Impact of New Vaccine Introduction on Developing Country Immunization Programs: A Review of the Grey Literature

Prepared by the USAID-funded Maternal and Child Health Integrated Program (MCHIP) for the World Health Organization

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Acronyms

AEFI	adverse event following immunization
AP	Andhra Pradesh
CDC	U.S. Centers for Disease Control and Prevention
CVI	Children's Vaccine Initiative
DTP	diphtheria, tetanus, pertussis vaccine
EPI	Expanded Program on Immunization
GAVI	Global Alliance on Vaccines and Immunization
Hep B	hepatitis B (virus)
HBV	hepatitis B vaccine
Hib	*Haemophilus influenzae* type B (vaccine)
HPV	human papillomavirus virus (vaccine)
IPV	inactivated polio vaccine
MCHIP	Maternal and Child Health Integrated Program
MMR	Measles, mumps, rubella (vaccine)
MoF	Ministry of Finance
MOH/MoH	Ministry of Health
MTEF	Mid-term expenditure framework
NGO	non-governmental organization
NUVI	new and underutilized vaccine introduction
OPV	oral polio vaccine
PATH	Program for Appropriate Technology in Health
PCV	pneumococcal vaccine
PIE	post-introduction evaluation
RV	rotavirus vaccine
SAGE	Strategic Advisory Group of Experts
VVM	vaccine vial monitor
WHO	World Health Organization
WHO/AFRO	WHO Africa Regional Office

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Executive Summary

As part of a multi-pronged effort to extract lessons and provide improved guidance to countries on new vaccine introduction, experiences described in the grey literature were identified and summarized. Despite several challenges in extracting solid information, many interesting and useful findings emerged. The ease of introduction and its effects on EPIs and ministries of health appear to be significantly related to: the vaccine, its formulation, presentation, and packaging; the strength of the EPI at the time of introduction; and the duration and quality of preparations for vaccine introduction. In general, the main areas in which new vaccine introduction appears to strengthen EPIs are in public perceptions (with some notable exceptions), cold chain hardware and storage capacity, and potential impact on morbidity and mortality. The main areas in which new vaccine introduction can stress or potentially harm EPIs are in cold chain logistics and long-term financing of new vaccines and their associated costs. More time and attention devoted to planning and preparations – as well as a taking a longer-tem view towards system improvement -- would allow EPIs to take better advantage of new vaccine introduction to strengthen weak system components.

1. Introduction

Under the auspices of WHO's Impact of New Vaccine Introduction workgroup, and in response to a request by WHO's Strategic Advisory Group of Experts (SAGE), the USAID-funded Maternal and Child Health Integrated Program (MCHIP) undertook a review of the grey literature on the effects of new and underutilized vaccine introduction on national EPIs and health systems. This review is part of a larger assessment that includes a review of published literature (by the U.S. Centers for Disease Control and Prevention), an analysis of national data by the Johns Hopkins University School of Public Health, and country case studies (by the London School of Hygiene and Tropical Medicine and PATH). The results are intended to inform new tools and guidance from WHO and partners on how countries can undertake smooth new-vaccine introductions that have ongoing benefits to health services.

2. Methodology

The MCHIP team consisted of a senior researcher and a young researcher with excellent computer skills. Their review focused on the experiences of lower and middle-income countries, because of the major international effort to support vaccine introduction in those countries and because of the likelihood that the issues and experiences in the richer countries would be quite different.

MCHIP undertook numerous literature searches on the Internet, requested documents from personal contacts, and posted a call for documents on TechNet and in Global Immunization News. Besides helping identify documents, other MCHIP staff and members of the working group on new vaccines provided comments and suggestions on the draft report. The systematic search strategy focused on literature dating from January 2000 to October 2010, although a few relevant documents dated prior to 2000 were identified and included. The team supplemented the grey literature documents with two interviews with persons who had been involved in planning or assessments of vaccine introduction.[29, 30]

A substantial effort was made to search databases using the mix of free text and MESH terms. The databases searched were Popline, PubMED, Cochrane Library, ELDIS, System for Information on Grey Literature in Europe (SIGLE), CAB Abstracts, and WHO regional office databases. The team also carried out a three-way search of the Internet, which included free text searches in Google using the same keywords; a search of conference proceedings, such as the New and Under-utilized Vaccine Retreats; a search of web pages of international organizations, bilateral agencies, nongovernmental organizations (NGOs), consultancy firms, and universities involved in the vaccine introduction, such as the Global Alliance for Vaccines and Immunization (GAVI Alliance), WHO, UNICEF, MCHIP, the Program for Appropriate Technology in Health (PATH), and the Johns Hopkins University School of Public Health.

The literature search comprised keyword terms relating to vaccines and freetext terms relating to health systems, immunization systems, health planning, and capacity. Additionally, searches were carried out using the following terms: hepatitis B, Hep B, *Haemophilus* vaccine, Hib vaccine, pneumococcal vaccine, pneumo, PCV, rotavirus vaccine, rota vaccine, meningococcal vaccine, yellow fever vaccine, Japanese encephalitis vaccine, papillomavirus vaccine, HPV vaccine, new vaccine introduction, cold chain, delivery of healthcare, "delivery of healthcare" AND immunization, "capacity building" AND immunization, and numerous other terms used interchangeably.

The review team considered as grey literature hard- or soft-copy documents that were not peer-reviewed or published commercially. From the hundreds of documents examined, the MCHIP team included 59 that contained information on the impact of new vaccine introduction on immunization programs and, in a few cases, the broader health system. Major document types were post-introduction evaluations (PIEs) led by WHO, trip reports, studies, organizational reports, and meeting presentations and summaries. Documents that only discussed the decision-making process to introduce new vaccines, but that did not discuss the effects of the introduction afterwards, were excluded. The team carried out some Internet searches to expand or corroborate other information. They had to make judgments on the reliability of information on websites, including newspaper articles, and excluded many such sources. In general the team accepted relevant documents, including PowerPoint presentations, that were associated with respected international organizations such as WHO, UNICEF, USAID and PATH.

The review team summarized relevant information using the health systems components in the WHO health systems framework (described in WHO, *Key components of a well functioning health system*, May 2010).

Assessing the impact of vaccine introductions on EPIs and on broader health systems, on the basis of the documents reviewed, was challenging for several reasons:
►Three of the vaccines of particular interest – pneumococcal vaccine (PCV), rotavirus vaccine (RV) and human papillomavirus vaccine (HPV) – have been introduced into developing countries only in the last few years, so it is too soon to obtain substantial, in-depth feedback.
►Most documents that describe national immunization programs, but that are not *about* new vaccine introduction, fail to mention the effects of new vaccine introductions on EPIs or health systems.
►PIEs, conducted six to 12 months post-introduction, focus more on preparations for and occurrences during the introductory phase than on long-term effects. PIEs and other documents describe strengths and weaknesses of EPIs but may not link these directly with the introductions.
►PIEs and other assessments of vaccine introductions report on a particular point in time. A report shortly after an introduction might find problems of insufficient transportation capacity to move the new vaccine to districts around the country, but a report a year later might not corroborate these early problems.
►PIEs are considered by WHO as confidential documents, prepared to guide country actions, and not intended to be widely disseminated. While very useful sources, in many cases only PIE summaries from WHO were available, rather than full documents, and they sometimes contained contradictory or incomplete information.
►It was also difficult to separate out the effects of the new vaccine introduction from the effects of funding from the GAVI Alliance or other donors that often accompanied the introduction.

Undoubtedly, the active search strategy followed failed to capture some documentation housed on shelves and in the files of persons involved in vaccine introduction.In particualr, little information was found linking changes in broader health systems with new vaccine introduction, and the team did not conduct broad, but likely fruitless, searches on health systems. Finally, simultaneous government and donor initiatives and other contextual factors make it challenging to link new vaccine introduction with changes in overall health systems.

Despite these challenges, this review was able to capture much useful information, which, triangulated with findings from from the other studies commissioned by the Impact of New Vaccine Introduction workgroup, should provide useful lessons learned and guidance for the future.

3. Findings

3.1 Determinants of the Impact of Vaccine Introduction on Immunization Programs

In Brief: Based on the grey literature examined, it appears that the major determinants of the impact of new vaccine introduction on national immunization systems include: (1) the vaccine introduced, its formulation, presentation, and packaging; (2) how well planned, managed, and funded the existing EPI was at the time of introduction; and (3) how well planned and executed the vaccine introduction process was.

