

# the polio pipeline

A quarterly update of ongoing research in the Global Polio Eradication Initiative

## Dear Research Colleagues,

A year has passed since the inaugural meeting of the Polio Research Committee (PRC), a year in which we have witnessed a virtual revolution in research activities for polio eradication.

Researchers are evaluating new vaccines and exploring novel uses of existing vaccines. The Global Polio Laboratory Network is implementing faster diagnostic procedures to speed up the rate of detection of poliovirus. Molecular epidemiology and transmission studies help to track virus circulation. Seroprevalence surveys are offering new insight into programme performance and vaccine efficacy. New surveillance strategies are being assessed in key reservoirs. These are just some of the research activities being coordinated by the Global Polio Eradication Initiative (GPEI), under the strategic guidance of the PRC.

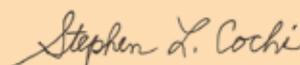
To those of us who are members of the Advisory Committee on Poliomyelitis Eradication (ACPE), the global independent advisory body to the GPEI, this research is absolutely vital. It helps make sure we have the sharpest and most up-to-date epidemiological and virological picture, allowing us to determine the most appropriate targeted eradication strategies.

Having this research-enhanced sharp picture is more crucial now than it has ever been in the 20-year history of the GPEI. We can see the finish line, but it has thus far eluded us. This year, however, two ongoing research projects in particular may well revolutionize the way we do business from here on. The first is the much-anticipated evaluation of a bivalent oral polio vaccine (bOPV) containing both type 1 and type 3 serotypes, which could have significant advantages in areas where both remaining wild serotypes co-circulate.

The second is a five-arm clinical trial to assess new vaccine strategies in western Uttar Pradesh, India, arguably the most technically challenging place on earth to eradicate polio and where we have seen the efficacy of OPV compromised time and again. The outcomes of these studies - along with the recommendations of a major independent evaluation into the remaining barriers to polio eradication - will help inform the finalization of a new multi-year GPEI Strategic Plan, expected for publication in January 2010.

Given the critical importance of these and other research projects, this issue of the *Polio Pipeline* provides an overview of the outcomes and conclusions of the most recent PRC, which convened on 2-3 June in Geneva, Switzerland. It is an exciting time to be sure, as the vast research activities give ever-more solid evidence into what works, what doesn't, and what can and should be done differently. I for one am convinced that it will be research and innovation - perhaps more than anything else - that will lead us in the final steps to a lasting polio-free world.

With best wishes,



Dr Steve Cochi  
Chair of the ACPE

## Polio Research Committee reviews ongoing activities; endorses new research studies

The third meeting of the Polio Research Committee (PRC) convened in Geneva, Switzerland on 2-3 June 2009. Discussions focused on various ongoing and proposed research topics relating to both the pre- and post-eradication era. Reviewed research topics included addressing compromised oral polio vaccine (OPV) efficacy (eg zinc supplementation to improve OPV efficacy; zinc has been shown to be associated with a reduction of diarrhoeal disease); developing 'affordable' inactivated polio vaccine (IPV) options (eg IPV production from non-infectious seed strains, adjuvants and Sabin-IPV development); and, use of IPV in northern India to fill residual immunity gaps among very young children and enhancing surveillance for acute flaccid paralysis (AFP).

In its deliberations, the PRC endorsed the following external research proposals for funding:

- 1. Antiviral drug development:** The proposal is to identify new antiviral compounds against polioviruses through industrial-scale mass screening of compounds and

Continued on page 2

### Polio Pipeline:

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## PRC Call for Research Proposals

### Submission guidelines

The Polio Research Committee (PRC) is currently soliciting research proposals focusing on topics outlined in Table 1. Proposals will be reviewed at the next PRC meeting, to be held in November 2009 in Geneva, Switzerland.

Researchers are invited to submit proposals by 30 September 2009 to Dr Hiro Okayasu, Research and Product Development, Global Polio Eradication Initiative, WHO Geneva, email: [okayasuhi@who.int](mailto:okayasuhi@who.int). The standard research proposal form is available in downloadable format at [www.polioeradication.org/content/fixd/opvcessation/opvc\\_researchproposals.asp](http://www.polioeradication.org/content/fixd/opvcessation/opvc_researchproposals.asp).

