Evaluation of Microarray Patches for Human Factors—Considerations and Program Feasibility

Results of simulated-use testing in clinics in Ghana

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Introduction

Microarray patches (MAPs) consist of an array of micron-scale projections that painlessly penetrate the outermost layer of the skin (the stratum corneum) to deliver vaccines and pharmaceuticals intradermally. They may be applied directly to the skin due to the adhesive backing to hold the patch in place. A wide range of vaccines and pharmaceuticals have been tested preclinically with MAP technologies by academic and industry developers, including some vaccines of global health importance such as inactivated poliovirus (IPV), measles, rotavirus, influenza, dengue, yellow fever, and tetanus toxoid vaccines. Advantages of this method of delivery include increased thermostability, ease of delivery, reduction in sharps waste, and the possibility of increased efficacy or dose sparing. As a result, MAPs have the potential to expand access through enabling delivery in alternative immunization scenarios such as house-to-house delivery by lesser-trained health care workers (HCWs).

Micron and the Georgia Institute of Technology (GT) have developed a MAP using a dissolvable microarray to deliver vaccine into the top layer of the dermis. The vaccine on the patch penetrates the skin by the push of the thumb to manually press down on the back of the patch until a “click” is heard. PATH has previously conducted preliminary user testing, expert interviews, and heuristics analysis of the GT MAP using mock MAPs, which consisted of a patch with a plastic-encased metal backing and a commercially available, hypoallergenic medical skin adhesive. The results of the evaluation were reported to the device manufacturer for further product development and were used to inform the design of the separately funded field evaluation. The patches used in both the preliminary and field evaluations had no microarray or other mechanism for penetrating the skin or other mechanism of biological action and therefore no vaccine, drug, or placebo was administered during the evaluation.

In order to assess the acceptability, usability, and logistical fit of the GT MAP in low- and middle-income countries (LMIC), PATH conducted a simulated-use evaluation in Ghana to assess the user requirements and potential operational fit of the MAP for vaccine delivery. FDA guidance to industry on human factors considerations for designing medical devices notes that such a study “demonstrates that the device can be used by the intended users without serious use errors or problems, for the intended uses and under the expected use conditions.” Conducting the study in a simulated-use environment is a recommended best practice and allows for a more complete exploration of potential failure modes and opportunities for program innovation.
GOAL AND OBJECTIVES

The goal of this study was to evaluate the ease of use, acceptability, and programmatic fit of the GT mock MAPs for vaccine delivery in:

- Campaign immunization for pandemic/outbreak response.
- Routine immunization of children.
- Maternal immunization.

The objectives of the research were to:

1. Define the human factors and operational requirements for delivering vaccine using MAP technology.
2. Provide product and packaging design and training recommendations to MAP developers.
3. Describe the programmatic considerations for immunization using MAP technology.

Methods

ETHICAL CONSIDERATIONS

The research protocol for this study was reviewed and approved by the PATH Research Ethics Committee and the Kintampo Health Research Centre (KHRC) Ethics Committee. Informed consent was obtained from every participant, and a separate media release statement was signed by every participant, permitting use of the videos and photos taken during this study for inclusion in reports and presentations on this work and similar PATH projects.

COUNTRY SELECTION

Several factors were considered in the selection of Ghana for the conduct of the evaluation. Of primary importance to the conduct of this research was an experienced local research partner with qualitative and quantitative research expertise and established connections to public and private health care providers. To ensure the MAPs would be tested in a variety of contexts, we sought a country in which varying types of facilities, health providers, and immunization strategies would be accessible for inclusion in the evaluation. Lastly, we sought a country in which PATH has a country office or established country presence to facilitate necessary connections at the local level. From prior experience and PATH staff recommendations, we identified KHRC in Ghana as the best research partner for this evaluation.
SITE SELECTION

Research sites for conducting the evaluation were identified based on the following criteria:

- Accessible in a day from the KHRC main offices.
- Representative of a range of levels of infrastructure (urban/rural, reliable/unreliable electricity, indoor/outdoor settings for patient and client visits, etc.).
- Representative of a range of levels of the Ghana health system: primary, secondary, and tertiary health centers and private facilities.
- Reflective of the different ways in which vaccine supplies are distributed to and stored at facilities.
- Reflective of different patient flow patterns and volumes.

From these criteria, a list of potential sites was generated and site managers were contacted regarding participation. Final site selection was dependent on staff availability at the time of the evaluation and availability of potential recipients for participating in the evaluation—many clinics alternate the types of services offered on varying days and so patient volumes were not always aligned with target participant types.