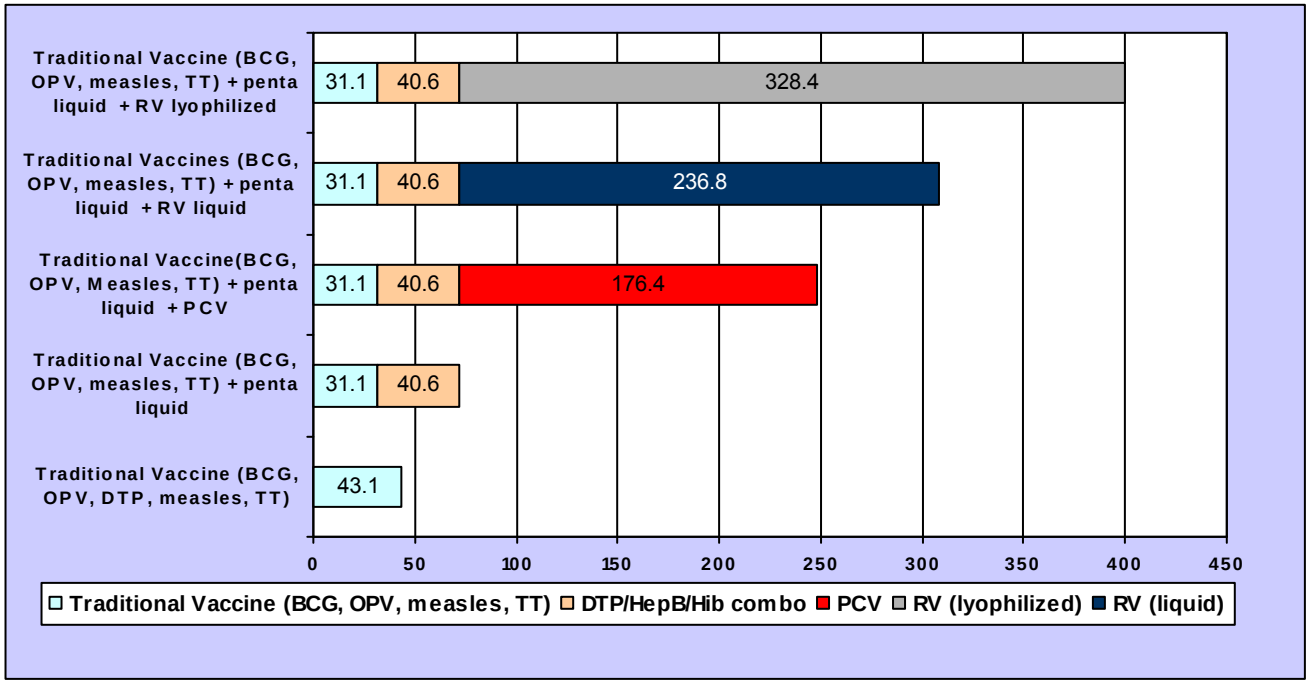
3.1.1 The vaccine, its formulation, presentation, and packaging. The grey literature indicated that vaccine formulation, presentation, and packaging can ease or complicate the incorporation of new (or under-used) vaccines into an immunization system and their effects afterwards. Generally, transitioning either from DTP to DTP-HepB (liquid tetravalent) or from DTP or liquid tetravalent DTP-HepB to liquid DTP-HBV+Hib (the most common form of pentavalent) are relatively easy changes, although: (1) introducing DTP-HepB+Hib becames slightly more complicated if Hib comes in lyophilized (freeze-dried) form, which requires new health worker skills as well as use of syringes for reconstitution and their safe disposal; and (2) the liquid form of monovalent Hib requires substantially increased cold chain storage and distribution capacity (see Figure 1).

Most EPIs also appear to handle well adding liquid hepatitis B vaccine (HBV) or Hib as separate monovalent injections. However, a birth dose of HBV, which should be given within 24 hours after birth, can present a major challenge where most births do not take place in facilities or are not attended by skilled birth attendents.

A few of the documents indicated that adding a new monovalent vaccine was a concern to some parents and/or health staff because it implies an additional injection on the same visit, but this did not emerge consistently as a significant issue.

The introduction of RV, PCV, or HPV has the potential to stress limited budgets, and the cold chain (storage capacity, volume of vaccine and frequency of distribution, fuel for and maintenance of new equipment). The latter problems emerged even in lower middle-income countries with strong EPIs, although generally they were resolved within a year or so.The graph below illustrates the impact of the relatively huge volume of several new vaccines.

Figure 1: Vaccine Volumes Per Fully-Immunized Child (cm³)



Source: Re-created from a graph in S. Kone and M. Dicko, Preparing the Cold Chain for New Vaccine Introduction, 3rd Global Immunization Meeting, CICG/Geneva, 19 - 21 February, 2008.[35] *Note: storage volumes per dose for PCV and RV have been reduced in the past year through more streamlined presentations and packaging.*

The box below summarizes how vaccine characteristics can either support or hinder smooth introduction.

Box 1: Preferred Vaccine Characteristics

►Vaccine and diluents that can be stored at temperatures above +8ºC, esp. freeze-sensitive vaccines
►Vaccines that come in ready-to-use formats
►Multi-component vaccines that have a short and simple preparation process
►Vaccine that comes in small, standardized volume-per-dose and that have a small packed volume
►Multi-dose vials without preservative that have one or very few doses per vial
►Multi-dose vials with preservative that have <=20 doses per vial
►Packaging of vaccine and diluent with the same number of doses per package; e.g. if lyophilized vaccine vials are packaged in secondary containers 100 to a box, the vial of diluents should not be packed 30 to a box, as this will inevitably lead to unmatched quantities sent from level to level
►Primary and secondary packing and injection materials that minimize environmental impact
►Where appropriate, components that are packed and shipped together (bundled)
►Vaccine that is affordable in the short and longer term

Problematic Vaccine Characteristics

►Pre-filled syringes that have a large cold chain volume, not auto-disabled, no vaccine vial monitors (VVMs), difficult to dispose safely
► Liquid vaccine in multi-dose vials, without preservative, which presents an unknown risk of health workers keeping opened vials for future sessions
►Oral vaccines whose packaging that may be confused with pre-filled devices, so they are erroneously injected
►Multi-component vaccines whose different components differ in heat stability, resulting in difficulty in assigning VVMs
►Vaccines that are not affordable after an initial period of donor support

Adapted from: Rudi Eggers, WHO/EPI, "How do we get the vaccine presentations that we need?" Presentation to TechNet Meeting, 30 Nov – 2 Dec 2010.[25]

Near-term introduction of PCV in some countries may be in the form of PCV-10, which comes in a liquid two-dose vial *without* preservative. This may challenge the current understanding of health workers accustomed to keeping opened, multi-dose vials of liquid vaccines (such as penta) for use on subsequent days. Consequently, efforts are underway to design a visual cue on the vial label to alert health workers that this particular liquid vaccine must be discarded at the end of the session or within six hours of its opening, whichever comes first. Transmitting this safety information entails a considerable training burden, as well as enhanced adverse events monitoring to detect if adverse events do arise.[54]

3.1.2 Strength of the EPI at the time of introduction. Better-managed EPIs with stronger system components appear to accommodate vaccine introduction more easily than poorly managed and under-resourced EPIs. Many programs did expand their cold chain storage and equipment inventories as part of preparations for new vaccine introductions, and most implemented technical training focused on the new vaccine as well as broader immunization skills. Despite these positive steps, PIEs of weaker EPIs typically found performance problems in cold chain management, data collection and use, and other areas. It should be mentioned, however, that even relatively strong EPIs, such as those in Brazil and Turkey, experienced short-term stresses because of the storage and transportation requirements of the bulky new vaccines they introduced.

3.1.3 Duration and quality of preparations for vaccine introduction. Some new vaccine introductions are well planned and executed, but it appears to be fairly common for mild chaos to emerge as the launch date approaches. Some EPIs carry out appropriate assessments and make corresponding plans to prepare for the introduction, but then lack sufficient time, staff or other resources to complete planned training, construction of new cold storage rooms, revision of forms, etc. Others have sufficient planning time (a year or more), but the EPI and partners do not feel the urgency of action until the launch approaches. A few countries, including South Africa and Rwanda, felt compelled to implement a rolling introduction because, when the time came, they were not ready for a national one. One southern African country, which introduced PCV, RV, and pentavalent vaccines together in 2008/9, encountered a number of challenges, including staff shortages, late delivery and installation of refrigerators, and the need for training on a huge scale. Key recommendations of the EPI manager afterwards were: multi-year planning that included securing broad financing and guaranteed vaccine financing at all levels, and more time to address human resource, cold chain, and regulatory issues.[56] One South American country that introduced PCV, RV, and influenza vaccines together in 2008, appears to have garnered sufficient political commitment and funding and to have carried out effective preparations so the multi-antigen introduction came off smoothly and even "strengthened local management."[11]