All research proposals should include the following information:

1. **Research question/objectives** (eg clarity of questions, reference to published literature and cutting edge science, description of how the results will be utilized).
2. **Qualification of investigators and collaborators** (eg track record of researchers, capability of laboratory, necessary contractual arrangements).
3. **Budget request** (eg appropriate for work anticipated).
4. **Study design and methodology** (eg clarity of activities, availability of institutions, feasibility of methods, compliance with Good Clinical Practice guidelines, plans for ethical and regulatory approvals).

### PRC Reviews - continued

evaluation of candidate compounds in-vitro and in mouse models.

2. **Assessment of alternate polio strains for vaccine production:** This project will create efficient poliovirus packaging cell lines and produce encapsidated poliovirus replicons as seed material for IPV production. Those replicons lack the capsid encoding genome segment, and are therefore unable to form virus particles. Additionally, replicons are considered to be identical in antigenicity, stability and biophysical properties to wild polio virus.
3. **Impact of zinc supplementation on OPV efficacy:** This proposal will investigate whether low zinc status in infants contributes to diminished immune response to OPV; and, evaluate the impact of zinc supplementation among infants on immune response to OPV.

The next PRC meeting is scheduled for 10-11 November in Geneva, and will focus on pre-eradication issues, low vaccine efficacy and risk factors contributing to low vaccination coverage.

## India vaccine trials prompt major strategic shift

A recently-completed multi-centre clinical trial in India (Chennai, Indore, and Pune), sponsored by Panacea Biotech Ltd, initiated based on a recommendation by the Advisory Committee on Poliomyelitis Eradication (ACPE) and with extensive technical and financial support by the World Health Organization (WHO), has demonstrated the non-inferiority of a bivalent (types 1 + 3) oral poliovirus vaccine (bOPV) compared with monovalent type 1 oral poliovirus vaccine (mOPV1) and monovalent type 3 oral poliovirus vaccine (mOPV3). The trial also demonstrated the superiority of bOPV compared to the respective Sabin type 1 and 3 strains contained in the trivalent oral poliovirus vaccine (tOPV). Immediately after the trial results were available, the ACPE convened by conference call and reviewed the trial outcomes and current epidemiology of wild poliovirus globally. It concluded that the use of bOPV in supplementary immunization activities (SIAs) constitutes an important new tool for the Global Polio Eradication Initiative to complement the use of tOPV for routine immunization and SIAs as well as the use of mOPVs in SIAs (see Weekly Epidemiological Record 17 July 2009; vol. 84, 29, pp289-300). The clinical trial report was made available in

July 2009 by the sponsor to other manufacturers interested in bOPV production. To date, at least four manufacturers are seeking national licensure for bOPV and a process has been initiated to review in parallel the regulatory dossiers for WHO-prequalification of these products for United Nations purchase. It is anticipated that the first newly-licensed bOPV could be used in supplemental immunization activities as early as November 2009.

In addition, the Global Polio Eradication Initiative is also awaiting the results of another clinical trial that was conducted in Moradabad district, western Uttar Pradesh, India. The trial evaluated five arms, a regular- and higher-potency mOPV1 and three inactivated poliovirus vaccine (IPV) arms. Unprecedented collaboration by Panacea Biotech Ltd, the sponsor (with IPV-bulk supplied by the Netherlands Vaccine Institute), GlaxoSmithKline,

and Sanofi Pasteur made the trial possible. The results of this trial should be available in mid-September 2009 and should answer the following questions:

- 1) Is higher-potency mOPV1 more immunogenic than regular-potency mOPV1 in northern India?
- 2) Does IPV have a role to play in closing remaining immunity gaps?
- 3) Will a fractional dose of IPV (1/5<sup>th</sup> of a full dose) given intramuscularly by needle-free device perform as well as a full dose of IPV?

As with the case of bOPV, the ACPE will review the data on higher-potency mOPV1 and on full- and fractional-dose IPV as soon as these will be available. It is expected,

depending on the outcome of this trial, that major strategic shifts in the use of these products should be anticipated (as is the case with bOPV). These clinical trials will help inform the finalization of the new Global Polio Eradication Initiative five-year Strategic Plan (expected for publication in January 2010).



Bivalent OPV: an important new tool for the Global Polio Eradication Initiative.

