Technology overview of microarray patches

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Dr. Jessica Mistilis
Senior Technical Officer
https://www.path.org/programs/mdht/mapresources/
PATH is a global team of innovators working to eliminate health inequities so people, communities, and economies can thrive.
PATH’S MISSION

Advance health equity through innovation and partnerships.
One PATH, one mission, many experts

More than 1,500 strong, our global team includes experts and thought leaders from dozens of specialties including:

- **Product development**—contraceptives, rapid diagnostics, and other devices.
- **Primary health care**—people-centered health systems strengthening.
- **Vaccines and essential medicines**—development, formulation, manufacturing, and rollout.
- **Digital transformation**—electronic immunization registries and other real-time systems.
- **Epidemic preparedness and response**—disease surveillance, responder training, and coordination.
- **Advocacy and communications**—elevating community priorities, influencing local and global stakeholders.
Packaging and delivery technologies at PATH

We identify, advance, and assess primary packaging and delivery devices for vaccines and essential medicines that have the potential to maximize safety and efficacy, expand equitable access, and minimize costs.
Microarray patch (MAP) technology overview

- A patch may have **hundreds or thousands of tiny projections**.
- The projections can be **coated with or composed of a drug and excipients** (dry formulation).
- The **patch is applied to the skin and pressed down** so that the projections penetrate the top of the skin. The patch is worn for a few minutes during which the drug releases into the skin, and then the patch can be removed.
- The projections only **penetrate the top layers of the skin** to deliver the drug.
- It is typically perceived as **less painful than an injection**.
- Some platforms require an **applicator** for delivery (integrated or separate).
MAPs could increase access to vaccination and essential medicines in low-resource settings

Attributes
- Ease of use
- No reconstitution
- No needles or sharps waste
- No ancillary supplies
- Enhanced thermostability
- Single-dose presentation

Potential benefits
- Improved acceptability
- Allows for delivery by lesser-trained health workers or self-administration
- Enables new delivery scenarios (house-to-house campaigns, self-administered)
- Reduces vaccine wastage
- Avoid first-pass metabolism

Potential impact
- Increased access and equity
Types of microneedles

**Step one:** Microprojections are applied.

**Step two:** Pharmaceutical is released.

**Microarray patches (MAPs)**

**Liquid delivery via microneedles**
MAP landscape: Examples by development phase

**Preclinical**
- Contraception (multiple APIs)
- HIV ARVs (multiple APIs)
- Diabetes (insulin)
- mAbs
  - HPV vaccine
  - Typhoid conjugate vaccine
  - IPV vaccine
  - HIV vaccine

**Phase 1**
- Warts (bleomycin)
- COVID-19 vaccine
- Influenza vaccine
- Japanese encephalitis vaccine
- Hepatitis B vaccine
- Cystic fibrosis diagnostic (pilocarpine)

**Phase 2**
- Diabetes (semaglutide)
- Skin cancer (doxorubicin)
- Osteoporosis (parathyroid hormone)*
- Measles-rubella vaccine

**Phase 3**
- Migraine (zolmitriptan)*
- Osteoporosis (abaloparatide)*
- Scarring (siRNA)

**Marketed**
- Cosmetic (hyaluronic acid)

**Key**
- Small molecule
- Biologic
- Non-pharma
- *Discontinued
First clinical proof of concept of vaccine MAPs in infants

- First completed Phase 1 & 2 clinical trial in unprimed 9-month-olds with a microarray patch (MAP) for measles-rubella (MR) vaccine in 2021–2022 in The Gambia, a country where measles is endemic.

- Double-blind, double-dummy design where participants received either an MR MAP and placebo subcutaneous (SC) injection or a placebo MAP and MR SC injection.

- Vaccination by MAP was safe and well tolerated, with no allergic reactions or related serious adverse events.

- Over 90% of the parents of toddlers and infants enrolled in the trial, who took part in an acceptability survey, said the MAP technology would be better than SC injection.
Measles-rubella vaccine MAPs were safe and effective in infants

Mild skin reactions such as induration and discoloration, seen in the active MAP group, all resolved during the study.

High and similar seroprotection and seroconversion rates for MR were shown in all cohorts for both the MAP and SC injection.
PATH has evaluated MAPs for **long-acting antiretroviral delivery** for adult pre-exposure prophylaxis (PrEP) and pediatric treatment.

User/stakeholder studies in Kenya, South Africa, and Uganda showed **high acceptability of MAP prototype designs for HIV PrEP**. Most potential users preferred the smallest-sized MAP and protection ranging from 1 to 3 months.

For **pediatric HIV treatment**, global, US, and Ugandan HIV experts preferred monthly or weekly MAPs over daily oral treatment.

Our preclinical rat studies and physiologically based pharmacokinetic modeling has indicated that **highly potent antiretroviral drugs are required** to balance dosing frequency and size of MAP.

MAP for HIV PrEP is on hold until a more potent ARV is available for development.