Box 2: Pressure to Launch

The *reasons* for intensive, last-minute efforts to meet an immunization launch date vary. Launch dates may be as much a political as a technical decision, and once set, high officials are reluctant to delay them, even when such problems as late arrival of vaccine or refrigerators arise. Pressure to launch comes from various sources: perceived pressure from donors and vaccine manufacturers, who occasionally enlist support from the media; national officials who desire to have their country be the first to introduce a new vaccine or who need a visible public achievement; the availability of sizeable funding support from GAVI Alliance or other donors, which country officials feel compelled to take advantage of.[31, 32, 33]

Several of these factors came into play in stimulating the introduction of hepatitis B vaccine in the

Philippines in the early 1990s. An assesment 10 years later reported that: "… many political, financial and procurement problems were encountered which have prevented the full integration of HBV into EPI and full coverage of the target population after almost ten years. This experience was cited as a barrier to consideration of other vaccines…. Financing the purchase of HBV has been an on-going problem and … Government had been unable to purchase enough HBV for 100% of the target population…."[33]

3.2 Service Delivery

In Brief: Most new vaccines have little impact on vaccination schedules. Exceptions are HPV, which targets adolescent or pre-adolescent girls, the birth dose of HBP, and the challenge of the strict upper age limits of RV. There are some data and strong perceptions that new vaccine introductions have helped improve coverage, but overall evidence is mixed. Global or national shortages of new vaccines have temporarily harmed coverage in a few countries, and at least initially RV coverage lagged behind DTP in Latin America. Wastage of new vaccines appears to be minimal because they often come in one-or-two-dose presentations, and health staff are reportedly motivated to avoid wasting expensive vaccines. Public acceptance of new vaccines has been strong in most countries, regardless of the extent or quality of social mobilization/communication activities. There are a few reports that vaccine introductions improved the image or perceived importance of the EPI. In a relatively small number of countries, anti-vaccine or anti-government movements have vocally opposed new vaccines and the EPI. Overall, vaccine introductions appear to have had little impact, positive or negative, on communtiy involvement in immunization.

3.2.1 The vaccination schedule. With few exceptions, the impact of new vaccines on national immunization schedules appears to be minimal, since administration of HBV, Hib, PCV, and RV generally conforms to existing contacts for DTP. However, the birth dose of HBV should be given in the first 24 hours of life, a period that is much more stringent than the recommended periods for OPV0 (within 14 days of birth) and BCG (as soon as possible after birth). WHO recommends that RV "…be administered between the ages of 6 weeks and 15 weeks, and that the maximum age for administering the last dose of either vaccine should be 32 weeks. In June 2009, the Global Advisory Committee on Vaccine Safety conducted a review and found that no data offered statistically significant evidence that the increased relative risk of intussusception associated with the earlier rotavirus vaccine was associated with the age of administration of the first or last dose." *Weekly epidemiological record*, 22 July 2011, No. 30, 2011, 86, p. 320.

Some EPIs have to deal with an additional injection being given during regular visits. In Rwanda, this was explored in formative research and dealt with well in health worker training and communication to caregivers. In Ukraine, there was some resistance among health workers to administer an additional injection (Hib monovalent vaccine).

The main impact of new vaccines on the schedule in most countries has simply been the need to modify forms, registers, and cards to accommodate the new vaccine. PIEs indicate that this has usually, but not always, been completed before the introduction.

3.2.2 Coverage, missed opportunities, vaccine wastage. Many PIEs report that health workers and officials felt that the introduction had improved attitudes towards the EPI and had increased coverage. A synopsis of seven African PIEs reported that, "…introduction actually positively affected coverage in most countries…. It was reported that many caretakers whose children had already received DTP or had just exited the DTP series came to facilities asking for hepatitis B vaccine for their children. In countries where monovalent presentation of vaccines was introduced (e.g., Benin) coverage was much higher with hepatitis B compared to the DTP."[38] A WHO group also noted that, "New vaccines have improved the overall coverage of routine EPI vaccines," although noting that in some countries, such as Pakistan, this did not

happen. This source suggested that combination vaccines have been associated with improved timeliness of the administration of both routine and new vaccines."[2]

In some cases these perceptions were based on data, in others on impressions. There are also a number of instances in the literature in which, at least temporarily, new vaccine introduction had a detrimental effect on coverage – generally because of vaccine-supply problems related to global shortages or national inability to distribute the bulky new vaccine rapidly enough. It is possible that the strict lower and upper age limits for RV adminstration may result in lower coverage than hold down coverage than for DTP-containing vaccine.

In the absence of studies of coverage data that control for confounding factors, the grey literature indicates that the publicity, enhanced image of the EPI, and quality improvements associated with new vaccine introduction *can* lead to a rise in coverage in some countries, but this does not appear to have happened consistently. Possibly, the more reliable the supply of vaccine and stronger the public interest in the disease the new vaccine addresses, the more likely such increases will occur.

One analysis found that two years following HBV introduction, coverage levels for the new vaccine reached the level of DTP3 in about two-thirds of countries Coverage at the time of introduction and GAVI support were strong predictors of rapid catch-up.[57]

Most evidence points to less wastage of new vaccines than traditional ones, due to generally fewer doses per vial and/or health worker concern with wasting such expensive vaccines. In Benin and Malawi in particular, the latter concern also led to reduced number of vaccination days and to more missed opportunities.(AFRO 2004)

Box 3: Country Experiences/Coverage, Wastage

People interviewed for the *Mozambique* PIE (2002), approximately a year after tetravalent vaccine introduction, expressed the view that **"**…the introduction of new vaccine had increased the overall attendance at immunization sessions."[45]

In the Republic of *Georgia*, uptake of HBV in 2002 was slow due to negative media publicity regarding suspected cases of adverse events following immunisation (AEFI). This publicity also prompted a drop in DTP3 coverage. Financial and management issues that arose from decentralization further complicated the progress of HBV coverage.[57]

The WHO/AFRO EPI Mid-Term Review in *Ghana* conducted in August 2003 found that the pentavalent vaccine introduced in 2002, with GAVI financial assistance, had been effectively incorporated into the system and had resulted in increased coverage, reduced wastage, and improved operations for routine immunization. However, a 2004 EPI review found high dropout rates in some districts. Wastage rates, meanwhile, had decreased since the introduction of pentavalent vaccine, due primarily to the shift to two-dose vials and the added focus on training, supervision, and reporting.[42]

An EPI review in the *Gambia*, four years after the introduction of HBV and Hib in 1997, found that coverage had generally fallen since the introduction. One factor was the erratic supply of new vaccines, especially of Hib: "Children have been denied the four antigens (DTP + Hib) although the DTP was available."[24]

A review of experience in African countries noted that "In some countries, in *Benin* and *Malawi* in particular, the effort to reduce vaccine wastage led to reduction in the number of immunizations day[s] per week as health workers would prefer regrouping children on a given day to fit the number of doses in vaccine vials." This occurred particularly with lyophilized vaccines and may have resulted in "a lot of missed opportunity that could have resulted in reduced coverage."[38] A similar phenomenon was reported

in the Ukraine with the 10-dose tetravalent vaccine.[44]

3.2.3 Public perceptions of the EPI. There are some reports that the publicity around the new vaccine launch, including the involvement of national leaders, along with an intense information campaign, led to more EPI visibility within government and an improved image among the public, e.g. in Rwanda and the Dominican Republic. In a few countries, shortages of the newly introduced vaccine had detrimental short-term effects on community confidence in immunization services, as in Kenya and Gambia, which suffered the consequences of global shortages of pentavalent vaccine.[22, 24] There were also a few reports of confusion among both health workers and the public about whether children who had started their DTP series should or should not receive the new tetravalent or pentavalent vaccine.

Most countries plan and implement some level of communication to explain their new vaccine introductions to the public. Channels typically include radio, print materials, and information from health workers. Only a few countries (such as the Dominican Republic and Rwanda) based based communication activities on in-depth formative research with health workers, leaders and families. Some communication plans were not fully implemented because the preparatory period was too short.

One interesting pattern found in many of the approximately 30 PIEs reviewed was good public acceptance of the new vaccine despite limited communication efforts and poor parental knowledge about the vaccine and disease it addresses (see Box 4).