PARTICIPANT TYPES

Target users

We recruited two groups of HCWs to participate as users in the simulated-use components of this evaluation:

- Midwives and community health nurses (CHNs) or community health officers (CHO)s who provide antenatal care (ANC) services to pregnant women at clinics and in the community.
- CHNs and CHOos offering immunization services to children at clinics and in community outreach.

In addition, community-based surveillance volunteers (CBSVs), who help with campaigns, outreach, and some clinic services and who work closely with the CHOos and CHNs, were also recruited for participation in group interviews. Likewise, CHOos and CHNs who did not participate in the simulated use but who also work in the target-use environments were recruited for participation in group interviews.

* Image from: Awoonor-Williams JK, Tindana P, Dalinjong PA, et al. Does the operations of the National Health Insurance Scheme (NHIS) in Ghana align with the goals of Primary Health Care? Perspectives of key stakeholders in northern Ghana. BMC International Health and Human Rights. 2016 5;16(1):23. Creative Commons License http://creativecommons.org/licenses/by/4.0/, no changes made.
**Simulated-use recipients**

For the target users to have experience applying the MAP in a simulated-use scenario, we recruited two types of MAP recipients, representative of the two target-use scenarios: pregnant women attending ANC clinics, and children from nine months to three years, with their parents, who were attending child welfare clinics where Expanded Programme on Immunization (EPI) services are provided. Because there had not previously been patch applications to children before, the lower age threshold (nine months) for the children was determined by the study team following a previous assessment that included expert interviews with neonatologists and nurses, who unanimously agreed that the mock patches would be suitable for children aged nine months and older.

The community members (pregnant women and parent/child pairs) were selected based on attendance at the clinic and willingness to participate in the study. The inclusion of pregnant women and children in this evaluation presented the opportunity to collect valuable information on the acceptability and operational fit of the MAP for maternal immunization and routine childhood immunization, the two primary intended applications of the MAP. As the devices used in the evaluation were mock MAPs without microneedles, the inclusion of these high-risk populations posed no undue risk.

**SAMPLE SIZE**

This qualitative evaluation did not include statistical analysis of data. Therefore, the sample size reflects a convenience sampling strategy based on qualitative sampling theory. To calculate sample size, we used the Blink UX sample size calculator for usability research, which calculates sample size based on the evaluation’s design parameters. It is grounded in established, peer-reviewed qualitative research theory and best practices.9

The recommended sample size generated by the Blink UX calculator for the simulated-use component of the evaluation was 16 users (8 per group). The robustness of data generated by a sample of this size is demonstrated by Faulkner’s 2003 meta-analysis of usability data, in which she shows that a sample size of 15 users will generate data reflecting 97% of all usability problems, with diminishing returns from larger sample sizes.10

To ensure each user had sufficient experience with the mock patch, we recruited an average of 3 recipients per user, resulting in a total of 48 recipients participating in the simulated-use activity. Lastly, for the group interviews with other stakeholders (interview only, no simulated use) we targeted a sample size of four interviews per stakeholder type with an average of 3 participants per interview, for a total of 12 participants per stakeholder type. Because group interview data reflects the consensus of several individuals, it is considered a single data point per interview so that we would have eight data points from group interviews with stakeholders not involved in simulated use. Therefore, we targeted the following sample sizes for each group of participants:
Entrance & exit interviews with recipients

Entrance interviews were conducted with all recipients or parents of recipients participating in the simulated-use activity. The purpose of these interviews was to gauge recipients’ first impressions of the MAPs before they experience the simulated use, and then compare this with their impressions of MAPs after having received one during the course of their routine visit. This provides comparative data on any shift in acceptability or perceived utility of the product. This pre-/post comparison offers researchers added insight into the recipient’s experience that may not be articulated by the recipient, including highlighting potential moderator acceptance bias, where a participant responds to questions with what he or she believes the researcher wants to hear.

Simulated use during routine visit

Simulated-use of the MAPs was integrated into the standard clinic flow for the ANC and EPI patch recipients. Integrating the MAP application into the routine visit enabled collection of data on realistic wear times, task flow, fit within standard procedures, and staging and disposal of MAPs prior to use. It also enabled data collection on acceptability of patches in an environment that more closely mimics the target use environment than would be possible with standard usability exercises in a contrived use environment.

Exit interviews with users

Exit interviews were conducted with users at the end of each site visit to collect feedback on the HCW’s experiences using the MAPs during the course of their normal job duties. The data collected during the exit interviews offer a more detailed view of the impact of the introduction MAPs on routine task flow in the clinic setting. The exit interviews also offered researchers an opportunity to collect data on the potential impact of MAPs on other use-cases not directly observed during simulated use, such as in campaigns or outreach settings. Lastly, the exit interviews enabled deeper probing on the reasoning behind specific actions or comments made during the simulated use component of the study.
**Group interviews with HCWs providing non-clinic-based services**

In order to explore the potential fit of MAPs into use-cases beyond those observed at the study sites, group interviews were conducted with CBSVs, CHO, and CHNs who normally provide campaign, outreach, and other village-based services. In these interviews, data were collected on the operational feasibility, training requirements, and usability considerations for MAPs to be used in non-clinic based settings and by a broader range of cadre of HCW than is normally found in a clinic-use setting.

