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Review

Potential use of microarray patches for vaccine delivery in low- and middle- income countries

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ABSTRACT

Microarray patches (MAPs), also referred to as microneedle patches, are a novel methodology that have the potential to overcome barriers to vaccine delivery in low- and middle-income countries (LMICs), and transform the way that vaccines are delivered within immunization programs. The World Health Organization's Initiative for Vaccine Research and its partners are working to understand how MAPs could ease vaccine delivery and increase equitable access to vaccines in LMICs. Global stakeholders have been engaged to evaluate technical, economic, and programmatic challenges; to validate assumptions where possible; and to propose areas of focus to facilitate future vaccine-MAP product development. This report summarizes those learnings.

Contents

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1. The public health need for vaccine delivery by microarray patches (MAPs)

In line with the 2011–2020 Global Vaccine Action Plan (GVAP) strategic goals and the 2030 Sustainable Development Goals (SDG), the World Health Organization (WHO) aims to increase vaccine coverage, so that the benefits of immunization are provided equitably to all people [1]. WHO also works to accelerate development and approval of new vaccines and delivery technologies, as well as to assist low- and middle- income countries (LMICs) in implementing their immunization programs [2–4]. Microarray patches (MAPs), also referred to as microneedle patches, are a novel methodology that have the potential to transform the way that vaccines are delivered within immunization programs in LMICs, where vaccine delivery faces several challenges [5]. These include the requirement for an uninterrupted cold chain from manufacturer to point of delivery and the need for appropriate reconstitution and safe sharps disposal. Another barrier to higher vaccine coverage in these settings is the common multi-dose vial presentation, which can result in missed opportunities because of reluctance to "waste" vaccine by opening a vial to vaccinate only one or two infants. MAPs have features that can potentially address many of these difficulties.

A MAP consists of a cluster of tens to thousands of projections less than one millimeter in length attached to a backing that can be applied to the skin with finger pressure or an applicator. When applied, the projections pierce the stratum corneum to deliver vaccines to the epidermis or dermis, depending on the length of the microprojections (Fig. 1). There they encounter a high density of antigen-presenting cells (e.g., dermal dendritic cells), where vaccine delivery can evoke a strong immune response. In this review we will focus on two types of MAPs: coated and dissolving [6–8]. Coated MAPs are solid projections coated with vaccine that is then dried. After a patch is applied to the skin, vaccine diffuses into the dermis and epidermis and the projections remain attached to the backing when the MAP is removed, typically several seconds or a few minutes later. For dissolvable MAPs, the projections are formed from a polymer/vaccine-antigen blend and are designed to dissolve into the skin after penetration [7–10].

Other types of technologies also fall under the umbrella term of microneedles, including hollow microneedles that facilitate active injection of a liquid formulation and patches that use the "poke-and-patch" approach, wherein the skin is pierced with microneedles before application of a transdermal patch or topical gel/cream containing the active ingredient. However, these have substantially different characteristics from coated and dissolvable MAPs and will not be examined here [8–12].

WHO's Initiative for Vaccine Research is working to understand how MAPs can facilitate vaccine delivery and increase equitable access to vaccines in LMICs. To this end, in 2015 WHO held a consultation to evaluate technical, economic, and programmatic challenges; to validate assumptions where possible; and to propose areas of focus to facilitate future vaccine-MAP product development [1]. Among topics discussed at the meeting were preferred product characteristics, as well as the manufacturing, clinical development, regulatory and commercialization considerations since vaccine-MAPs are considered novel vaccine combination products [13,14]. The potential commercial value for vaccine-MAPs in LMIC vs. high-income country (HIC) markets may differ with respect to assessment of need, willingness to pay and acceptability of vaccine-MAPs by end-users, including vaccine recipients, their caregivers, and health care providers. This uncertainty of perceived value of vaccine-MAPs (known as the value proposition), results in complexity for developers as they contemplate investment in the product development of this innovative technology. This is particularly the case for vaccine-MAPs where there is a clear public health need for the technology in LMICs, but for which it is challenging to identify the market for a vaccine that is likely to cost more than the existing product [15]. Therefore, in cases where MAPs might be used to deliver existing vaccines, their product attributes must offer significant advantages over the existing presentations to rationalise the costs that will be required for product development and use in immunization programs.