Box 4: Good Acceptance despite Limited Public Communication

The PIE following HBV (tetravalent) introduction in a southern African country (2001) described some social mobilization and communication activities at the time of launch and in facilities; however, "exit interviews … at immunization sessions revealed that none of the mothers interviewed knew either the vaccines their children had received or the target diseases they have been vaccinated against…..Mothers had no idea that a new vaccine [was] being introduced into the programme." Despite this, "…the introduction went smoothly and was successful."[45]

A PIE summary from West Africa noted that "Penta [was] well accepted by parents," although "[n]o communication activities [were] conducted by regional or district heatlh authorities." In another country, there was some communication before the launch but little afterwards. "[The m]ajority of caregivers interviewed did not know what diseases PCV-7 vaccine prevented." Still, the vaccine was "generally well accepted." In yet another west African country, "although …[health workers were] well prepared to provide information," there was "[w]eak interpersonal programme communication" and a "[g]eneral lack of awareness by mothers regarding diseases prevented by the vaccine." Still, the "Vaccine [was] well received by [the] community – no refusals." In yet another West African country, health workers did not know the benefits of the new vaccine…and parents had minimal knowledge of the vaccine or diseases. Nonetheless, there was "[g]ood acceptance of penta by parents."[40]

A PIE summary from central Africa noted that the "[n]ew vaccine [was] well accepted by population…and by health personnel," despite "[m]others' lack of knowledge of the diseases for which children are vaccinated." In another central African country, there were "[n]o communication activities conducted by health provinces or zones," but "Penta vaccine [was] well accepted by parents."[40]

A PIE summary from the Horn of Africa noted some mass media, print materials, and (weak) interpersonal communication, but "no promotion of new vaccine in the community." Mothers realized the importance of vaccination but not which illnesses they prevented." There was "[n]o resistanace to the new vaccine [Hib] in the community." In a neighboring country, "Social mobilization using media and printed materials [was] limited at peripheral levels," and "[h]ealth workers [were] unaware of and not providing key messages o[n] the benefits of penta to caregivers." The vaccine was "well accepted."[40]

Some, but fewer, countries reported both strong communication and good acceptance (Box 5).

Box 5: Strong Communication with Good Acceptance

In a South American country, there were well-planned and executed communication activities, and "92% of health units report having experienced no resistance in the community on rotavirus vaccine."[40]

In Rwanda there was both strong communication, based on formative research, and good acceptance of PCV.[49]

In Sudan also, there was strong communication, good parental knowledge, and good acceptance of the new vaccine (Hib). The PIE judged that "The new vaccine has renewed trust in immunization…and [reduced the] number of injections."[40]

Finally, there are the cases of poor acceptance with or without well-planned communication efforts, mainly in eastern Europe. The introduction of monovalent Hib lyophilized vaccine and then lyophilized tetravalent DTP-Hib in Ukraine led to sustained vocal opposition by the active anti-vaccination community in that country. There was little preparation of the public on the need for Hib vaccine. No information packets with educational materials targeting parents and the medical community were developed at the central level. Education of parents was left to health workers, but this effort was clearly inadequate.[44]

A UNICEF assessment of public attitudes towards vaccination in eight countries in Central and Eastern Europe and the Commonwealth of Independent States found:

- **"…**a collapse of public trust in health systems including public trust in primary health care workers and services, as well as key health messages."
- Because of such attitudes, several countries have introduced new vaccines in services with no communication activities for the public. Health workers had briefings and/or training.
- Strong anti-vaccination sentiment among younger, better educated, urban populations predisposed to resisting state interventions
- Many different communication activities taking place but with little coordination, strategy or national ownership (they were mainly donor driven)
- None of the eight countries assessed have any dedicated budget for health promotion beyond operational costs.[19]

Where there is an active anti-vaccine movement, or where political opposition might use vaccine introduction as a wedge against the ruling party, significant pre-introduction communication and advocacy may be needed. However, in other cases, particularly where vaccination and the EPI are well accepted and the new vaccine requires no changes in the vaccination schedule, number of injections, or venues for vaccination, communication efforts can focus on informing people about the introduction, the benefits to them, the vaccine's safety, and the idea that they will get more protection with no additional effort. Every EPI, however, should have materials and health staff ready in case of negative publicity and should periodically interact with key media figures. It is also advisable for health workers to be trained on how to address resistance or misinformation when they encounter it.

An example of an effective "counter-attack" occurred in Ghana, where a front-page newspaper article, prepared by the anti-vaccination movement, stated that Ghanaian children were being

used as “guinea pigs” for a new combination vaccine donated by pharmaceutical companies. The Ministry of Health effectively countered the article by taking a public stand.[38]

3.2.4 Community involvement in immunization. WHO/AFRO recommends engaging community-based structures to mobilize the community for acceptance of new vaccines and increase the uptake of traditional EPI vaccines. With sufficient preparation time, there is potential for the introduction process to more fully engage community leaders and groups in supporting immunization. Traditional chiefs in some African countries were briefed about new vaccines and given responsibility for mobilizing their communities. The Mozambique EPI prepared a booklet to help community leaders respond to people’s questions about tetravalent introduction, although a subsequent PIE found mimimal evidence of community-level advocacy. In the Dominican Republic, there was minimal participation by community leaders in promoting immunization and immunization services either before or after pentavalent introduction.[16]

Overall, vaccine introductions appear to have had little impact, positive or negative, on community involvement. One exception is Ghana, where the 2004 EPI review reported that there was a strong community involvement in the programme through district assemblies and community structures/community volunteers and that DTP3/Penta3 has been selected as a major indicator for monitoring the district assemblies’ performances.[42]

3.3 Health Workforce

In Brief: Many countries have taken advantage of vaccine introductions to provide additional training, and support materials to health staff. Although useful, in many countries these steps did not sufficiently address deficiencies in such areas as vaccine management and in collection and use of data persist. In a few countries, staff complained about extra work that vaccine introduction brought. Funding that accompanied vaccine introduction enabled increased supervision in many countries, usually for a fixed period. There were many reports that supervision was not systematic (with no checklists) and that supervisors left no documentation of findings and recommendations at facilities.

3.3.1 Staff knowledge, skills, and attitudes. Most countries prepared written introduction plans that included training of health staff. Training covered key information on handling, administering, communicating about, and recording doses of the new vaccine. Most training also included other vaccination topics, in some cases based on a needs assessment. Some EPIs (such as Rwanda’s) prepared job aids and reference materials to accompany vaccine introduction.[43] As part of RV introduction in Brazil, guidelines on the vaccination schedule, vaccine storage and distribution, surveillance for adverse events, and the epidemiology of rotavirus were distributed nationwide.[17] In the Dominican Republic a donor grant for vaccine introduction supported the revision and standarization of EPI norms and procedures, which were disseminated via nationwide training.[16] In some countries, manuals prepared to accompany training were not present in many health facilities six to 12 months post-introduction.

Based on information in the PIEs, it appears that the overall impact of training and other capacity-building steps associated with vaccine introduction was positive, although still insufficient in most countries to bring health worker skills to desirable levels. Commonly deficient skills noted were in management of EPI: estimating target populations; calculating coverage, dropout rates, and wastage rates; managing the cold chain; and monitoring immunization activities. In most countries, health workers observed during PIEs demonstrated good knowledge of the new vaccine. Assessments found health workers’ interpersonal communication on new vaccines to be effective in some countries and weak in others.

To prepare for vaccine introduction, most countries used a cascade training approach, with varying degrees of effectiveness. There are reports of training associated with vaccine introduction being too short, not sufficiently practical, and not reaching all peripheral facilities. Health workers in several countries complained that the new vaccine was not available for practice during training. Training was "insufficient" for some district personnel for Hib introduction in one West African country, and some did not demonstrate recommended vaccine-administration procedures and vaccine-management skills. Training in two nearby countries was said to be insufficient on aspects of pentavalent vaccine and/or not to have reached many field staff. Immunization planning and management skills remained weak afterwards. In one of those countries, all pentavalent vaccinations observed were administered intramuscularly in the buttocks.[40] In one southern African country, health staff felt that the training was rushed and felt more like a briefing. Moreover, there was no training for new staff followng the introduction.[56] In a nearby country, training of trainers was done at the national level, but there were inadequate funds for cascade training. Some health workers had limited knowledge on benefits of HBV vaccine as well as on how to respond to myths and rumors about the vaccine. There was confusion among health workers on where to tally, which led to problems in data collection.[34]

A 2004 WHO/AFRO assessment summarized various common problems in new-vaccine training.[38] Most countries did not budget or allocate resources for training, particularly at sub-national levels. GAVI funds reached some countries only after training had been completed. Training materials were not very appropriate, technical content was questionable, and most training was conducted without any new vaccine samples or AD syringes for demonstrations. Health workers complained that training was rushed and covered too much information.

