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Review

Strategies to advance vaccine technologies for resource-poor settings

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ABSTRACT

New vaccine platform and delivery technologies that can have significant positive impacts on the effectiveness, acceptability, and safety of immunizations in developing countries are increasingly available. Although donor support for vaccine technology development is strong, the uptake of proven technologies by the vaccine industry and demand for them by purchasers continues to lag. This article explains the challenges and opportunities associated with accelerating the availability of innovative and beneficial vaccine technologies to meet critical needs in resource-poor settings over the next decade. Progress will require increased dialog between the public and private sectors around vaccine product attributes; establishment of specifications for vaccines that mirror programmatic needs; stronger encouragement of vaccine developers to consider novel technologies early in the product development process; broader facilitation of research and access to technologies through the formation of centers of excellence; the basing of vaccine purchase decisions on immunization systems costs rather than price per dose alone; possible subsidization of early technology adoption costs for vaccine producers that take on the risks of new technologies of importance to the public sector; and the provision of data to purchasers, better enabling them to make informed decisions that take into account the value of specific product attributes.

Contents

Abbreviations: AD, autodisable; LIC, low-income country; LMIC, lower-middle-income country; OPV, oral polio vaccine; PDP, product development partnership; R&D, research and development; UNICEF, United Nations Children's Fund; VPPAG, Vaccine Presentation and Packaging Advisory Group; WHO, World Health Organization.

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1. Introduction

1.1. Background

New methods to formulate, produce, package, and deliver vaccines can have significant positive impact on the effectiveness, acceptability, and safety of immunizations. They also can influence cost and speed of product availability—sometimes in negative ways. This document provides a high-level overview of representative previous efforts to advance new vaccine platform and delivery technologies in low-income country (LIC) and lower-middle-income country (LMIC) markets. It highlights achievements and failures, major themes in terms of barriers and challenges, opportunities, and proposed strategies and actions to accelerate the availability of innovative and beneficial technologies to meet critical needs in resource-poor settings.

1.2. Current situation

In recent decades, a number of vaccine technologies have traveled the long road from discovery to successful global use. These include autodisable (AD) syringes, stability improvements to measles vaccines, and vaccine vial monitors. In contrast, many other vaccine technologies have either failed or have not yet achieved their potential. An example of a failure includes past efforts to improve the stability of oral polio vaccines. Existing technologies that have not reached their potential include the Uniject™[2] compact prefilled AD injection system, needlestick-prevention devices, and new adjuvants.

The current environment for vaccine technologies is a paradox. Donor support for vaccine research is strong, both through direct grants on focused technologies and investments in product development partnerships (PDPs) [1,2]. Fascinating research and development (R&D) efforts are under way offering an array of potential improvements to vaccine products. Never before have so many biotechnology and device companies, academic institutions, non-governmental organizations, and individual inventors been so focused on vaccine technologies in the context of the needs of developing countries. Global advocacy around these issues is, indeed, paying off. The other half of the paradox is the lack of uptake of these novel technologies by the vaccine industry and the lack of demand by purchasers.

The following is an attempt to explain and illustrate the key drivers behind this paradox and to discern a way forward that would take advantage of the rich R&D pipeline, identifying and supporting technologies worthy of investment and adoption.

2. Main barriers and challenges

2.1. Scientific

2.1.1. Difficulties assessing the impact of technologies applied to antigens

Some scientific challenges for vaccine technologies are inextricably entwined with the challenges associated with the antigens to which the technologies are applied. The application of a new technology to a vaccine must be carefully assessed for its impact on the potency and safety of the vaccine using the best available methods. Technology developers either require access to the antigens and test methods or need to rely on vaccine producers to conduct the testing. Some technology developers lack sufficient pharmaceutical industry expertise to carry out the work on their own. To further complicate matters, strong correlates of immunity are simply not available for some vaccines such as whole-cell pertussis.

Example: *changes to an existing vaccine*. Reformulation of a vaccine with new stabilizers, a new adjuvant, a new container, or new format (such as microneedle patches) would require testing the new formulation against an entire battery of in vitro and in vivo assays. For multivalent vaccines, each antigen would need to be tested and deleterious effects on one antigen could negate neutral or positive effects on another antigen. If laboratory data are promising, then clinical trials would be a required next step. The later the change is made to the vaccine in the product development process, the more costly and difficult it is likely to be.

2.2. Commercial

2.2.1. Many technologies require vaccine industry adoption

Many categories of vaccine technologies—including formulation, production, packaging, and integrated delivery technologies—require incorporation directly into vaccine manufacturing processes or products and cannot move forward without vaccine industry uptake. Such adoption usually requires laboratory and clinical studies, capital expenditures, intellectual property (IP) evaluation, and licensing arrangements. In contrast, stand-alone vaccine technologies can be distributed independently from the vaccine industry and can often be fast-tracked to global availability.

Examples: *AD syringes and the Uniject™ injection system.* In 1987 the World Health Organization (WHO) called for designs of AD syringes with features to prevent inadvertent or intentional reuse. In response, a technology (SoloShot™)[3] was developed, underwent field testing in 1990, and was commercially available in 1992 [3,4]. Competitive brands quickly emerged thereafter and average prices dropped from a United Nations Children's Fund (UNICEF)-subsidized price of US$0.13 in 1992 to an open market price of about US$0.06 per syringe [5,6]. One reason for the quick success and broad availability is that AD syringes are purchased directly from the syringe manufacturers and do not require adoption by the vaccine industry.

In contrast, the Uniject injection system must be adopted by vaccine producers as a new container for vaccine products. Work on the Uniject injection system also began in 1987; however, the device was not commercially available to producers until 2000 due to the lengthy processes required to prepare and validate the device for use with specific vaccines in collaboration with vaccine producers. This work included developing Uniject filling equipment, conducting pilot filling, conducting clinical studies, and obtaining regulatory approvals. Although shown to be cost-effective [7] and beneficial in multiple countries with both tetanus toxoid [8] and hepatitis B vaccines [9,10] and advantageous over end-user-filled AD syringes [11], today, only one vaccine producer, BioFarma (Indonesia), commercially supplies these vaccines in Uniject [12]. Another, Crucell, is working toward

[2] Uniject is a trademark of BD.

[3] SoloShot is a trademark of BD.