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**TABLE 1: UNMET RESEARCH NEEDS**

Highest priority

| Category                            | Program priority                                       | Current research activities  | Unmet needs  |
|-------------------------------------|--|--|--|
| <b>Pre-eradication</b>              |  |  |  |
| Assessment of emerging polio risks  | Minimizing VDPV risks and circulation                  | <ul style="list-style-type: none"> <li>- iVDPV studies in 10 countries (i.e., Bangladesh, China, Iran, Madagascar, Russia, Senegal, Sri Lanka, Philippines, Egypt, Tunisia)</li> <li>- Outbreak investigation for cVDPV in Nigeria</li> <li>- Evaluation of risk factors for VDPV emergence in Africa</li> </ul>   | <ul style="list-style-type: none"> <li>- Animal model to determine transmissibility of poliovirus</li> </ul>   |
| Accelerate eradication              | Evaluating programme performance in endemic countries  | <ul style="list-style-type: none"> <li>- Seroprevalence survey in Pakistan</li> <li>- "Quick and dirty" seroprevalence protocols</li> </ul>  | <ul style="list-style-type: none"> <li>- Further mathematical modeling                             <ul style="list-style-type: none"> <li>. Estimation of efficacy of monovalent OPV type 3 in India and Nigeria</li> <li>. Evaluation of vaccine efficacy at sub-region level in India</li> </ul> </li> </ul>   |
|                                     | Improving vaccine efficacy in northern India           | <ul style="list-style-type: none"> <li>- A pilot study of zinc supplementation to improve immunogenicity</li> <li>- Clinical trial of bivalent OPV</li> <li>- Clinical trial of IPV (IM and ID) and higher-potency mOPV1</li> <li>- Evaluation of roles of older person (&gt;5 yrs) in wild poliovirus circulation in India (two projects)</li> </ul>                  | <ul style="list-style-type: none"> <li>- Studying the cause of vaccine failures (e.g., epidemiologic, immunologic assessment)</li> <li>- Development of surrogate test to measure mucosal immunity</li> </ul>  |
|                                     | Overcoming failure to vaccinate (e.g., Nigeria)        | <ul style="list-style-type: none"> <li>- Communication (KAP) research</li> </ul>   | <ul style="list-style-type: none"> <li>- Operational research of vaccine delivery (e.g., identification of barriers that prevent higher SIA coverage)</li> <li>- Social research on improving community acceptance and vaccine delivery</li> </ul>   |
|                                     | Enhancing surveillance                                 | <ul style="list-style-type: none"> <li>- Environmental surveillance in Pakistan and expansion in India (Delhi)</li> </ul>  | <ul style="list-style-type: none"> <li>- Development of simpler and more efficient methods for detecting poliovirus in environmental samples</li> <li>- Evaluation of alternative approaches to evaluate surveillance in low-performance areas</li> <li>- Operational research on the effectiveness of reverse cold-chain for AFP surveillance specimen transport in Nigeria</li> </ul>  |
| <b>Containment</b>                  |  |  |  |
| Long-term containment               | Ensuring polio virus is properly contained             | <ul style="list-style-type: none"> <li>- (Not applicable)</li> </ul>   | <ul style="list-style-type: none"> <li>- Polio-specific biosafety research (e.g., rapid technique for validating disinfection, alternative methods for poliovirus disinfection, utility of low humidity as a disinfection method, validation of proposed biosafety requirements for post-eradication poliovirus facilities)</li> <li>- Determining barriers to achieving containment</li> <li>- Evaluation of containment implementation status</li> </ul> |
| <b>Post-eradication</b>             |  |  |  |
| Long-term surveillance and response | Preparing response for potential outbreak              | <ul style="list-style-type: none"> <li>- Evaluation and implementation of mOPV stockpile</li> <li>- Development of antiviral compounds</li> <li>- Evaluation of block-ELISA to measure antibody profile (e.g., IPV, OPV, wild virus)</li> </ul>  | <ul style="list-style-type: none"> <li>- Evaluation of alternative surveillance strategies in post-eradication era</li> </ul>  |
| Safer and more affordable IPV       | Developing a better protection in post-eradication era | <ul style="list-style-type: none"> <li>- Sabin IPV development</li> <li>- Evaluation of alternative inactivation method in IPV production</li> <li>- Evaluation of alternate IPV strains</li> <li>- Assessment of IPV adjuvants</li> <li>- Evaluation of fractional IPV dose with needle-free device</li> <li>- Non-infectious approaches to IPV production</li> </ul> |  |
| Options for OPV cessation           | Developing and selecting OPV cessation option          | <ul style="list-style-type: none"> <li>- Evaluation of OPV cessation options with mathematical modelling</li> <li>- IPV demonstration project in Indonesia</li> </ul>  | <ul style="list-style-type: none"> <li>- Establish a second IPV demonstration project</li> <li>- Evaluation of operational and technical feasibility of IPV use to control cVDPV outbreak</li> <li>- Evaluation of VDPV emergence and risk factors in low-middle income countries switching from OPV to IPV (e.g. Mexico)</li> </ul>   |

## CDC: leading research for pre- and post-eradication issues

The US Centers for Disease Control and Prevention (CDC) is performing and collaborating on various polio eradication research projects which are directed toward accelerating the interruption of wild poliovirus transmission as well as supporting the risk assessment and management for the post-eradication period.