There were also more positive capacity-building experiences (e.g. in Brazil, Gambia, Sudan, Tanzania, and Swaziland). In Ghana, GAVI financial support enabled intensive training at all levels with the introduction of pentavalent vaccine. Health staff were satisfied with the content on how to reconstitute and administer the vaccine, use and proper disposal of the auto-disable (AD) syringes, vaccine storage and management, attention to reporting and tracking of vaccine to reduce drop-out and wastage, and communication on the "five-in-one" vaccine.[42] Training for RV in Ecuador included the innovative use of a 19-minute adult education DVD that addressed all components of the program, reinforced by questions and answers, a skills test, and correction with participatory responses at all levels.[40] A similar DVD was used for training for RV introduction in Brazil.[17] The 2010 vaccine introduction in The Gambia was also judged to have had a clear positive impact on staff capacities. Staff demonstrated good knowledge of the new vaccine (PCV7), AEFIs, and use of VVMs, although some deficiencies in skills remained, particularly in planning and data use. Cascade training in Sudan was well received and contributed to good health worker knowledge of Hib and the immunization schedule. In Swaziland, trained nurses continued to conduct on-the-job training on Hib for new staff after the introductory phase.[40]

Health workers in Tanzania felt that their refresher training associated with hepatitis B introduction in 2002 prepared them well for the transition. In the field, they showed good knowledge and skills in many areas but also a lack of interest and ability to use targets and monitoring charts. There was also some confusion about eligibility for the new vaccine during the transition period (which was mentioned in many countries).[37]

Health workers in some countries (e.g. Malawi, Kenya, Ghana, and Ukraine) complained that a new vaccine had increased their workloads or confused them because of reconstitution requirements, having to give additional injections, or learning to use and properly dispose of AD syringes.[38, 44]

3.3.2 Supervision, monitoring and evaluation. In some countries funding from the GAVI Alliance or other donors that accompanied vaccine introduction allowed increased supervisory visits, usually for a limited time period. Most supervision visits took place as planned in some countries, but not in others. In many countries supervision teams did not leave a report of findings and recommendations at the facility, as per procedures. Many supervision systems lacked a supervision checklist and/or consistent use of a checklist.

Most supervision visits appear to have been for immunization only, although in some countries (e.g. Gambia, Sierra Leone, Swaziland) they covered broader health activities. Supervision seemed to be well functioning in Sudan ("well planned and well organized… logbooks used at all HFs…feedback and recommendations documented…follow-up visits….").[40] Supervision in Ukraine was also reported to be effective.

The PIEs indicate that with few exceptions, vaccine introduction did not have a noticeable impact on the quality of monitoring within various EPIs. In general, the collection, manipulation, analysis, intepretation, and use of data on program inputs (vaccine forecasts, inventory, usage rates for vaccine and supplies, and equipment), vaccination (target populations, coverage, timeliness, dropout, wastage), and impact on disease (surveillance) remain weak areas in many programs, and new vaccine introduction did not redress these pre-existing gaps. Even when there were clear procedures and tools, many reviews often found health staff capabilities in this area to be weak.

In the Dominican Republic, the grant to support pentavalent introduction was used to strengthen the infrastructure, operation, monitoring and evaluation of the EPI at all levels; and to establish a system of acreditation of public and private facilities, which assessed standards of quality, equity, efficiency, and effectiveness.[16]

Djibouti is an interesting case in which 100% of health centers completed their daily log, 100% of reports were fully completed and received on time, a defaulter tracking system was in place, and all vaccinated children had a vaccination card. However, facilities did not have official target figures or coverage charts; staff did not calcultate coverage, dropout, or wastage rates; and outreach vaccinations were not included in the data that facilities report.[40]

3.4 Information, Records and Forms

Efficient and effective collection, compilation, analysis, and use of data remain challenges for many EPIs. There is no indication that vaccine introduction has worsened the problem -- generally, needed changes in forms, registers, vaccination cards, and reporting formats are anticipated and made before the introduction – but there are also few indications that the introduction process took advantage of the opportunity to *improve* data collection and use.

The PIE for a southern European country noted ongoing problems with lack of standardization of the information system among different facilities and levels as well as major problems with numerators and denominators. One west African country updated its reporting forms, vaccination registers, and cards before the introduction, but suffered a shortage of immunization cards and forms at the local level, as well as sometimes late receipt of coverage figures that were then updated repeatedly during the year.[40] At the time of the PIE in the Ukraine, there was a national electronic data system for EPI down to the district (but not to the facility) level. Hib information had to be added manually to vaccine logs, registries, and immunization cards. Similarly, PCV information had to be added manually to monitoring charts in Rwanda. The

reporting system in Sudan generally was found to be much better than most (100% timeliness and completeness of monthly reporting), although some areas still needed improvement.

Based on the PIEs, many countries' AEFI systems (e.g. the Central African Republic, Chad, DRC, and Ethiopia) had poorly or non-functioning procedures both before and after the introduction. Many other countries had some, but not all, essential pieces of a good AEFI system: they had the forms but not the detailed guidelines for reporting, investigation, and follow-up; the procedures but not the forms or the emergency drugs/kits to respond, or the health workers who knew and followed procedures; or practical mechanisms for timely notications. In one Horn of Africa country, personnel knew minor AEFIs and were prepared to report AEFIs, yet there were no national guidelines or notification forms. From limited information in the PIE summary, Sudan appears to have one of the stronger AEFI systems. In Rwanda, there was an AEFI surveillance protocol and report forms available at health facilities, yet no AEFI cases reported and no system of zero reporting. The April 2008 PIE in the Ukraine reported a strong AEFI policy and system, which was critical due to the strong anti-vaccine movement in that country. A WHO/AFRO review of multiple PIEs concurred that "…AEFI recording and reporting was not systematically done" but also that health staff felt that there were fewer side effects from tetravalent and pentavalent vaccines than from DTP alone.[38]

Rwanda, Ukraine, and other countries gathered and analyzed existing disease information as part of the assessment of need for new vaccines. Some countries took steps to establish or strengthen sentinel or district surveillance systems, particularly for pneumonia and meningitis. In general, the poorest countries have not prioritized disease surveillance.

3.5 Vaccine Supply, the Cold Chain, Injection Safety and Waste Management

In Brief: Vaccine introductions have enabled many EPIs to obtain new cold rooms, refrigerators, and AD syringes. Internal distribution of high-volume new vaccines has a major challenge, and vaccine-management practices remain deficient in many countries. Overall, vaccine introductions appear to have improved injection safety and, in some countries, waste management, although waste management remains poor in many countries.

Depending on the new vaccine introduced, its formulation, presentation, and packaging, the introduction process may put tremendous pressure on a country's cold chain and logistics. (See Figure 1, which illustrates how the addition of pentavalent, PCV, and RV increases the volume of vaccine storage by a factor of two to eight times.) On a global level, the efforts of manufacturers and agencies have led to more streamlined packaging to reduce the storage volume per dose, but the concern remains.

The majority of PIEs acknowledge both improvements in the cold chain as a result of preparing for new vaccine introductions as well as continued important deficiencies (Annex A summarizes findings from many PIEs). The improvements related to vaccine introduction mainly consisted of purchase and installation of equipment and greater storage capacity. While these contributions were valuable, support for two equally critcal needs was frequently inadequate: improving *health worker practices* related to the supply chain and *transportation* of vaccine and related supplies.

Box 6: Country Experiences/Cold Chain and Vaccine Management

Rwanda's EPI had to adjust to the challenges of introducing single-dose PCV7 in pre-filled glass syringes in bulky packaging with separate unattached needles. There were no problems with vaccine supply or storage at the central level, but it was recognized and planned that districts required more frequent (monthly) deliveries because of limited cold storage capacity. This was difficult to do consistently in part because of substantial space required in vehicles for the large volume of PCV in addition to the many

other medicines and supplies going monthly to districts. In fact, some districts required twice-monthly deliveries of the vaccine and other supplies. Immunization outreach via motorcycle also became problematic because of the bulky vaccine. The pre-filled glass syringes could be adequately incinerated at the requisite high temperatures in only one incinerator, which was located in the capital Kigali. Health workers were well oriented regarding waste management, and special safety boxes for the used PCV prefilled syringes were provided. However, the need to move those syringes to the capital on a regular basis put additional pressure on transport (vehicles and fuel). The program has now switched to a different PCV product that is more compatible with standard vaccine handling procedures.[29, 47, 48, 49]

The introduction of rotavirus vaccine in *Brazil* in 2006 overloaded the EPI's cold chain. In many locations below the state or large-city levels, cold chain storage capacity was unable to accommodate a month's vaccine supply. In some cases, vaccine distribution had to be done weekly, which had major cost implications. Many state coordinators reported great difficulty in transporting and storing large-volume vaccine boxes containing 25 single-dose vials and diluent together. Large boxes of vaccine would not fit in some types of vaccine carriers used in the field. Introduction of RV meant that four times the previous cold chain storage and transport capacity was required at national and state levels.[17]

Although a donor-supported project that supported pentavalent introduction in the Dominican Republic strengthened many aspects of the EPI, problems persisted in the cold chain at all levels. The central level needed four cold rooms with freezers for exclusive use of EPI, regular temperature monitoring, alarm systems, contingency plans, etc. "In the 3 fixed vaccination posts visited in one province serious cold chain deficiencies were observed, including temperatures below 2ºC, lack of a thermometer, lack of ability to read the thermometer, disorganized refrigerators, expired polio vaccine, lack of measles vaccine, and lack of a second gas tank."[16]