**Recipients study flow**

Recipients were recruited from among the eligible patient population at the clinic. In some cases, recipients were recruited the day prior to the study visit and returned to the clinic on the day of the study visit. This resulted in some simulated-use sessions occurring outside the flow of standard clinical care. In these cases the timing and process of a standard clinical visit was approximated.

Recipients were consented to participate in the study and then proceeded with the entrance interview, followed by resuming their place in cue for the clinic visit (or waiting the approximate time for a similar process), receiving the patch at the time they would receive other vaccines, completing their clinic visit (or approximate wait), and completing the exit interview.

**Users study flow**

Users were recruited from available and eligible staff at the clinics on the day of the study visit. They were then consented to participate in the study, after which they were trained on study procedures and how to use the patch. Patch training was designed to approximate the type and level of detail most users would receive in an actual-use scenario. This would likely include peer-to-peer training in a cascade training format, where HCWs (usually facility managers) would receive training from their district-level supervisors and then would provide similar training to their peers at the clinic. The training of the users included the following elements:

- Information provided on the package and the Instructions for Use.
- Presentation of the patches: 10-dose tray, five trays per carton.
- Removing the patch from the tray: lift by the tab, don’t touch the adhesive.
- Applying the patch: place adhesive down, press with tip of thumb until “click” is heard.
- Wait time: complete normal visit or wait 5–20 minutes.*
- Removing and disposing the patch with infectious waste.
- Application sites: ANC clients—medial deltoid, wrist, and iliac crest. EPI patients—anterolateral aspect of thigh, medial deltoid, and scapula.
- Site preparation: prepare the site as usual for “normal” injection, including swabbing the site if that is the normal practice.

* Users were instructed to integrate patch application/removal into the normal clinic routine. They were given a range for waiting of 5–20 minutes. This was to provide them with a benchmark for acceptable wait time, while allowing them to determine best flow for application and removal. The resulting timing data can help inform maximum and target acceptable wait times for the eventual product introduction into these use scenarios.
Following training, users resumed their normal duties while recipients were recruited and consented. There were two use scenarios explored in this evaluation, ANC and EPI. Simulated use for the application and removal of the patch varied between the two scenarios. For the ANC scenario, users were instructed to apply the patch during the palpation portion of the client’s visit. This timing was selected as this is the longest stretch of time when a single care provider interacts with the client. For the EPI scenario, users were instructed to apply the patch during the point in the visit when other vaccines are given to the child. The patient flow for each use scenario, and the potential time points at which the patch could be applied and removed, is discussed in the Results section of this report. Once a recipient was ready, the user would provide routine care to the recipient, apply the patch, continue routine care/other normal duties, and remove the patch at the specified time point. At the end of the day, users would complete an exit interview.

**DATA COLLECTION METHODS**

We used a mix of qualitative data collection methods that included direct observation and interviews. Both types of data were recorded in audio, video, and photo formats and analyzed later using MAXQDA (VERBI GmbH, Berlin Germany) qualitative analysis software. Interviews were conducted with HCWs on ease of use, ergonomic comfort (efficient and comfortable use), acceptability, and operational fit of the patch from the users’ perspectives. Likewise, entrance and exit interviews with recipients of the patch covered the acceptability and comfort of the patch. In addition, we conducted focus group discussions with stakeholders who provide ANC and immunization services in settings outside of the clinics, such as community ANC and community-based immunizations. Lastly, we documented information on the patient flow, infrastructure, layout, staffing structure, and resources used in the facility through direct observation and during the interviews with the HCWs.

**DATA ANALYSIS METHODS**

**Recipient interview data**

Notes from the pre/post interviews with recipients were transcribed into English by the local researchers. These notes were then loaded into MAXQDA for analysis. Data were coded according to a predefined coding
structure for acceptability as well as codes developed in vivo at the time of analysis.

Health care worker interview data
Audio and video recordings of the interviews with HCWs were loaded directly into MAXQDA for analysis. Data were then coded according to a predefined coding structure for usability, acceptability, and operational fit as well as codes developed in vivo at the time of analysis.

Observational data
Video, photo, and audio data collected during observation of use were reviewed and coded according to pass/fail of critical tasks and other observations. Operational data were coded in vivo, emphasizing those operational elements relevant to use of MAP in the target-use scenarios. In addition, usability data were coded according to a predefined coding structure reflecting the success or failure of the user to achieve set critical tasks, as defined here. In addition, further usability and operational fit codes were developed in vivo.