MAPs have the potential to offer many benefits to immunization programs and patients that are of particular relevance to LMICs. These include being less costly to transport and distribute (thermostable, small footprint), easier and safer to administer (no need for reconstitution), and greater acceptability and potentially less hesitancy by end-users (needle-free) because of the perception of being less painful than administration by needle and syringe [16–25]. Below we discuss the issues outlined above and the benefits and challenges associated with MAP vaccine delivery.

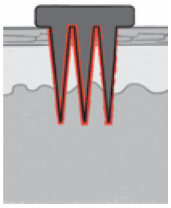
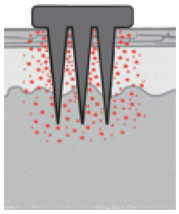
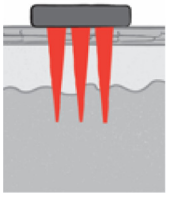
Type of MAP	MAP upon application into the skin	Release of vaccine from MAP into the skin
SOLID COATED Solid coated MAPs are made of non-biodegradable materials and coated with liquid formulation that is then dried. Upon contact with the skin's interstitial fluid, the dry formulation dissolves to release vaccine into the skin. After delivery, the intact solid projections are removed and discarded.		
DISSOLVING Dissolving MAPs are made of biocompatible, biodegradable micro-projections that encapsulate the vaccine and are designed to dissolve upon contact with the skin's interstitial fluid to release vaccine into the skin. Once dissolved, the MAP backing is removed and discarded.		

Fig. 1. Solid coated and dissolving MAPs.

2. MAP product development status and attributes for vaccine delivery

2.1. Vaccine MAPs under development

Vaccine MAPs are in clinical development for influenza and preclinical development for several vaccines. Additional vaccines have also been identified as viable MAP candidates that may be pursued in the future (Table 1). Several MAP developers have focused on seasonal influenza vaccine for the first clinical trials because of the well-accepted correlate of protection—the hemagglutination inhibition titer—that enables early demonstration of clinical proof of concept (POC), as well as the large and potentially lucrative market in HICs. The first clinical trials using three different MAP products to deliver vaccines have now been completed, with each using a form of influenza vaccine [19,25,26]. The trials demonstrated safety and similar immunogenicity for MAP administration compared with intramuscular injection using inactivated trivalent seasonal influenza vaccine (H1N1, H3N2 strain, and B strain) [19,26] or monovalent (H1N1) influenza vaccine [25].

MAPs are in preclinical development for several other existing vaccines, including measles and rubella (MR), inactivated poliovirus vaccine (IPV), tetanus toxoid, Bacille Calmette-Guérin, diphtheria, hepatitis B, human papillomavirus, and anthrax [27–34]. Researchers are also working on MAPs for vaccine candidates in early stage development, such as next generation rotavirus and dengue vaccines, malaria, hepatitis C, herpes simplex virus 2, West Nile virus, Chikungunya, HIV-1, and plague [35–42].

IPV- and MR-MAPs are the most advanced preclinical MAP candidates and non-human primate studies have been conducted with promising results [27,28]. Several MAP developers are working to develop MAPs for delivery of IPV and some have initiated manufacturing process development [28,56]. In addition, three developers, are working to advance an MR-MAP to the stage of readiness for phase 1 clinical trials [57–59]. For both applications, partnerships and strategies for product development and commercialization between vaccine manufacturers and the MAP developers will be needed to advance them beyond early phase clinical testing.

