed. If vaccine MAPs have different dosing schedules than their needle and syringe counterparts, acceptability should also be assessed (e.g., rabies, where some current regimens require two doses be administered at each visit).

### Optimal performance targets and programmatic acceptability

Across vaccine scenarios, the overall public health value proposition for MAPs resonated with stakeholders. The potential of a product that would simplify delivery, increase access, improve adherence, ensure greater coverage, and reduce vulnerability to vaccine-preventable diseases was welcomed. The promise of enhanced heat stability, particularly in discussions around increasing access, was a key value to participants, since it could address limitations related to the cold chain and potentially allow vaccines to be stored closer to populations in need, for example, having more immediate access to a rabies vaccine in remote areas or during outbreak response.

In addition, heat stability combined with the possibility of self-administration opened up possibilities for different delivery scenarios, such as mail delivery for a pandemic influenza vaccine or the initial or follow-up doses of a rabies vaccine being self-administered, which could increase coverage and address adherence. However, the technical feasibility of an out-of-the-cold-chain MAP and regulatory approvals for and acceptability of self-administration are open to question. As a result, it will be important to understand the potential impact on access, and therefore acceptability, of a MAP product that meets what are determined as the minimal versus optimal product requirements (see Table 1).

“Too many potential use cases depend on product stability.”

Table 1. Example optimal and minimal targets for a rabies microarray patch.

Optimal target Single-dose rabies vaccine MAP for delivery in a health care setting	Minimal target Three-dose rabies vaccine MAP labeled for CTC storage (minimum of 7 days)
<p><b>Benefits</b></p> <ul style="list-style-type: none"> <li>Simple protocol.</li> <li>Addresses adherence challenges.</li> <li>Reduces costs associated with multiple clinic visits.</li> </ul> <p><b>Challenges</b></p> <ul style="list-style-type: none"> <li>Requires a sustained-release formulation.</li> <li>More technically challenging and costly to develop.</li> </ul>	<p><b>Benefits</b></p> <ul style="list-style-type: none"> <li>Initial clinic delivery followed by self-administration.</li> <li>Promotes adherence.</li> <li>Reduces household costs.</li> </ul> <p><b>Challenges</b></p> <ul style="list-style-type: none"> <li>Regulatory approvals.</li> <li>Acceptability of self-administration and home controlled temperature chain (CTC) storage.</li> </ul>

### Understanding specific vaccines and use cases

As development efforts move forward with specific vaccines, it will be essential to understand both the realities and challenges related to program implementation as well as the perspectives of providers when developing target product requirements and understanding which features/product attributes are actual needs versus preferences/desires. Feedback from the rabies stakeholders in India highlighted product considerations that are specific both to the rabies vaccines and to the programmatic reality in India. Some providers made a distinction between the need for a feedback indicator, which provides confidence that the MAP

Rabies is “life or death.”

“No margin for error.”

has been applied correctly and are a feature of several MAPs in development, and a need for an indicator that the vaccine has been correctly and completely delivered. Under current World Health Organization (WHO) guidance,<sup>8</sup> “a visible and palpable ‘bleb’” should be raised in the skin following for intradermal rabies vaccine delivery. If a bleb does not appear, then a provider should administer a new dose. Therefore, for provider acceptability, a delivery indicator was seen as critical.

Another important consideration is the anticipated cost of a rabies vaccine MAP, as vaccine cost is currently a challenge for rabies elimination in India. While a national vaccination program may be able to absorb a small increase in the cost of purchasing vaccines (taking into account savings in other programmatic costs such as training or wastage), it is the patient who is most often paying for rabies vaccines in India. Therefore, the impact on people who already have limited access to resources and for whom the indirect costs of vaccination (such as travel time and lost income) are already a barrier could end up reducing rather than improving access to postexposure vaccination and care.