Results

SITES AND PARTICIPANTS
A total of seven sites were engaged in this research, with eight ANC HCWs and eight EPI HCWs participating in the simulated-use components of the study, with 24 pregnant women receiving the patch in the ANC scenario and 23 children in the EPI scenario. Therefore there was a total of 47 unique patch applications in the simulated-use portion of the study. In addition, 6 CHN/CHOs and 11 CBSVs participated in group interviews (at their respective sites, see below) but did not participate in simulated use of the patch.

GHANA VACCINE SUPPLY CHAIN
The immunization supply chain in Ghana is structured in a cascading hierarchy. Following its initial delivery to the national cold room storage facility, the vaccine is distributed to regional and then to district cold room storage facilities, with accompanying storage facilities for non–cold chain supplies such as needles and syringes, diluent, safety boxes, etc. From there, vaccine and supplies are transported to the clinics, where vaccines are delivered to patients or transferred to vaccine carriers for routine outreach immunization. Shipments of vaccines arrive at the national cold room twice a year and are largely funded by Gavi and other international nongovernmental organizations. On a quarterly basis, the regional cold room storage facilities collect a six-month supply of vaccine from the national cold room. District cold room storage facilities collect a three-month supply of vaccine from their regional cold room storage facility every month, according to the schedule provided. Clinics without refrigerators top up their one-month supply of vaccine from their district cold room facility weekly or several times per week. Clinics with refrigerators resupply from the district stores monthly. Typically, this top-up supply can fit in one to two vaccine carriers, but for larger facilities (secondary-level facilities) a cold box may be used to stock vaccine for several days. On average, HCWs estimate that a vaccine carrier can hold about 80 doses of various vaccines, depending

CRITICAL TASKS
The critical tasks for both scenarios are listed below, along with definitions of success for each task.

1. Remove: Removes the MAP from the tray without touching the adhesive backing and with all remaining MAPs intact.
2. Apply: Applies to the site as instructed.
3. Activate: Achieves the “click” by pressing on the top of the MAP.
4. Dispose: Removes and disposes as directed.
on the type of vaccine and how it is packaged. Whatever vaccine the clinic does not use during the day must be returned to the district facility for reallocation. Each vaccine is accounted for and recorded in a log at each facility level. These logs are carefully maintained to keep an ongoing record of the number and types of vaccine administered by each clinic.

Beyond the facility level, vaccines are distributed by CHNs and Field Technicians during outreach sessions, which occur on set days of the week, and during extended outreach to extremely rural areas, which are called “camp-outs” because the HCW goes for at least one overnight and stays at the community. During standard outreach sessions, CHNs or Field Technicians travel by bike to villages with vaccine carriers, usually two or three carriers per bike. The HCW returns the supplies to the facility at the end of the day for restocking in the refrigerator. During camp-outs, the HCW loads a small cold box (roughly 4 cubic feet interior) onto a bike and travels out to a remote area, then she camps or is hosted in the community for one or two overnights before returning the remaining supplies

A photo of the calendar that marks the days each district within the Brong Ahafo Region should collect its three-month allotment of vaccines and other medical supplies. Such calendars and other types of schedules are commonly displayed on the walls of clinics and community health facilities.
to the facility, where they are assessed for expiry and restocked or discarded as appropriate.

Only 17% (3/18) of clinics in Kintampo District have functioning refrigerators. These retrieve vaccine once per month from the district stores or subdistrict stores. This translates to 30% (2/7) of subdistricts that have refrigerators, from which local supplies may be drawn for facilities without refrigerators. Those that don’t have refrigerators store supply in vaccine carriers or cold boxes, resupplied on a schedule that is timed to coincide with published vaccine days, the standard days of the week or month during which routine immunization occurs.

SITE DESCRIPTIONS

The selection of the seven sites purposively included sites representing each level of the Ghana health system as well as a private facility providing ANC services, as 30% of all pregnant women in Kintampo seek ANC services in the private sector. The general characteristics of each type of facility are described below.

**Private maternity ward: 1—Perpetual Help Maternity Home**

Perpetual Help Maternity Home is located about a five-minute drive from the Apesika Community-based Health Planning Services Compound, an hour outside of Kintampo. This facility serves Apesika and seven rural communities nearby. In terms of vaccination activities, the vaccinators hold clinic activities at the facility but do not conduct outreach visits. The facility serves about 2,500 women of reproductive age within the area, including providing family planning and general gynecological and child wellness care. Provision of ANC services includes tracking basic vitals, providing health education and counseling, provision of intermittent preventive therapy for malaria, Td vaccination, physical examination, hemoglobin screening, and HIV and malaria testing.