2.2. The potential benefits of MAP product attributes for vaccination in low-resource settings

Vaccine delivery strategies in low-income contexts must contend with challenges that are less of a barrier to vaccine uptake in high-income countries. Among the novel packaging and delivery technologies in the pipeline—including jet injection, sublingual formulations, and dual-chamber devices—MAPs have emerged as potentially offering clear advantages for vaccine delivery over needle and syringe in routine immunization programs, particularly in LMICs [60]. These features include better vaccine thermostability, ease of delivery, and safer administration and disposal—possibly enabling delivery via minimally trained volunteers [5,61]. Such attributes could significantly ease the logistics and reduce the cost of vaccine delivery, which would increase the equitable coverage of vaccines that are highly effective and could be particularly advantageous in outbreak scenarios but are difficult to deliver [62]. The potentially favorable product attributes of MAPs could ultimately increase equitable coverage and facilitate administration in inaccessible areas, rendering MAPs of considerable interest for delivery of several vaccine antigens. However, in the case of MAP delivery for existing vaccines in LMICs, the vaccine-MAP would be competing with the existing, established presentation, so the vaccine-MAP would need to offer considerable benefits. The minimal and preferred attributes are being developed by WHO and an expert working group in the case of MAP delivery for MR vaccine, in the development of a target product profile (TPP). The MR-MAP TPP will be made publicly available in 2019. Some general benefits that MAPs could offer to improve programmatic vaccine delivery in LMICs are summarized in Table 2.

Table 1
Vaccine microarray patch product development status.

		Microarray patch development status		
		Conceptual applications	**Preclinical**	**Clinical**
Antigen status	**Approved antigen**	Pertussis Yellow fever Japanese encephalitis	Anthrax [34] BCG [30] Hepatitis B [32,43] HPV [33] Measles-rubella [27] Diphtheria [31,44] IPV [28,45,46] Tetanus toxoid [29,31] Rabies [47]	Seasonal influenza [19,25,26]
	Investigational antigen	Cholera (conjugate) MERS Lassa fever Enterotoxigenic Escherichia coli	Chikungunya [40] Hepatitis C [38] Herpes simplex virus 2 [39] West Nile virus [40] HIV-1 [41] Ebola [48] Rotavirus vaccine (IRV) [35,49] RSV [50,51] Zika [52] Pandemic influenza [53] Dengue [36] Malaria [31,37,54] Plague [67]	

Table 2
General considerations for programmatic vaccine delivery by MAPs.

MAP Attribute	General considerations
Ease of use	Since vaccine-MAP delivery removes the need for reconstitution, and is needle-free, MAPs may enable immunization via minimally-trained volunteers and community health volunteers. This approach may facilitate delivery to communities with weak health systems, through "house-to-house" campaigns and temporary or fixed post sites. MAPs are thus ideally suited to Supplementary Immunization Activities and outbreak response as well as routine immunization.
Safety in reconstitution/ administration	Risks related to operational errors and reconstitution using wrong diluents will be removed. The risk of contamination would be reduced. Risks of needle-stick injuries would be removed.
Single-dose presentation	The single-dose presentation will reduce hesitancy to open a vial related to missed opportunities for vaccination compared to the multi-dose presentation that is available for most vaccines in the EPI setting.
Thermostability	Stability profiles might offer enhanced thermostability and improvement upon current vaccine storage requirements, allowing the removal of the cold chain equipment at health posts and stocking of vaccines at unequipped facilities.
Pain-free/reduced pain of vaccine delivery	A decrease in pain upon administration would reduce vaccine hesitancy and increase vaccine (and MAP) acceptability over vaccines currently administered by needle and syringe.
Disposal	In response to a stakeholder survey, including members of WHO's Immunization Practices Advisory Committee, the assumption is that MAPs will be considered biohazard waste that can be disposed of within the clinical waste system [63].

3. Potential use cases for vaccine delivery in LMICs

MAPs could overcome some of the major bottlenecks facing the delivery of several currently available vaccines in LMICs, including IPV, rabies, MR, hepatitis B birth dose (HepB-BD), and maternal tetanus toxoid-containing vaccine, as well as investigational candidates such as inactivated rotavirus and malaria, providing technical hurdles in MAP development specific to each of these antigens can be overcome. Some vaccines, such as those delivered outside routine immunization during infant Expanded Programme on Immunization (EPI) visits—including yellow fever, human papillomavirus, and vaccines against outbreak pathogens such as Ebola—might be suitable for MAP delivery and would benefit from increased ease of delivery and potential task shifting to minimally-trained volunteers.