The introduction of pentavalent vaccine in single-dose vials in *Ethiopia* in 2007 went well. However, this bulky presentation increased the required frequency of vaccine replenishment from central to peripheral levels, which had cost implications, and increased needed storage capacity, which was expanded during the preparatory phase.[61]

The 2010 EPI review in *Tanzania* describes another case in which new vaccine introduction at least temporarily overwhelmed cold chain storage and vaccine distribution capacity. Before single-dose pentavalent vaccine was introduced in 2009, four vaccine deliveries per year to the country, including a 25% buffer stock, were sufficient. Because of the increased storage capacity needed to accommodate the pentavalent vaccine, the EPI no longer had room for a buffer stock at national level, and it had to institute "fast transportation … from the airport to the regions once vaccines arrive in the country." Stock-outs occurred "at all levels over the past 1 year."[12]

Introduction of pentavalent vaccine in one east African nation in 2002 posed major challenges to the cold chain in terms of storage space, temperature monitoring and dry storage space for injection materials. Change from the 20-dose DTP formulation to two-dose pentavalent vaccine vials meant a five-fold increase in needed storage space for the vaccine. Adequate steps were planned to address these needs but only partially implemented. After introduction, there were problems with pentavalent supplies needs, storage capacity, and recalling existing DTP stock.[13, 60]

An EPI review in a southern African nation, after the introduction of pentavalent vaccine, found notable deficiencies in vaccine management and the cold chain. These were not attributed to introduction of the new vaccine; however, the introduction process clearly highlighted and did not correct these problems, which included: stockouts in the last six months in all health facilities visited; storing non-EPI items in refrigerators; most refrigerators malfunctioning; many health workers unaware of correct storage temperatures; vaccines in every facility visited stored at below +2°C for more than a week; and unequal quantitites of lyophilized Hib and DTP-Hep B, which may have resulted in vaccination of some children without Hib.[36]

In 2008/2009, South Africa introduced three vaccines simultaneously – PCV7, RV, and pentavalent (DTaP-IPV-Hib). This challenged every component of the EPI, including the cold chain, whose capacity

for the PCV and RV alone had to increase by more than 450%. The national treasury provided limited funds in 2008, and two provinces managed to provide additional funding through replacement of redundant refrigerators. Two vaccine companies provided funding to procure 3,000 refrigerators; however, they arrived very late, and there were initial set-up problems (some did not function due to power surges). One issue was that Provincial Cold Chain Managers had other responsibilities besides EPI, including for such high priority programs as tuberculosis and HIV/AIDS. Some depots had limited capacity to increase orders due to limited cold chain capacity, resulting in facilities having to order more frequently. So overall both costs and personnel needed for cold chain operation increased substantially.[56]

Even in Turkey, a country with a strong EPI, the introduction of MMR, pentavalent, and PCV over a four-year period presented challenges to the cold chain. Cold rooms had to be rented and cooled vans used while cold rooms were built at the intermediate level. Storage volume expanded from 26.2 cm^3 to 550 cm^3per fully immunized child at subnational levels; and vaccine distribution increased from four to eight times per year and from one to three rounds over each distribution route.[50]

At a recent workshop, the team from Kenya advised other countries to consider the "hidden costs" (e.g., gas and electricity) required to run new cold chain equipment installed to prepare for new vaccine introduction. In Kenya the funding did not cover all such costs, leading to a serious depletion of resources: facilities ran out of gas to operate the additional cold chain equipment. For up to two weeks all immunization services were stopped for all antigens, so that debts could be cleared and gas cylinders could be refilled.[55]

In general, the combination of AD syringes and training that accompanied vaccine introductions in most countries appears to have led to improvements in injection safety, although poor practices, such as recapping, were still observed during PIEs.[40] A recent evaluation credits GAVI Injection Safety Support (INS) with "the adoption/ increased uptake of injection safety equipment across GAVI countries. Further, this program has demonstrated the highest sustainability in terms of sustained use and financing …after GAVI support…."[21] The introduction of new vaccines does not appear to have had a notable impact on waste management in most countries: both hardware and practices still needed substantial attention after new vaccines were introduced in most countries.[40]

3.6 Financing and Sustainability

In Brief: Despite substantial international attention, and some positive steps such as co-financing and reduced PCV prices for GAVI countries, the cost of new vaccines (plus their distribution and storage) remain unaffordable to many governments. Some EPIs remain overwhelmingly dependent on donor-financing. Long-term financing of new vaccines and the impact of new vaccines and their associated costs on national health budgets remain critical issues.

Most new vaccines are many times more costly than traditional EPI vaccines: extrapolating from information in *SnapShots* (Issue 8, July 2008), it would appear that the cost of new vaccines in a fully-loaded district refrigerator may be 50 times the cost of the refrigerator. Moreover, the introduction of new vaccines implies many collateral costs. The PIE for one Horn of Africa country noted unexpected or under-estimated costs for: transport (fuel and per diem because of the greatly increased volume of pentavalent vaccine in small-dose vials), cold chain (airport storage), training (materials, staff time), and equipment and maintenance. In general countries that add one of the high-volume vaccines incur substantial new capital and recurrent costs for cold storage, transport, and vaccine carriers and cold boxes for outreach. While a donor may

fund hundreds of new refrigerators for a new vaccine introduction, it is the EPI (or district health budgets) that must fund ongoing expenses for fuel, maintenance, and repair.

Donor financial support (although time-limited) has certainly eased the "sticker shock" in many countries. GAVI Alliance funding, for which some 70 countries with the lowest per capita income are eligible, has included: new vaccine support, immunization services support (ISS), health system strengthening (HSS), injection safety support, and civil society organization (CSO) support. JICA (Japanese aid), AusAID, USAID, and other donors have also provided funding to support immunization programs in some countries. (For most countries, ISS funding ended over the past few years, and injection safety funding has already been phased out.)

The GAVI co-financing policy, initiated in 2008, is intended to help countries move along a trajectory toward greater financial sustainability for the costs of new vaccines. Countries are required to co-finance (co-procure) a portion of their new vaccines from the beginning of introduction, and, in accordance with their income level, increase this proportion over time. Support for new vaccine introduction also includes a vaccine introduction grant of US$0.30 per infant in the year's birth cohort, with a minimum award of $100,000.[28] In addition the Advanced Market Commitment has achieved the guaranteed low price of $3.50 per dose of PCV for GAVI-eligible countries that purchase vaccine through UNICEF.[14]

As of 2009, the lowest price for non-GAVI countries of PCV7 was $25 to $26 per dose and around $16 for the full series (two or three doses) of rotavirus vaccine.[55] A preliminary WHO analysis of country data in 2009 found that the average cost per child immunized with DTP3 would increase from $11 to $30 in going from DTP to DTP-HepB to DTP-Hib-HepB. On average, WHO calculated that vaccine supply and logistics were expected to increase from 57% in 2008 to 71% in 2012 of immunization expenditures, with a much less significant increase in non-vaccine costs.[5]

In a 2009 workshop, various African country staff felt that co-financing had helped increase country ownership and commitment to immunization and enhanced evidence-based decision-making. Still, a number of those governments are struggling to meet their co-financing obligations. Many national programs are extremely concerned about how they will cover the costs of their immunization programs once GAVI support ends, in part because future vaccine prices remain uncertain.[55]

The GAVI phase two evaluation stated: "All evidence points to the conclusion that the prospects for financial sustainability for low-income GAVI-eligible countries is very low indeed. Financial sustainability is expected to be a more surmountable challenge in low-middle income GAVI eligible countries. We also conclude that GAVI's choice of vaccines and presentations (i.e. combination vaccines) has not in practice been based on a realistic consideration of the potential for low-income countries to take on financing of these vaccines after GAVI support ends (whether through their own or other donor resources). In our view, there has been a failure to recognise explicitly, or communicate clearly, that financial sustainability (for low-income countries at least) would not be achievable in the medium term for the vaccines that GAVI supports."[21] GAVI's strategic plan for 2011-2015 does acknowledge and express the intention to address this situation.

Many health and immunization budgets in low-income countries are extremely donor-dependent; in 2010, it was estimated that only 15% of vaccine financing in these countries originates from country budgets.[4] Government contributions to EPI mentioned at a workshop of 16 African countries were as low as 3.6%.[55] Besides limited overall government budgets,

financing of immunization in many countries faces such obstacles as inefficient national disbursement procedures and the recent creation of many new districts, which implies substantial expenses and human resources. Major and effective advocacy, within ministries of health and with ministries of finance for additional immunization funding, is required if the cost of new vaccines and their delivery are to be covered on a sustainable basis in the poorest countries.[55]

Box 7: Country Experiences/New Vaccine Financing

The Government of Bosnia and Herzegovina finances all routine vaccines but welcomed GAVI support for Hib introduction in 2009. In late 2009, the MOH was concerned about funds for vaccine procurement for 2010 and for financing Hib in particular after 2012.