The facility has electricity as well as a refrigerator. Given the proximity to the nearby CHPS facility, HCWs usually retrieve vaccines from that facility and leftover vaccines are then returned to the Apesika CHPS compound for storage. Vaccines that are collected from the Kintampo South Disease Control cold room are generally restocked monthly.

**Primary facilities: 2—Apesika and Babator CHPS Compounds**

There were two primary-level facilities included in the evaluation. These are also known as community-based health planning services (CHPS) compounds and are primary care facilities owned and operated by the government. These tend to be in more rural areas—the two included in this evaluation were roughly a 30-minute to one-hour drive from Kintampo township. The CHPS compounds serve about five to ten rural communities in the district. Vaccinators hold static vaccination activities at the clinic and also go on
outreach visits within the communities served by the CHPS compound. In general, outreach services rotate through the surrounding communities so that each village receives a visit once per month. There are two or three primary vaccinators at CHPS facilities, and the vaccinators in this assessment were all more junior staff with less than ten years’ experience. The facilities visited for this assessment varied significantly in the sizes of catchment populations, with Apesika serving roughly 12,000 people including 2,500 children under five years, while Babator serves roughly 7,000 people with 1,400 children under five years. The two facilities see on average 80 and 30 children, respectively, for immunization services each month.

The CHPS facilities have electricity from a mains power supply; however, only one (Apesika, the larger) had a refrigerator for keeping vaccines. Vaccinators from Apesika travel to the Kintampo South District cold room monthly to resupply the refrigerator (these vaccines may then be shared with the nearby private ANC clinic, as mentioned above, as well as other nearby clinics). At Babator, where there is no refrigerator, vaccines are retrieved from the Kintampo Municipal Cold Stores (a different cold room facility) and stored in cold boxes, at timing intervals to coincide with monthly immunization days and scheduled outreach sessions. Unused vaccine is returned to the Municipal Cold Stores at the end of the day or the following morning.

Secondary facilities: 3—Newlongoro Health Center, Anima Health Center, Dawadawa Health Center

There were three secondary-level facilities included in this evaluation. The secondary-level facilities are larger and more well resourced than the CHPS compounds, but not all have refrigerators. In this assessment, only one of the facilities had a functional refrigerator (New Longoro), but this refrigerator was not used for EPI vaccines, which were instead stored in a cold box. The facilities were all roughly one hour by car from the Kintampo District stores, where vaccine resupply occurs monthly for the facility with the refrigerator and biweekly for those without. The secondary facilities serve as first-level referral facilities for the subdistricts in which they are located and also serve a small catchment population (roughly 5,000) of their own in addition to referral services. Vaccination services are offered on fixed days at the facilities without refrigerators, coinciding with biweekly resupply days. In addition, vaccinators will travel to nearby villages for static-point outreach visits and will also travel to remote areas for outreach services. At the facilities without refrigerators, vaccines are stored in vaccine carriers between resupply days. In general, secondary-level facilities have teams of three to five primary vaccinators along with other auxiliary staff who assist with well-child visits and record keeping by registering patients, recording the child’s weight, and making a note of which vaccines are due at the visit.
Tertiary facilities

The evaluation included data collection at one tertiary-level facility, the Kintampo Municipal District Hospital, where ANC services and EPI services are offered in separate wings. The hospital serves as the referral hospital for all of Kintampo District, in addition to serving the residents of the Kintampo municipality. The ANC unit serves an average of 80 pregnant women per week and ANC services are offered daily, but Wednesdays are market days for the district, and so this day has the highest number of women at the clinic. Client records are managed on paper and entered electronically. ANC services include urinalysis, basic vitals, physical exam, tetanus toxoid (TT) vaccine, and patient education. Although there is a small refrigerator inside the ANC clinic, TT vaccine is not stored there—it is collected daily from the nearby Municipal Cold Stores and stored in a vaccine carrier, and the remainder is returned at the end of the day. The cold room facility is about a five-minute walk from the ANC facility.

The Reproductive and Child Health Unit (RCH) within the Kintampo District Hospital is where EPI vaccination sessions occur, 4 times per week. This unit serves over 6,000 children under five and gives approximately 300 vaccines per month. There are seven primary vaccinators on staff, in addition to ancillary staff who assist with record keeping. Three of the primary vaccinators are assigned to the facility while the remaining four are assigned to outreach services. Outreach services include static-point immunization services at specified times, including a table at the market on market days. The three facility-based vaccinators are responsible for the children attending well-child visits at the RCH unit as well as hepatitis B birth-dose and BCG vaccines for newborns in the maternity ward. Although there is power, there is no refrigerator in the RCH unit and vaccines are retrieved from the district cold stores and stored in vaccine carriers for daily use, with remainders returned in the evening. As with the ANC unit, the district cold stores are a five-minute walk from the RCH unit.