3.1. Inactivated polio vaccine

As part of the polio eradication strategy, countries are transitioning from use of oral poliovirus vaccine to IPV, which is more challenging to deliver as it is parenteral and therefore requires trained health care workers to give the injection and safely dispose of sharps waste. From a public health perspective, an IPV-MAP could help to maintain high population immunity against polio as oral poliovirus is phased out and would contribute to efficient stockpiling and deployment for outbreaks [61,64].

3.2. Rabies vaccine

For rabies vaccine, adherence with the full post-exposure prophylaxis regimen is challenging due to the number of injections and stringent schedule [65]. Intradermal delivery reduces the length of the full course; however, multiple injections are required during each visit, which can decrease acceptability. Delivery of post-exposure rabies vaccine by a thermostable MAP that is easy to administer, possibly by a community health volunteer, and relatively painless could improve acceptability by eliminating multiple injections, and could allow the vaccine to be stored locally, increasing accessibility and compliance. In addition, a MAP may be applicable to pre-exposure prophylaxis for individuals who are at risk of exposure in highly endemic rabies settings.

3.3. Measles-rubella vaccine

Delivery of MR vaccine by MAP would confront a clear and urgent public health need, with approximately 90,000 deaths from measles and 100,000 cases of congenital rubella syndrome occurring annually despite the availability of a safe, effective, and affordable vaccine [66,67]. The reasons for the immunization gap may include reluctance to open multi-dose vials for one or two infants, loss of vaccine potency due to stringent cold chain requirements, and the need for use within six hours following reconstitution. For these reasons, house-to-house campaigns to deliver MR by needle and syringe are not feasible, and a methodology that overcomes these issues, such as MAPs, is needed. The predicted thermostability and ease of use of MR-MAPs would offer significant benefits in outbreak scenarios as well as routine immunization at the community level, especially in rural areas where the infrastructure for vaccination is often poor and vaccines shortages might occur more frequently [27]. In fact, it has been argued that without the availability of an MR MAP for delivery to the most remote populations and during outbreaks, regional elimination goals for these diseases will not be met [68].

3.4. Hepatitis B birth dose

To prevent perinatal or early postnatal transmission, the most important source of chronic hepatitis B infection, WHO's Strategic Advisory Group of Experts (SAGE) on immunization recommends a birth dose of hepatitis B vaccine (HepB-BD) as soon as possible after birth [69]. Although HepB-BD is considered a cost-effective or cost-saving intervention, coverage worldwide is persistently low, estimated at only 39% in 2015 [69–71]. Transport and cold chain storage limitations, as well as the lack of trained health staff represent the main obstacles to administering HepB-BD in low-resource settings [69]. A thermostable vaccine that could be stored at the community-level and administered by a community health volunteer or birth attendant could improve coverage and equity [32]. These attributes would enable—and hopefully, encourage—the home delivery of HepB-BD through innovative outreach strategies to newborns born outside of health facilities in LMICs.

3.5. Maternal tetanus toxoid-containing vaccine

Neonatal tetanus is an often fatal infection typically occurring when contaminated material is used to cut or cover the umbilical cord in neonates born to women with incomplete vaccination against tetanus [72]. Despite the significant improvement in the use of tetanus toxoid-containing vaccines for maternal immunization resulting from the Maternal and Neonatal Tetanus (MNT) Elimination Initiative and a 96% reduction in tetanus cases since 1988, it was estimated in 2015 that neonatal tetanus deaths worldwide range from 19,937 to 34,019 [73,74]. The uncertainty in these estimates reflects the poor vital registration and tetanus disease surveillance systems in most countries, where many neonatal deaths are not reported. A tetanus-MAP could improve complete

coverage with the challenging five-dose schedule required for full immunisation of women of reproductive age and pregnant women by improving access to the vaccine at the community level, where thermostable vaccine might be kept for several weeks. Vaccination campaigns might also be simplified, as health care workers will not need safe injection training.