Understanding the social and cultural context around specific vaccines and programs is also important to consider when exploring the MAP platform for specific vaccines. In the discussions around MAPs for HPV and outbreak response, stakeholders highlighted existing challenges, such as misinformation, rumors, vaccine hesitancy, community and social mobilization, and sustainable funding for community awareness and education activities. These issues have the potential to be exacerbated if a new technology is used. During an outbreak, when time and speed of delivery are critically important, the time and resources needed for community sensitization and awareness of a novel MAP vaccine may be an even bigger barrier. In addition, the ease of use of MAP products could also be seen as a disadvantage/liability, since a patch may be perceived as too simple (described as “low tech”) by some, with more complex methods being seen as more acceptable or efficacious. Finally, more than one stakeholder emphasized that the challenge of introducing a *disruptive innovation* during an outbreak should not be understated.

## Critical assumptions/unknowns

### Cost and cost-effectiveness

The cost—not only of the vaccine but also the delivery strategy—is a key driver for country programs when considering the introduction of a new vaccine or delivery method. Costs related to social mobilization and outreach, for example, for HPV and outbreak response, also need to be considered. In addition, how the program is financed and who pays also needs to be considered. In the case of HPV, there is strong donor support for vaccine introduction. However, the costs of maintaining an ongoing immunization program and the need for continued social mobilization, as new cohorts become eligible for the vaccine, need to be incorporated into the country’s own budgets and school health programs. For rabies vaccine delivery in India, outside of the public sector (where access and availability are problematic, especially in smaller facilities and remote areas), it is the client who is paying for the vaccine. Therefore, any increase in costs for a MAP product would likely be borne by a population that is already facing multiple challenges due to lack of access to financial resources.

“Innovation only makes sense if it is economically viable.”

### Impact on cold chain

Stakeholders have an expectation of increased heat stability for MAPs compared to the vaccines’ current formulations (discussed above), but this may not be feasible for all vaccines. A key aspect of the value proposition for a vaccine MAP is a reduced need for the cold chain and smaller packaging and storage volumes compared to a vial plus a separate needle and syringe. However, a vaccine MAP that takes up more space per dose in the cold chain could be significantly less desirable, even if the total storage size

including the needle and syringe is reduced or if the MAP could be stored in a controlled temperature chain for a few days before use. For example, in the case of HPV, a potential increase in packaging volume for MAP technology compared to single-dose glass vials was described as increasing rather than decreasing barriers to access.

### **Data availability and regulatory approval**

Given the overall status of product development of the MAP platform, where vaccine efficacy or noninferiority have not yet been demonstrated in humans for any vaccine, as noted above, both regulators and stakeholders are expected to be cautious. Some of the first questions providers in India had, when talking about a potential rabies vaccine MAP, were about the immunogenicity and safety data for a MAP product. Since MAPs are applied directly to the skin, there were also concerns about potential reactogenicity and the impact on client acceptability.

### **Conclusion**

The user and program needs activities of the MAP Center of Excellence have illustrated the potential benefits of the MAP platform in supporting LMIC immunization programs and increasing access to vaccines. Similar anticipated benefits were highlighted through the Vaccine Innovation Prioritisation Strategy (VIPS)—an unprecedented three-year collaboration to prioritize and drive vaccine product innovations to better meet country needs and support coverage and equity goals—led by Gavi, WHO, PATH, United Nations Children’s Fund, and the Bill & Melinda Gates Foundation.<sup>9</sup>

A key finding from our interviews was the importance of the perceived *ease of use* for improving access, by reducing the need for training and expanding the types of providers who could administer vaccines through alternative delivery scenarios outside of a health facility. Acceptability by providers and patients was generally expected to be high for a needle-free and pain-free solution. Providers in India like the idea of MAPs for vaccine delivery once safety and immunogenicity have been proven, although note that the adoption of a new technology is a process. However, the regulatory and policymaker acceptability of a self-administration use case is less certain.

In addition, the technical feasibility of increasing stability needs to be determined on a vaccine-specific basis and is key to the value proposition of a MAP. The costs of a vaccine MAP are both important and unknown, particularly for vaccines that require more than one dose. Identifying vaccine delivery alternatives that are safe, easy to administer, reduce cold chain impact, and increase access remains an important goal both for high-income countries as well as LMICs.<sup>10</sup>

To ensure that MAP products that are developed are successfully introduced and have the intended public health impact, it is essential to understand the unique needs of each vaccine and to determine the feasibility of attaining desired product attributes.

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