PARTICIPANT DESCRIPTIONS

EPI vaccinator (Community Health Officer/Community Health Nurse)

Vaccinators within the EPI program are usually more junior staff, in the first ten years of their careers, and are both male and female. CHOs and CHNs each have a secondary diploma, a two-year nursing degree, and a community health certificate. CHNs and CHOs have the same functional roles, but CHOs are also trained in management of the CHPS compounds and can operate autonomously while CHNs must be supervised by a CHO, midwife, or medic. The EPI vaccinators are responsible for well-child exams, vaccination, and administering other vitamins/therapies as needed as part of well-child visits. They may be posted to a clinic only, or conduct outreach at the village level, often alongside CBSVs.
**Midwife**

Midwives are generally more senior staff at the clinic and are usually the in-charge nurse for the facility. Beyond secondary school, midwives have a midwifery degree that includes three years of coursework plus a one-year internship. They are responsible for antenatal and postnatal services, although they generally do not provide vaccines beyond TT. ANC services include blood pressure/vitals, palpation, malaria diagnosis, intermittent preventive therapy, and bednet distribution.

**CBSV**

Community-based surveillance volunteers are representatives from the local communities who are in positions of respect and authority, usually a village leader or elder. They are recommended by their peers and nominated by the District Health Management Teams. They serve as a liaison from their community to assist the CHOs/CHNs with health activities within the community. The selected volunteers undergo a one- to three-day training on how to fill forms and detect disease cases. CBSV responsibilities include assisting CHOs/CHNs with outreach immunization and campaigns by recruiting and gathering children for vaccination, record keeping, and supply management. Prior to OPV withdrawl from campaigns, CBSVs would also give OPV vaccine in campaign settings.

**OPERATIONAL FIT CONSIDERATIONS FOR MAP**

**STUDY TASK FLOW**

- User encounters participant during routine visit.
- Briefs participant on MAP placement and wear time (> 5 minutes).
- Swabs application site.
- Removes MAP from container.
- Applies to site and activates (“click”).
- Participant completes routine visit.
- MAP removed at end of routine visit.
- Discarded in infectious waste.

**Wear time**

MAP application, wear time, and removal were integrated into routine clinic flow or, if this was not feasible, the routine flow was approximated within the context of the study. The mean wear time for the MAPs in ANC use was 10:51 minutes (range 1:25–36:14) and for EPI use was 10:46 minutes (range 3:13–21:20).* In the cases of very short wear times, the patch recipient generally had already completed most of the routine visit before the patch was applied or otherwise had a short clinic visit, such as a child who was coming in for a well-child visit but was not due for vaccination. In all cases, the MAP remained intact on the application site until it was time for removal: there were no cases of a patch falling off before removal.
Users and recipients found the wear time acceptable; however, the construct of the study and the study participants’ willingness to add on to their normal routine in order to participate may have favorably biased their perceptions of acceptable wear time.

**Clinic flow**

The fit of MAPs within the task flows of the various clinic settings varied widely by setting. This introduces a unique challenge for MAP use, in that the 11-minute average wear time may, in some cases, be split across more than one provider. That is, one provider may apply the patch and send the patient back into the clinic flow, and another provider would remove the patch. This is best illustrated by the “assembly line” approach to well-child days witnessed at Apesika and New Longoro clinics. In these cases, multiple HCWs (three and five, at each clinic respectively) would register, weigh, vaccinate, provide other vitamins and therapies, and counsel on specific well-child messages. In each case the child spent roughly three minutes with each provider, and providers ranged from minimally trained volunteers with basic literacy (weigh-ins) to clinic supervisors providing counseling to parents (often in groups). How MAPs can integrate seamlessly into widely varying clinic flows will depend largely on the final wear time for the product and the capacity of HCWs at the clinics. It may also depend on the willingness of the clinic managers and country-level EPI managers to allow for more than one person to be responsible for completing a single immunization in the cases where clinic flow demands that one HCW note what vaccines are required and apply the appropriate patch and the other removes the patch and records the completed vaccination.

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**“ASSEMBLY LINE” EPI FLOW:**

- Arrive and wait
- Weigh child

  *Lesser trained HCW records weight in child health booklet.*

- Wait 30 min
- See vaccinator

* Excludes two outliers caused by study artifacts.