The PIE for one central African nation found that there was no financing available for purchasing traditional vaccines and injection equipment, late payment of co-financing, and insufficient funds for transportation of vaccine and other essential expenses.

The pentavalent introduction and EPI improvements in the Dominican Republic were mainly financed by JICA, the World Bank, and USAID. At the time of an assessment in late 2004, when the donor projects were due to expire, there had been little effort to plan for or secure funding for EPI operations for the next year. The health sector in general was underfunded, with shortages of basic needs such as electricity and water.[16]

The Ukraine PIE (2008) found that "Introduction of Hib containing vaccines led to considerable increase in the cost of the immunization programme, and there concerns in the MoH regarding sustainability of vaccine procurement for the year 2008."[44]

Like many other nations, the Government of the Gambia pays for traditional vaccines and supplies, and co-finances new vaccines supported by the GAVI Alliance.

The Government of Swaziland funds all vaccine procurement, including of Hib, and 90% of routine immunization funding overall is from the government budget.

In one east African nation, new vaccines accounted for 92% of vaccine costs in 2009 (currently mostly financed by GAVI). The proportion of the country's health budget allocated to the EPI has fallen substantially, and the proportion of the EPI budget for routine immunization services (vis a vis polio and measles campaigns) has been around 20%. The EPI has also had to deal with the creation of many new districts, each needing its own human and material infrastructure for immunization. There is a severe shortage of funds for routine EPI operational costs, which contributes to "longstanding deficiencies, such as inadequate supervision, absence of monitoring and use of data for detecting and correcting problems, irregular supplies, and infrequently trained health workers." Coverage has fallen in recent years, due to these and other factors. Although the continued effect of vaccine introduction on the EPI is unclear, the budgetary implications of vaccine introductions are very troubling. Introduction of both RV and PCV are in the current five-year EPI plan, and there is growing political pressure to introduce HPV.[13, 60]

The documents reviewed show that GAVI and other donor funding has enabled many countries to introduce new vaccines and has supported improvements in financial planning and budgeting, but these supports have not solved the basic problem that poor countries cannot afford the current prices of new vaccines and their delivery. Thus, to take advantage of the promise of new vaccines to save lives, many countries must take on expenses that they cannot reasonably afford. Financing of new vaccines and their collateral expenses remains a critical issue to resolve in order to prevent new vaccine introductions from reducing funding for other crucial expenditures of EPIs and ministries of health. There is growing awareness and concern, at both the international and country levels, of financing and sustainabilty issues but only short-term or partial solutions thus far. It would seem that solutions need to combine continued efforts

to reduce vaccine prices along with more effective advocacy within countries by EPIs and their partners.[5, 55]

3.7 Leadership and Governance

In Brief: New vaccine introduction appears to have resulted in steps in some countries towards better financial planning and expanded links between the MOH and other ministries. There is an untapped potential for wider partnerships and strategies within the MOH for diarrheal disease and pneumonia control.

As mentioned above, new vaccine introduction in some countries did at least temporarily raise the EPI's profile and image. The first families of many countries participated in new vaccine launches, but in only one case was there information on whether this opportunity led to ongoing political support for the EPI. The strong partnership for pentavalent introduction in Ethiopia among the MOH and donors was reported to have led to sustained commitment by national authorities at all levels for immunization services.[61]

There are some indications in the grey literature reviewed that the large costs that most new vaccines entail, as well as common requirements such as cMYPs and co-financing, have influenced some EPIs to improve financial planning and relations with ministries of financing and planning (see Box 8). A grant from the Bill & Melinda Gates Foundation is enablling the Sabin Vaccine Institute's new Sustainable Immunization Financing program to encourage key stakeholders in twelve African and three Asian countries to work together to identify sustainable financing mechanisms for immunization.

Box 8: Improved Governance in Zambia

"The development of the cMYP was evidence-based and critical for convincing the government to fund immunization. A participatory process was implemented, with a particular involvement of the MoF and the Planning Unit of the MoH. [The t]imeframe was aligned to the National Health Strategic Plan and the National Development Plan (2006-2010). While conceiving the budget, annual costs were calculated and reflected in the three-year rolling operational plans of the mid-term expenditure framework (MTEF), which in turn appeared in annual plans and budgets. EPI vaccine and logistics costs, including traditional vaccines and co-financing for new vaccines (about USD 2 million), are reflected in the MTEF and annual budget for 2008."[55]

Ideally, the introduction of PCV should be planned and carried out with a broad coalition of MOH units and other partners focussed on addressing childhood pneumonia, and RV introduction should include similar partners to address childhood diarrhea. The documents reviewed did not describe such broad coalition-building, although this may change due to a growing international movement to encourage and faciitate such integration. The Gambia PIE praised the integrated activities between the MOH's EPI and disease control units in supportive supervision for child health, but it is unclear if this was related to new vaccine introduction.

4. Discussion and Conclusions

The basic conclusion of this review is that, over the last 10 to 15 years, the process of introducing new vaccines has both strengthened and stressed EPIs, although, in most cases, not to a major extent in either direction. The grey literature reviewed indicates that if the introductions were better planned, with sufficient time for assessments and preparations, they could have substantially greater positive impact in most countries. At present, vaccine introductions typically have had some, but insufficient, success in addressing problems in cold chain, collection and use of information, and other commonly weak areas.

The main positive impacts of new vaccine introduction are: (1) protecting many people from illness and death; and (2) in many countries making some level of improvement in vaccination hardware, tools, systems and staff capabilities – although further improvements are needed. Perhaps an additional positive result is more national attention to immunization financing issues, although these are far from being resolved. New vaccine introductions often entail a several-fold increase in vaccine costs as well as other costs to the EPI budget. The initial availability of donor funding does not obviate the need for better long-term financial planning that must include higher commitments from governments and donors. Although there are indications that attitudes are changing, there have been too many cases in the last decade of EPIs assuming that the money would be found somewhere.

After reviewing lessons learned from recent PIEs following PCV and RV introductions, the GAVI Alliance Board Meeting (16-17 June 2010) noted that: "Vaccine specific system strengthening is required in terms of disease and Adverse Events Following Immunization (AEFI) surveillance, Expanded Program on Immunization (EPI) training, vaccine and cold chain management."[27]

Reflecting on RV introduction in 14 countries between 2006 and 2009, PAHO concluded that: "Many lessons were learned from the introduction of rotavirus vaccine in the Region of the Americas: for example, the need for adequate evaluation of the cold chain and the logistics of the immunization progarm prior to introducing a new vaccine, the need for training at all levels, the importance of strengthening the network for ESAVI [AEFI] reporting and investigating, the importance of ensuring the sustainability of the EPI vaccine in the national budget, and the establishment of rotavirus diarrhea surveillance prior to the introduction of the vaccine and the subsequent maintenance of that surveillance as fundamental to decision-making."[51]

Major determinants of the ease of vaccine introduction and its effects on EPIs appear to be:

- what vaccine, formulation, presentation, and packaging is being introduced, and how simple or complicated the transition is
- the quality of planning for vaccine introduction and amount of time for preparations
- the pre-introduction strength of the EPI and its components
- public perceptions of the EPI, which are positive in most, but unfortunately not all, countries.

In general, particularly when the EPI is reasonably well functioning, sufficient time and effort are allotted to planning, and the new vaccine characteristics are appropriate for the EPIs' capacity and capabilities, the introduction is a reasonably smooth process, which in many cases contributes to at least short-term improvements in the EPI and public perceptions. Unfortunately, in many of the introductions studied, one or more of these conditions were not met. Local political situations or an active anti-government or anti-vaccine movement can greatly complicate the introduction and its aftermath, even when other key conditions are favorable.

A key change in perception would also enhance the likelihood that new vaccine introduction will strengthenthe EPI and health system. While planning must try to ensure that the introduction goes smoothly, it should also be considered an opportunity deliberately to assess and address weak system components. The objective of system strengthening tied to new vaccine introduction should not be conceived as a rapid, intense process for a few months before and

after introduction, but rather as a well planned multi-year undertaking, as in the example of Andhra Pradesh (Box 8).