### Pre-eradication: supporting Nigeria and India's eradication efforts

Because a high proportion of children in high-risk states of northern Nigeria continue to be unvaccinated against polio, a comprehensive risk factor assessment has been initiated in collaboration with the Ministry of Health's National Primary Health Care Development Agency, the World Health Organization (WHO), UNICEF and other partners. This assessment will evaluate characteristics of the child who is unvaccinated and its family, in comparison with a child who is vaccinated. The assessment will further explore the comparative issues relating to immunization delivery in routine health services and supplementary immunization activities (SIAs) and community support. Initial results of this assessment are expected by end-2009.

In India, the wild poliovirus (WPV) case numbers are low and the geographic extent of transmission is limited. Interrupting the transmission of WPV simultaneously in the two remaining endemic states - Uttar Pradesh and Bihar - is key to ultimate success. To help achieve this, in addition to various research projects aimed at improving the effectiveness of polio vaccination, CDC - in joint collaboration with WHO's National Polio Surveillance Project (NPSP) - has designed two projects to expand surveillance of WPV in high-risk areas of those two states to older age groups, including adults. The projects aim to find if fecal specimens (and pharyngeal swabs in some settings) from persons aged >five years in households and/or neighborhoods of recent WPV cases suggest any participation of older aged individuals in WPV transmission. If substantial evidence is found and WPV transmission persists, this could inform a possible expansion of the target age group

for SIAs in these areas. Initial results of this expanded age group surveillance are expected by September.

### Post-eradication: helping gain crucial insight to secure a lasting polio-free world

Mexico in 2008 has switched polio vaccination policy to routine use of inactivated poliovirus vaccine (IPV) while continuing with twice annual campaigns with oral poliovirus vaccine (OPV). CDC, in collaboration with the Pan American Health Organization (PAHO), has initiated a project with the Ministry of Health's Centro Nacional para la Salud de la Infancia y la Adolescencia in which sewage is sampled before, during and after OPV campaigns to determine the persistence of OPV virus excretion in the population in this setting and to follow this over time. The poliovirus national reference laboratory at the Instituto Nacional de Diagnóstico y Referencia Epidemiológicos will be conducting the testing. Preliminary results are expected in 2010.

The Global Polio Laboratory Network (GPLN) has continued to adopt new methodologies and approaches to improve the timeliness and accuracy of poliovirus detection from acute flaccid paralysis (AFP) specimens. This has been most evident in the development, evaluation and implementation of new molecular techniques using new algorithms to rapidly identify and characterize polioviruses. Using methods developed in the CDC polio laboratory based on real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), it is now possible to replace previous methods with ones that are simpler, more reliable and can identify both wild polioviruses and vaccine-derived polioviruses (VDPVs) more quickly. The implementation of these methods is now in progress with joint CDC/WHO workshops conducted in two regions, with three more scheduled for late 2009. It is envisaged that these new methods will be introduced into all polio-endemic regions by end-2009.

In addition to developing laboratory methods to address current AFP surveillance activities, two projects are also in progress to address potential future polio surveillance systems. The first project

focuses on the continued expansion of the use of molecular methods to replace time-consuming and resource intensive steps in the process of poliovirus isolation. Current steps that are dependent on growing the virus in cell culture could be replaced by PCR methods that can directly detect the virus from the original fecal specimen, further improving the speed of polio detection. The second project will examine the use of immunological markers to look for evidence of poliovirus infection once polio has been eradicated and OPV immunization has ceased. This could greatly expand the ability to use simple ELISA tests to bring poliovirus diagnostics to many more sites and possibly integrate this laboratory testing with already existing measles laboratories that are performing similar tests.

## Global post-eradication IPV supply and demand assessment conducted

The Bill & Melinda Gates Foundation, in discussion with The World Health Organization, commissioned an assessment of global post-eradication inactivated polio vaccine (IPV) supply and demand, with a focus on identifying supply strategy implications for developing world populations. The insights and conclusions from this assessment were intended to help inform policy and aid country decision making.