**Child receives vaccines as needed. Skilled HCW delivers vaccines and records in booklet.**

- Wait 30 min
- See patient educator

  *Parent receives key health messages from skilled HCW, often in a group setting.*

- Depart
Vaccine and supplies storage

In all ANC clinics, TT vaccine was retrieved from the routine EPI supply and in all but one clinic it was stored in vaccine carriers near where ANC services were provided and then returned to the EPI supply at the end of the day. None of the ANC facilities procured or tracked their TT vaccine separately from the facility EPI supply. Only one secondary facility (New Longoro) stored TT vaccine in a domestic (non-EPI) refrigerator alongside limited supplies of other pharmaceuticals and multivitamins (EPI vaccines were stored in cold boxes nearby). As noted above, facilities restocked vaccine supplies on a biweekly or monthly schedule and scheduled immunization days to coincide with vaccine supply schedules. The resulting variations in supply availability at the clinic level could result in significant lost opportunities for vaccination between resupply days. This would be particularly true among ANC clients, whose visit schedules are not synchronized with vaccine supply availability the way they are with EPI days. Thus, the ability to store TT vaccine outside the cold chain for at least two weeks would be a particular asset to ANC workers, who would no longer have to seek out TT vaccine from outside their immediate clinic setting and could forecast and draw on vaccine supplies independently from EPI procurement, enabling more readily available access to vaccine during the course of daily tasks. Longer term, an EPI setting that uses MAPs for all vaccines could enable an available supply of vaccine at a clinic at all times, instead of following only biweekly or monthly resupply.

Village-based use

CBSVs and CHOs provide varying village-based services, depending on the scenario. During campaigns, CBSVs are used to recruit and gather village children for immunization, and during use of OPV (recently withdrawn from campaigns in Ghana) CBSVs delivered OPV and kept basic immunization records. During routine outreach services, CBSVs may travel with CHOs to villages to provide routine EPI vaccines. In this context they may serve as an extra set of hands for recruiting, patient flow management, and record keeping.

CBSVs were asked to try out the MAPs and provide feedback during group interviews. These potential users unanimously remarked on the preference for MAPs, and all appeared to correctly use the MAPs after one or two demonstrations (no data were collected on critical failures among the CBSVs due to the group environment). They noted that the MAP’s potential for storage outside the cold chain would make it easier to carry supplies to the village, and the needle-free aspect of MAPs would make them more acceptable to village children than standard vaccines. When asked about the wear time, CBSVs noted that lining up children in series to receive and then remove the patches after the designated wear time would not be a problem; however, not all CBSVs owned watches or phones to track the timing for removal. To enable MAP use in outreach scenarios, some sort of wear-time indicator would be required.
USABILITY OF MAP

In total, 16 users applied 47 MAPs to ANC clients and EPI patients during this evaluation. In the 47 applications, there were no critical errors. All users correctly handled the patches without touching or contaminating the adhesive side where the microarray would be, applied and activated the patch by pressing until the click was heard, and removed the patch. Only one user incorrectly placed the patch on the hip instead of the lower back of one ANC client recipient.

In some cases, users varied their hand placement when applying the patch. Although all users succeeded in achieving the click, in some cases this was preceded by the skin and muscle at the application site slipping over the bone as pressure was applied. Although the MAP remained in place on the site, this slippage could potentially damage the microarray, as forces applied to the array would vary in direction and strength before the array is fully embedded. This slippage was during application to children’s arms and thighs. Slippage is avoided by activating the MAP with the tip of the thumb and bracing the back side of the child’s arm or thigh with the fingers of the same hand. While this was emphasized in training, in several instances users chose variations on this hand placement, such as using a finger and bracing with the thumb, or using a finger and bracing with a second hand.

On average, MAPs were worn for approximately 11 minutes in both use scenarios in this evaluation, with a significant range in actual wear times (see Operational fit section). In all cases, the MAPs remained on the skin until the time of removal—none fell off, although in some cases parents had to monitor children to keep them from removing the MAP from the arm or thigh. Sweat was evident at the MAP site upon removal, but this did not affect the adhesion of the patch.

In addition, three of eight EPI HCWs swabbed the site with dry cotton before applying the patch, while five did not. Only one of the ANC users swabbed the site at all, and none of the users from either group used alcohol or other disinfectant to swab the site before application. No alcohol or other disinfectant was observed at any of the work stations in either group, although EPI workers had hand sanitizer that was used on their own hands between patients. In one instance, a user had removed the MAP from the tray before thinking to swab the site with dry cotton, and the subsequent shifting of the MAP between hands resulted in a piece of cotton stuck to the patch. However, upon removal and inspection, no cotton was visible in the center of the patch where the microarray would be, so this was not counted as a critical error.
ACCEPTABILITY OF MAP

No pain

MAPs were considered highly acceptable by users and recipients alike. Users preferred the simple, one-step application process and the fact that the MAP would be pain free for their patients. This was particularly emphasized among the EPI users, who noted that children won’t cry with a MAP vaccination. Parents of EPI recipients echoed this sentiment, and in several instances children slept through the entire MAP application process, confirmation that the MAP application didn’t cause discomfort to young children. CBSVs responded positively to the patch because a pain-free vaccination would be less likely to cause resistance among the village children who they are responsible for recruiting and grouping when out on campaign or outreach visits.