### Table: Antiretroviral Drug Options

<table>
<thead>
<tr>
<th>Antiretroviral drug</th>
<th>Adult PrEP</th>
<th>Pediatric treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabotegravir</td>
<td>Monthly: Not feasible</td>
<td>Weekly schedule for postnatal prophylaxis</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>Monthly: Not feasible</td>
<td>Weekly or monthly: Not feasible</td>
</tr>
<tr>
<td>Islatravir</td>
<td>Every 3 months: Feasible, if Islatravir developed for PrEP</td>
<td>Monthly schedule for young children is feasible</td>
</tr>
<tr>
<td>Lenacapavir</td>
<td>Every 3 months: Not feasible</td>
<td>TBD with oral loading dose</td>
</tr>
</tbody>
</table>

In collaboration with Queen’s University Belfast, US Centers for Disease Control and Prevention, and Pharmetheus.


Preclinical development of contraceptive MAPs

Several organizations have published findings on developing MAPs to deliver **hormonal contraceptive**—levonorgestrel.

Data in preclinical models indicate that MAPs could need to be applied **monthly, every 2 months, or even every 6 months**.

Based on the design of the MAP, the **wear time** can range from several seconds to several minutes.

Developers are working on designs that can be **self-administered**, providing women with an option for long-acting, user-controlled contraception.


**Abbreviations:** LNG, levonorgestrel; MN, microneedles.
## Challenges to develop MAPs for treatment and prevention

| Manufacturing scale-up | • This novel combination product requires new manufacturing facilities and test methods, leading to high initial investment.  
• Benchtop processes need to be scaled up to enable late-stage clinical and commercial production. |
|------------------------|---------------------------------------------------------------------------------------------------------------|
| Regulatory pathway     | • Regulators will need to be consulted on clinical and CMC plans.  
• A novel device will require new testing methods, critical quality attributes (CQAs), etc. |
| Drug amounts needed for treatment and prevention | • MAPs can deliver a limited amount of drug, about 1 mg per cm\(^2\).  
• Treatment and prevention of HIV, tuberculosis, HCV, etc. require higher doses, which limits MAP feasibility.  
• There is a need to balance potency of drug, MAP size, and treatment length. |
| Market feasibility     | • Unknown market size and demand for these products. Unknown if the demand will enable sustainable markets for MAP manufacturers.  
• MAPs will cost more than a vaccine vial or oral pills. Total cost of delivery may be less, given other attributes of the product.  
• Given the higher costs and potential benefits, need to understand the willingness to pay for a MAP. |
| Introduction and adoption | • Raise awareness among community and decision-makers.  
• Understand opportunities and challenges for MAP introduction in LMICs to integrate into the health care system. Understand how self-administration of a MAP could fit into the health systems.  
• Clarify value proposition relative to existing products. |

14 Abbreviations: CMC, chemistry, manufacturing, and controls; CQA, critical quality attribute; HCV, hepatitis C virus; LMICs, low- and middle-income countries.
Newsletters: Please contact MAPs@path.org to be adding to the mailing list.

MAP Resources page: For more information on PATH’s work on microarray patches, go to https://www.path.org/programs/mdht/mapresources/.

VIPS site: For more information on the VIPS Alliance and the technologies, go to https://www.gavi.org/our-alliance/market-shaping/vaccine-innovation-prioritisation-strategy

Target product profiles: To review and provide input on MAP target product profiles, go to https://www.path.org/resources/microarray-patch-target-product-profiles-tpp/.

For more information contact:

Dr. Jessica Mistilis
Senior Technical Officer, PATH
jmistilis@path.org
maps@path.org
PATH
Appendix
Global Microarray Patch Developers

96 microarray patch developers worldwide

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PATH’s role and impact: Microarray patch field

Abbreviations: BARDA, Biomedical Advanced Research and Development Authority; CEPI, Coalition for Epidemic Preparedness Innovations; DCVMN, Developing Countries Vaccine Manufacturers Network; FDA, US Food and Drug Administration; Gavi, Gavi, the Vaccine Alliance; PADO, Paediatric Antiretroviral Drug Optimization; USP, United States Pharmacopeia; UNICEF; United Nations Children’s Fund; VIPS, Vaccine Innovation Prioritisation Strategy.
User and stakeholder perspectives used to assess and refine HIV PrEP and MPT MAP prototypes

PATH and country partners implemented iterative user and stakeholder assessments in Kenya, Uganda, and South Africa. Women and men (18–40 years, n = 430 participants) participated in focus group discussions and mock use exercises. Key informant interviews gauged the decision-maker ecosystem for MAPs.

1. Explored user/stakeholder perspectives about MAPs
2. Assessed acceptability, usability, and programmatic fit for HIV PrEP or MPT
3. Explored needs and preferences for key features among various audiences

- Size
- Duration of protection
- Application site
- Wear time
- Delivery indicator
- Potential for discreet use
- Other features (packaging, instructions, etc.)
- Cost considerations

Abbreviations: MPT, Multipurpose prevention technologies.