The assessment was completed by Oliver Wyman, an international management consulting firm, over a ten month period and involved numerous consultations with existing and potential IPV suppliers as well as demand experts. A paper summarizing the assessment's findings was released in March and is available for download on the Global Polio Eradication Initiative website [www.polioeradication.org](http://www.polioeradication.org).

In the paper, the authors define future demand scenarios for IPV use, characterize the current and evolving supply base, and recommend a path forward to ensure access for developing world populations.

## Call for recruitment

The Research and Product Development Team of the Polio Eradication Group at the World Health Organization (WHO) is currently recruiting to fill a number of positions, including: an Epidemiologist/Medical Officer (for candidates with relevant clinical backgrounds); a Programme Officer (for candidates with relevant management/finance experience); recruitment for a Product Development post (for candidates with relevant medical/pharmacological backgrounds) will begin soon. Full job descriptions, requirements and the official post vacancies can be viewed at [www.who.int/employment/vacancies/en/](http://www.who.int/employment/vacancies/en/).

## Frequently asked questions

- Q:** What are the quality and safety standards that the World Health Organization (WHO) polio research abides by and must these be applied to external research supported by the Polio Research Committee (PRC)?
- A:** All research funded by WHO and involving human participants is subject to clearance by the WHO Research Ethics Review Committee, as well as approval by a local institutional review board. The clinical trials also require approval by national regulatory agencies. That therefore includes any research supported by the PRC. In addition to this, all the polio clinical trials sponsored by WHO are designed and implemented in compliance with Good Clinical Practise (GCP) standards, as per the 1996 International Conference on Harmonisation (ICH). Lastly, an independent Data and Safety Monitoring Board was established to ensure the scientific and ethical integrity of the polio clinical trials funded and sponsored by WHO.

## The Polio Research Committee: one year on...

In May 2008, the Polio Research Committee (PRC) was established by the Global Polio Eradication Initiative (GPEI), with experts in the fields of virology, epidemiology, sociology and public health from around the world. The PRC reports to the Advisory Committee on Poliomyelitis Eradication (ACPE), the global independent advisory body to the GPEI, and is providing strategic guidance to the extensive programme of research, coordinated by the Research and Product Development team of the GPEI at the World Health Organization (WHO).

Since its inception, the PRC has endorsed and provided funds to the following 17 research projects:

- two IPV adjuvant development projects (Infectious Disease Research Institute, Seattle, USA; Global Vaccines, Research Triangle Park, USA);
  - three antiviral drug development projects (CDC, Atlanta, USA; National Institute of Infectious Diseases, Tokyo, Japan; University of Leuven, Leuven, Belgium);
  - two mathematical modelling projects (Imperial College London, London, UK; Kids Risk, Boston, USA);
  - two surveillance and monitoring projects in Pakistan (National Institute of Health Pakistan, Islamabad; Aga Khan University, Karachi; Pakistan Medical Research Council, Islamabad; Khyber Medical University, Peshawar); and,
  - one evaluation of zinc supplementation's effect on OPV (Aga Khan University, Karachi, Pakistan).
- five alternate IPV strain development projects (National Institute for Biological Standards and Control, Hertfordshire, UK; US Centers for Disease Control and Prevention - CDC, Atlanta, USA; University of California at San Francisco, USA; and two projects with the State University of New York - SUNY, Stonybrook, USA);
  - one alternative inactivation method for IPV production (Netherlands Vaccine Institute, Bilthoven, the Netherlands);
  - one communication research project (UNICEF);

The PRC has highlighted a number of remaining unmet research needs, in particular relating to further investigating underlying causes for compromised vaccine efficacy in northern India, and operational research on risk factors to vaccine delivery in areas of low vaccination coverage (see Table 1 for an updated list of unmet research needs).

## Courtyard women strategy: innovative approach to community outreach in conflict-affected areas of Afghanistan

Conflict in Afghanistan and Pakistan has made efforts to immunize children more difficult and perilous for health workers and citizens alike. Although polio workers are not often directly targeted, in areas of active conflict polio eradication partners face immense challenges in extending services without compromising the safety of the immunization workers.

In this type of environment, polio teams have looked to define ways to take advantage of quiet periods when

fighting has abated, and to encourage people to be more pro-active in immunizing their children whenever an opportunity exists. One strategy relies on opportunistic immunization that occurs when polio workers see a lull in fighting in an area that was previously inaccessible, and then quickly marshal their forces to immunize children in those communities.