Acceptable pressure

There were no instances of local site reactions at the application sites, although without a vaccine-containing microarray, there are limited factors that could cause irritation. There were also no reports of bruising or other adverse events following the evaluation, and parents were satisfied that the application of the patch did not hurt their child, implying the amount of pressure required to apply the MAP is acceptable for children > 9 months.

“Abscess” (skin infection)

Several users commented on the perceived safety of the MAP for preventing abscessed vaccination sites. While this perception is not yet verified, the frequency of this comment indicates the importance placed on preventing abscess among vaccine recipients and may also imply that abscess is a somewhat common occurrence among vaccine recipients in this area. The absence of disinfection of injection sites may contribute to this. To date, preclinical and clinical studies of MAPs have not found risk of infection at the application site. Safety data on whether MAPs applied without disinfection may result in skin infection would help EPI managers prioritize ancillary resources such as disinfectant for application sites.

Preferred application sites

Among pregnant women, users unanimously preferred the wrist application site due to the ease of access—no clothing needed to be removed to access the wrist, while the arm, and particularly the low back, required recipients to remove their dresses and/or lift their hijab. Since most ANC services are offered in a group setting, this introduced considerable inconvenience as a private space was needed to apply the MAP.

Among EPI users, opinions varied, with some users selecting the thigh and others the scapula as the

—CBSV

When the children see us coming, they run away and tell all their friends to hide because they know we bring the injections. With this, they would not run away from us!
preferred application site. Those who preferred the thigh stated that this is the site where other vaccines are given, so it’s easily accessed when applying MAP alongside injections. Those who preferred the scapula noted that children would be unable to remove the patch from this site, while they may peel it off the thigh or the arm. Likewise it was noted that on the scapula it is easier to “activate” the patch.

**Recommendations for future MAP development**

MAPs were perceived as preferable to standard injection for use in immunization settings, but depending on the wear time, their introduction may require significant adaptations to existing task flows at both the facility and community levels. Application and removal of the MAPs may be done by different individuals with varying levels of training, so ensuring Instructions for Use for any future product can accommodate minimally literate HCWs, such as CBSVs in Ghana, will facilitate their introduction and uptake. Likewise, designing Instructions for Use and any other training materials for use in peer-to-peer training scenarios would help ensure that critical information is conveyed regardless of the trainer and training setting.

Several features would improve operational fit of MAPs but incorporating added features may need to be balanced against price, durability, and supply chain footprint. One such feature would be a wear time indicator: if wear time cannot be reduced to under one minute, then incorporating a time indicator, such as a color-change patch triggered by application pressure, would help ensure acceptable wear time in outreach settings and would also simplify the timing for users in clinic settings. Likewise, incorporating into the design of the patch a means for confirming completed vaccine delivery could help with task sharing in settings where MAP application and removal follows an “assembly line” approach.

Developing a product with a two-week tolerance to 40°C temperatures would enable the MAPs to be used in clinics without refrigerators between EPI resupply days. In the immediate term, where only TT and occasionally IIV are regularly used in ANC settings, this would improve maternal immunization coverage by ensuring these vaccines are available whenever a woman seeks out ANC, which may not coincide with vaccine resupply schedules.

The results of this evaluation confirm that the wrist and the scapula are the preferred application sites for women and children, respectively. More data are needed on the frequency of disinfection of application/injection sites in EPI and maternal immunization settings. If the frequency of disinfection is significantly lower than expected, exploring the safety implications of applying MAPs to nondisinfected sites may be a prudent step prior to introduction. This information may inform EPI managers’ decision-making for allocating ancillary resources such as disinfectant solution.

**RECOMMENDATIONS**

- A means for confirming complete delivery, such as dye in the microneedles
- A means for indicating appropriate wear time, such as color-change on the top of the patch
- Target wear time <1 minute
- Thermostability > 2 weeks
- Recommended sites:
  - women: wrist
  - children: scapula
- Safety data for no disinfection prior to application
Conclusion

The potential of MAPs for increased acceptability among recipients, greater ease of use among vaccinators, and extended thermostability at tropical ambient temperatures have promising implications for their introduction into EPI and maternal immunization programs. The results of this evaluation will inform the further development of the GT MAP product and, more broadly, will inform dialogue, provide recommendations for product development, and help guide MAP manufacturers to create products that fit into the global public health context. MAPs have significant potential to disrupt the current immunization supply chain and subsequently reinvent how and where vaccines can be delivered, increasing the reach of immunization services.
References