4. Microarray patch end-user acceptability studies in LMICs

In a systematic review of factors affecting vaccine uptake in young children in developed countries, there was a strong association between uptake and the perception that vaccines are safe [75]. In regard to discomfort experienced with vaccination, the lower pain level observed with MAP administration may reduce vaccine hesitancy in children, compared with conventional needle and syringe injections [17,76]. The success of the MAP platform in pediatric vaccination will depend on its acceptance among stakeholders such as healthcare workers, caretakers, and children. Endorsement by community leaders may also encourage use of this new technology. Barriers to the acceptance of MAPs in pediatric populations must be identified and reduced by providing information and education to stakeholders [17,76].

As vaccine MAPs are still in early development, most studies of acceptability used either projection-only MAPs (without vaccine) or backing-only MAPs (without vaccine or projections) [10,16–18,20,24]. Two such studies have been conducted recently to assess the anticipated end-user acceptability of vaccine-MAPs in low-resource settings. In one study conducted in Ghana, the usability, acceptability, and programmatic fit of a dissolving MAP was assessed [77]. The MAPs consisted of prototype packaging and patches with no projections. An applicator was not required for delivery, but an audible feedback indicator was incorporated into the patch backings to provide users with assurance of correct application pressure. These mock MAPs were incorporated into standard EPI and antenatal clinic visits and were applied by health care workers to children aged 9 months to 3 years and adult women. All health care workers were able to apply MAPs correctly, and in focus group discussions, community-based surveillance volunteers also felt confident they could successfully apply MAPs in campaign settings. MAP application was acceptable to the recipients, and health care workers also appreciated the potential for thermostability, which they felt could enable vaccines to be provided without refrigeration during the periods between resupply visits. Monitoring the time that the MAP must be worn for complete immunization was identified as a logistical challenge.

A second study performed in Benin, Nepal, and Vietnam assessed the perception of MR-MAP acceptability among EPI managers and national stakeholders (i.e., district and central levels), healthcare workers, community health volunteers, community representatives, and caretakers/parents of children aged 9–23 months (Guillermet et al., accepted for publication in this issue). A simulation was performed with a mock prototype solid-coated MAP (without projections) with an integrated, single-use, spring-powered applicator, used on the upper arm and left in place for 10 s. The device was accepted with enthusiasm by most stakeholders interviewed in the study. While the device was found to be easy to use, respondents felt vaccination would be more acceptable if supervised by a HCW even for a house-to-house strategy. A concern for the need to set up a separate supply chain for maintaining vaccine potency was also raised if the MR-MAP were to be used out of the cold chain due to an improved thermostability profile.

In addition to the studies in LMICs, acceptability information was collected during projection-only MAP studies in human volunteers as well as clinical trials of an inactivated influenza vaccine MAP. These were all performed in developed countries, involving only healthy adults and using either coated or dissolvable projections. Both types of projection-only MAPs provoked mild erythema, sometimes associated with tenderness and pruritus at the application site [18,20,22]. However, the presence of influenza vaccine on MAPs increased the incidence and duration of reactogenicity, and while found to be acceptable to participants in these clinical trials, reactogenicity and acceptance may vary by antigen and recipient population [19,25,26].

In general, MAP acceptability studies to date have shown the devices to be well accepted by end-users both recipients and caregivers—and MAP administration was the preferred delivery device compared with the needle and syringe injection route [16–18,20,24]. However, the acceptability of a MR-MAP by the EPI, the community, and health workers is likely to be a major factor in the success of its implementation. The factors that support a change in current behavioral practices must be identified and considered in the product development and implementation strategy.