To succeed, it is critical to ensure child caregivers receive information on the need to immunize their children and of

Continued on page 6

## Frequently asked questions (continue)

- Q:** What are the principal review criteria by the Polio Research Committee (PRC) on submitted research proposals?
- A:** As indicated in the 'PRC Call for Proposals' (see page 2), the PRC requests each proposal to include information relating to: 1) research question/objectives; 2) qualification of investigators and collaborators; 3) budget request; and, 4) study design and methodology. Key to successful application must be to ensure the completeness of research proposals, following the submission guidelines. Incomplete proposals cannot be considered for approval by the PRC. Any anticipated challenges, with proposed solutions, should be elucidated. Proposals requesting significant funding (ie >US\$100,000) should include detailed, divided budgets presented by phases of the proposed research activity. Research collaborators with relevant experience in the field of the proposed research activity is advantageous. The PRC encourages proposals meeting identified unmet research needs (see Table 1, page 3).

## Upcoming Events

- September 29-30 2009 (tentative): Investigator's Meeting, Moradabad, India
- October 21-22 2009: Data and Safety Monitoring Board (DSMB), Geneva, Switzerland
- October 27-29 2009: Strategic Advisory Group of Experts on Immunization (SAGE), Geneva, Switzerland
- October 30 2009: 8<sup>th</sup> WHO/ UNICEF Consultation with OPV/IPV Manufacturers and NRAs, Geneva, Switzerland
- November 10-11 2009: Polio Research Committee (PRC), Geneva, Switzerland
- November 18-19 2009: 6<sup>th</sup> Session of the Advisory Committee on Poliomyelitis Eradication (ACPE), Geneva, Switzerland

### Courtyard women strategy - continued

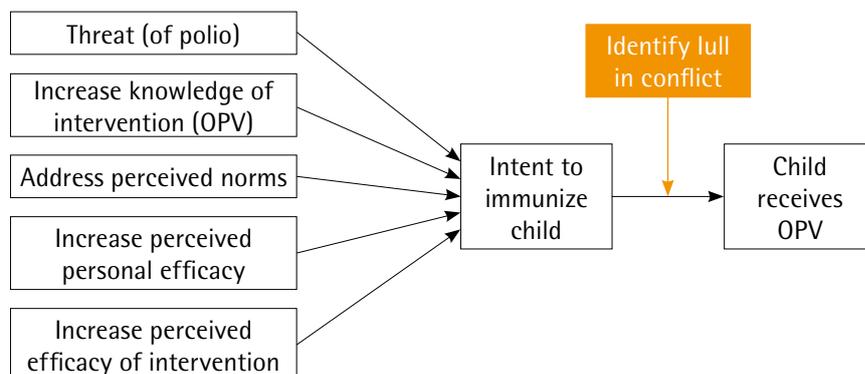
immunization services. To help increase this awareness requires local leadership to own and actively support polio eradication efforts. Local leaders can inform polio workers of lulls in conflict, and also use local networks to inform people in communities about available immunization services.

The demand for oral polio vaccine (OPV) is further driven by the deployment of local social mobilizers who work with communities to help them understand the threat of polio and the necessity of immunization, both during supplementary immunization activities (SIAs) and routine immunization.

A key innovative strategy in place to further drive this demand is the

'courtyard women strategy'. This activity brings trained female health workers into compounds to meet with mothers and other female child caregivers to engage in guided discussions about polio eradication, routine immunization and other basic child survival topics. As mothers are the primary caregivers of young children (the most vulnerable to polio), it is essential to increase an understanding among this target group of the need to immunize and increase empowerment to ensure children receive OPV and other vaccines. In areas where the 'courtyard women strategy' has been put in place, there is evidence that routine immunization and coverage during polio SIAs has increased.

### Community outreach and engagement



#### About this Newsletter:

At the annual meeting of the Advisory Committee on Poliomyelitis Eradication (ACPE) in November 2007, dozens of ongoing or pending research trials and multiple potential new products were discussed. Many of these studies were being managed by the Research and Product Development team at WHO, but a large number of important studies in the overall strategy of GPEI research are being conducted in conjunction with partner organizations such as the US Centers for Disease Control and Prevention (CDC) and UNICEF, as well as collaborators in industry and academics. This increased complexity has made it difficult for the global polio eradication scientific community to remain apprised of the overall research strategy and the ongoing projects within the research agenda. For this reason the ACPE recommended that WHO develop a GPEI research newsletter for the scientific community. This will be integrated with broader inclusion on [www.polioueradication.org](http://www.polioueradication.org).

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