Box 9: Country Experience/
Using Vaccine Introductions to Strengthen the Routine Immunization Program

Funded by the Bill & Melinda Gates Foundation and state government resources, the Andhra Pradesh (AP) Partnership Project on Immunization (2001-2006) was implemented through a strong partnership between the Government of AP and PATH. The project successfully bolstered routine immunization in the process of introducing HBV in the 23 districts of the state, adding HBV and AD syringes while greatly strengthening most immunization system components. In three years coverage rates increased from 58 percent to 72 percent, and drop-out rates for measles vaccination decreased from 22 percent to 8 percent. While this was not a typical new vaccine introduction, the scale was equivalent or to or greater than that of most national introductions. Aspects worthy of replication by EPIs and their partners when introducing new vaccines, include: the strong, explicit focus on system strengthening; the longer-term vision that the process would take several years and not simply focus on a short preparation and introduction period; the availability of sufficient funding from several sources; development of strong monitoring and information systems and effective use of information on progress to build and sustain political support; and establishment and maintenance of a strong coalition of partners. This project was able achieve what vaccine introduction should ideally achieve everywhere, a smooth introduction of new vaccines in a manner that truly strengthens routine immunization.[23]

Based on the findings from the grey literature, we offer the following recommendations to EPIs and their partners:

- Make rational, unrushed decisions to introduce a new vaccine, based on both operational feasibility and good evidence of need – delay the introduction if necessary.
- Accept the new vaccine only in a formulation, presentation, and packaging that makes sense for the EPI, and for which the supply seems secure.
- Invest more in preventive maintenance, timely repair, and replacement of malfunctioning cold chain equipment protects investments in expensive vaccines.
- Take full advantage of the introduction preparations to strengthen weaker components of the EPI, both through short-term training, supplies, equipment, and supportive supervision, and through a long-term improvement strategy. Plan improvement steps as a sustained undertaking, not as actions concentrated in a few months before and after introduction.
- In addressing cold chain needs, go beyond purchasing refrigerators and cold storage; address the additional needs for more frequent transport, per diem, and staff time caused by bulky new vaccines, and address staff vaccine management skills and attitudes, in both the short and longer term. Plan for the added fuel costs that new equipment entails.
- Expand the focus to include the full financial implications of new vaccines, including associated costs of cold chain, training, and other critical components of the vaccination system, and advocate for more government resources to fill financing gaps.
- Gauge the level and nature of communication and mobilization regarding the vaccine introduction to the particular situation and setting. Base strategies and activities on rapid formative research when possible.
- Assess the political environment to ensure, as best as possible, that the vaccine introduction will not occasion controversy; and if there is a threat of controversy, reduce the risk *before* introduction by engaging in dialogue with all parties.
- To the extent possible, embed planning for RV and PCV introduction into broader coalitions and strategies addressing diarrheal and respiratory disease in the country.

- Use the introduction period to generate political support for the EPI and continue to advocate afterwards. The vaccination program needs greater national and sub-national ownership and support to take advantage of the new life-saving vaccines. The new vaccines do not deliver themselves.

There are several important questions on financing that this review could *not* answer, but that governments and donors should strive to answer:

- What is the effect of new vaccine introduction on both the size of and the proportional allocations in the EPI and ministry of health budgets, in the year of introduction and in subsequent years?
- Have the high costs of some new vaccines and their delivery led to reductions in funding for other vaccines, other EPI, or other health system expenses?
- What, if any, evidence exists of countries not being able to finance other health priorities because of the expenses on new vaccines?
- Has the process of new vaccine introduction led to improvements in financial planning and/or the effectivenses of the EPI/ministry of health's advocacy for funding with the ministry of finance or national legislature?

The new vaccines reviewed (HBV, Hib, RV, PCV, HPV and others) have a tremendous potential to reduce morbidity and mortality throughout the world. The challenge to EPIs is to achieve this goal in the most efficient and effective manner possible, so that the *process* of introduction will strengthen service delivery well beyond the period of introduction.

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Annex A: Summaries of Findings from Post-Introduction Evaluations on the Cold Chain, Injection Safety and Waste Management[40]

Region *New Vaccine*	*Synopsis of Findings*
Southern Africa: lyophilized penta, then liquid penta	Inadequate cold rooms at national level and cold chain capacity in provinces and districts; generally adequate vaccine storage space in facilities; good and bad practices in cold chain management; stockouts in some provinces and districts and expired vaccine in fewer places; no standardized vaccine forecasting; wastage not calculated; injection practices generally safe; deficiencies in waste management, particularly unprotected areas and shallow pits.
Southern Africa: Hib	Overall adequate and well-funcioning cold chain; many small upgrades in equipment, roofing, and practices needed; current central-level stockout of penta; mixture of stockouts and overstock at facility level; poor forecasting skills; vaccine wastage not monitored; injection safety supplies and practices good; waste management needs some improvements.
Southern Africa: Hepatitis B	Cold chain capacity and equipment were adequate to accommodate the new vaccine; frozen vaccine was found in one district; many refrigerators more than 10 years old needed to be replaced; users were not trained for the proper handling of the equipment, which led to problems nationwide; no functioning freeze watch indicators or cold chain maintenance records; vaccines inappropriately arranged in refrigerators.
Central Africa: Hib	Overall excellent cold chain equipment, supplies, and practices; generally <1% penta wastage rates (one-dose vials); no stockouts or expired vaccine in last 6 months; vaccine forecasting procedures and practices need strengthening; good injection safety; waste disposal good but policies not fully followed (e.g. fencing off disposal areas).
Central Africa: PCV	Donor-funded cold chain equipment distributed to all facilities; some practices need improvement (e.g. conditioning icepacks, monitoring cold store temperature, using monitors correctly, placing vaccines correctly, monitoring wastage); no stockouts or expired vaccine; waste management well handled despite special requirements for glass syringes; a few unsafe injection practices observed.
Central Africa: Hib	Penta introduction strengthened cold chain capacity; lack of sufficient storage space at all levels (due to high-volume, single-dose vials of penta); poor maintenance and management at central level; need to strengthen hardware and practices in many provinces and local areas; low penta wastage rate; 29% facilities had stockouts; bundling sometimes done; increased costs for vehicle hire, petrol, and maintenance due to need for more vaccine deliveries; injection safety and waste management tools available but many practices deficient.
Central Africa: Hib	Good cold chain hardware at all levels; many power outages; high wastage; frequent stockouts and expired vaccine; good vaccination practices; poor waste management.
Horn of Africa: Hib	Cold storage capacity expanded before introduction; penta generally stored correctly; refrigerator distribution not optimal; few refrigerators had internal thermometers; a few pentavalent stockouts; increased vaccine distribution needs not anticipated (additional petrol and per diem costs); outreach complicated by need for additional vaccine carriers; supplies and equipment for injection safety and waste disposal good but practices needed improvement.
Horn of Africa: Hib	Generally good hardware and practices; no major problems with stockouts, expired vaccine, injection safety, waste management, immunization practices.
West Africa: Hib	Cold chain assessment was part of planning but still insufficient cold storage capacity at national and district levels, resulting in moving vaccine around to keep in cold chain; national cold storage below recommended 2ºC; need more generators, fuel, and freeze watch monitors in facilities; generally efficient distribution so few stockouts (unanticipated transport costs); outreach complicated by need to carry additional vaccine carriers; good injection safety; waste disposal variable, with poor implementation in some places (burning without burying, exposed pits, needles/syringes

	on ground).
West Africa: Hib	Adequate storage capacity at most levels; penta generally stored at correct temperature but temperature commonly not monitored and recorded; some facilities overstocked with penta beyond safe capacity; no expired vaccine but some local stockouts; vaccine ordering and management need strengthening; injection safety practices okay but waste disposal practices need strengthening (fencing, complete burning).
West Africa: PCV	In preparation for vaccine introduction, solar refrigerators and other cold chain support provided to all facilities; both equipment and practices working well; need cold store for country's Western Region, more fuel for stand-by generators, and national cold van to deliver to sub-national levels; manuals and guidelines usually available; distribution efficient and no stockouts or expired vaccine; vaccine and equipment bundled; some vaccine management problems including lack of sound ordering practices; good injection safety and waste management, despite challenges (glass syringes, insufficient incinerators).
West Africa: Hib	Cold chain infrastructure in most facilities; some refrigerators not functioning well; storage capacity insufficient and storage practices deficient; one regional cold room not functioning; vaccine management problems: guidelines not updated, overstocking, use of vaccine in phase 3 and 4, etc.; poor waste disposal practices.
North Africa: Hib	Generally sufficient equipment but substantial problems with vaccine management practices; insufficient storage space; poor forecasting, bundling, VVM interpretation, etc.; some stockouts; injection safety good but many improper waste disposal practices.
Eastern Europe: Hib	Generally strong cold chain (hardware and practices); insufficient equipment in some facilities and lack of cold chain monitors; lack of bundling led to some stockouts of AD syringes; overstock of Hib in some areas and stockouts in others; safe injection supplies and practices generally good; national waste management policy could be strengthened.
Southern Europe: Hib	Cold chain functioning well; the vaccine introductioni put pressure on cold storage capacity and transport for vaccine distribution; various stockouts and a small amount of expired vaccine; no vaccine management guidelines; generally good injection safety; less than adequate waste disposal.
South America: RV	Generally good storage capacity, equipment, policies, and practices, although improvements needed in some practices (particularly temperature monitoring); no expired vaccines but reported shortages of various vaccines at provincial and local levels; no wastage of rotavirus vaccine; excellent injection safety and waste disposal, although some local practices need improvement.