5. Manufacturing considerations

Currently, regardless of their format, vaccine MAPs can be produced on a small scale (up to hundreds of devices per batch) in conditions suitable for use in early-stage clinical trials. The processes and equipment required to manufacture MAPs at large scale will vary, depending on the design of the device; e.g., solid-coated or dissolving projections, with or without an applicator, or aseptic vs low bio-burden Good Manufacturing Practice (GMP) conditions [78]. Once manufacturing facility plans are in place, the timeframe from breaking ground to a fully validated, operational pilot plant is anticipated to be 2–3 years [1]. A development strategy in which a large-scale GMP manufacturing process and facility are established in parallel with phase 2 clinical testing of the first vaccine MAPs would shorten the timeline to start phase 3 trials and, ultimately, the time to licensure of the first product. However, this would require significant capital investment to be made at risk.

Key considerations for MAP manufacturing for vaccines used in low-resource settings include the scalability of production processes and costs per unit when produced at large scale. Depending on the vaccine antigens used, antigen costs could be a large driver of manufacturing costs, so production yield at each step (including the concentrating of antigen, if required) will directly impact the cost of manufacturing a MAP in relation to other presentations. Facilities, equipment, and labor associated with aseptic production are also important cost factors. There has been much debate regarding the need to aseptically manufacture MAPs since the patches are exposed to a non-sterile environment upon administration and applied to non-sterile skin, which poses a low potential-risk of infection [79]. To date, regulators have accepted early stage clinical studies to be performed with low-bioburden clinical material in which general safety and endotoxin levels of the MAPs have been tested and shown to be acceptable [19,25,26]. Whether non-aseptic manufacturing would also be acceptable for a commercial product remains unclear and would be dependent on the generation of supporting data for regulatory review as well as the risk tolerance of the manufacturer. The more conservative approach would be to use an aseptic manufacturing process, even if it is not required by the regulatory authorities.

6. Regulatory pathways

From a regulatory perspective, a vaccine-MAP will most likely be considered a new combination product since it integrates a medical device with a biologic, and both form a single product designed to be used exclusively in the given combination and which are not re-usable or refillable, and therefore similar to pre-

filled syringes used for vaccine administration in high-income countries [13]. The formulations of licensed vaccines would, in most cases, need to be modified to enable production of solid-coated and dissolvable MAPs. In addition, some national regulatory authorities (NRAs) may require an extension of Marketing Authorization or a new application for Marketing Authorization or license if there is a change in the route of administration [80,81]. Therefore, safety and efficacy data comparing the approved vaccine to the new product—including its formulation and/or its new route of administration—will be required by NRAs [81].

In the case of a MAP for an existing vaccine, supporting data from bridging studies will be needed for comparison of the new product with the already licensed product, to decrease the complexity of the regulatory process. Immunological bridging studies to demonstrate non-inferiority between the MAP and an approved product might be sufficient if a correlate of protection exists, otherwise efficacy against relevant clinical outcomes in appropriate populations would likely be required to support licensure [81]. For some vaccines, it may be possible to demonstrate immunogenicity/efficacy in some age and population sub-groups and extrapolate to others based on immune response data.

An important potential concern is that the manufacturing and characterization processes of some licensed vaccines that have been approved for decades may not adhere to the current-day quality and characterization requirements. For example, the production process may include an obsolete filtration/purification process and/or unmet qualification of the cell bank or seed lot according to guidelines considered currently acceptable by the NRA for new licensure. This represents a risk for manufacturers who may have to update their bulk antigen production process for licensing a new MAP- based product [80–82].

For the purposes of pharmacovigilance, it is likely that the FDA's Biological Licensing Application or European Medicines Agency's (EMA's) Marketing Authorization Application for the vaccine-MAP will be submitted by the vaccine manufacturer who has a license to manufacture and commercialize the combination product [83]. The optimal regulatory pathway will depend on whether the vaccine-MAP is intended for use in LMICs only or will also be marketed in HIC. The WHO Vaccines Pre-Qualification (PQ) Programme is a service provided to UN purchasing agencies and member states, ensuring that candidate vaccines are suitable (quality, safety and efficacy) for the target population and the programme. As a prerequisite to the PQ application, the vaccine must be licensed by an NRA, such as FDA or EMA, or by an NRA that has been recognized as performing essential regulatory functions according to WHO indicators [84,85]. Therefore, vaccine-MAPs intended for delivery of Gavi-supported vaccines and most other vaccines included in LMIC immunization programs must be WHO-prequalified.

If the vaccine is to be used exclusively in LMICs, the EMA's Article 58 procedure may be appropriate. This is a mechanism that facilitates prequalification of the vaccine by WHO and the registration in the specific country outside the European Union [86]. The scientific review capabilities of the EMA's Committee for Medicinal Products for Human Use, in collaboration with the local epidemiology and disease expertise of WHO and national regulators in the target countries, provide a unique development and assessment pathway for human vaccines to prevent diseases of major public health interest, intended exclusively for markets outside of the European Union. This pathway targets innovative vaccines and new developments of already authorized vaccines [87,88]. Since vaccine-MAPs are considered new products, MAP developers, in collaboration with the vaccine manufacturers, are strongly recommended to discuss their development plans with NRAs, EMA/FDA, and the WHO PQ group from the very early stages of clinical development [1].

7. Value proposition of MAPs for vaccine delivery

The attributes of MAPs render them attractive for improved vaccine delivery and coverage in both HICs and LMICs, although the priority antigens for MAP delivery may differ. In HICs, a technology that can offer the possibility of minimal pain and self-administration (for adult immunizations, such as influenza vaccine) may increase uptake. However, this may be less important than attributes such as ease-of-use, cold chain footprint, and thermostability which are critical for LMIC contexts. The value proposition for vaccine-MAPs in LMICs will need to clearly articulate the public health benefit that MAPs will offer, as well as a clear market, or willingness to pay, once the product is made available. With an unclear return on investment for the MAP product, there is little incentive to invest in product development and commercialization. More specifically, there is currently a lack of enthusiasm to invest in the scale-up of pilot facility infrastructure that is needed for late-stage clinical trials and commercial manufacturing of vaccine-MAPs. Unless this investment can be made at risk or based on small-scale clinical trial data and an understanding of the demand and business case for a specific vaccine-MAP product, this step could be a barrier to technology advancement. The technology platform-based approach could support the value proposition if, for example, learnings from the development of vaccine-MAPs for one indication could be transferred to another and if one facility could be used to manufacture multiple MAP products. The timeline to commercialization will be significantly extended if the investment in manufacturing infrastructure is delayed until clinical POC data are available or if data from development of individual vaccine-MAPs cannot be leveraged to accelerate the technology platform, as a whole.

8. Summary

For several years, academic and industry groups have invested in research and development of MAPs, focusing on various vaccines that target high- and/or low-income markets. While developers are currently focusing on seasonal influenza vaccine with emphasis on HIC markets, MAPs are perceived to have significant potential to improve vaccination coverage of several other vaccines in LMICs as discussed above, thus decreasing the burden of these often-fatal diseases. Advantages such as needle-free, reconstitution-free, single-dose presentation, and minimal pain combined with enhanced thermostability and potential for dose-sparing render this new delivery technology attractive for many vaccines, potentially transforming their reach in LMICs by enabling novel vaccine delivery scenarios. However, articulation of the use case and potential demand for vaccine-MAP products is needed to define their potential value and encourage investment through to commercialization, introduction, and impact.

One approach to accelerate product development and avoid duplication of efforts, is to facilitate sharing of lessons learned among developers. PATH's Center of Excellence for Microarray Patch Technology promises to advance development of the MAP technology platform for priority global health needs by generating and disseminating information on product development, manufacturing, regulatory pathways, and commercial viability [89]. Furthermore, a new initiative has been formed between Gavi, WHO, the Bill & Melinda Gates Foundation, PATH, and UNICEF to prioritize innovative vaccine delivery technologies, such as MAPs, that will best meet programmatic needs and improve coverage and equity in LMICs. This effort is known as the Vaccination Innovation Prioritization Strategy (VIPS) [90].

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Conflict of interest

None declared.

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