



## Technology Solutions for Global Health





In the developing world, the difference between sickness and health for millions of babies and mothers can be as simple as a sterile needle and syringe, a reliable refrigerator for storing vaccines, or a diagnostic test at point of care. In reality, needles are not easily sterilized; refrigerators are expensive, require fuel, or are difficult for rural health workers to maintain; and laboratories where urine and blood are analyzed for infectious disease often are found only in major cities.

For the past 30 years, PATH has managed multiple projects focused on technology solutions to health needs. Working in many developing countries, PATH improves health by assessing needs and developing affordable and appropriate health, nutrition, and reproductive health technologies to solve them. Activities are carried out through effective partnerships with public-sector agencies (i.e., the World Health Organization) and private-sector companies. Involving the commercial sector improves the chances of developing low-cost, widely available, sustainable products. Technologies range from simple products which can be manufactured by small, local industries to highly sophisticated technologies produced with state-of-the-art industrial processes and materials.

PATH's areas of expertise include:

- Needs assessment
- Technology design and development
- Technology assessment and evaluation
- Technology transfer
- Local introduction, training and advancement of new technologies
- Technology-related technical assistance
- Commercialization and business development

To improve the safety and effectiveness of immunization services, PATH works on vaccine delivery devices and cold chain technologies. A vaccine heat-exposure indicator has been advanced and methods of stabilizing vaccines are being investigated. Injection devices include autodisable

syringes with features which prevent reuse; a prefill, single-dose syringe with an attached needle; and a needle-free injector. Technologies to deal with medical waste—especially used needles and syringes—are being developed and advanced, as are various refrigeration technologies to keep vaccines and pharmaceuticals cool throughout the distribution channels.

To improve maternal health and child health, low-cost technologies designed for use by low-literate health workers include a home birth kit, a portable scale to screen for low birthweight, and safe injection delivery devices for antibiotics for neonatal infections and for treatment of mothers with postpartum hemorrhage.

To improve reproductive health, new versions of diaphragms and female barriers are being designed and developed to protect women against HIV/AIDS, sexually transmitted diseases, and pregnancy. Work on effective delivery systems for microbicides is also a focus.

In the area of nutrition, PATH is working on a method of food fortification and low-cost ways of improving surveillance of vitamin A deficiency and other micronutrients among populations.

To improve diagnosis of major diseases, easy-to-use, low-cost test kits for tuberculosis, diarrheal diseases, fevers (including malaria), sexually transmitted infections, and cervical cancer for use at the point of care are being developed and advanced. For treatment of HIV/AIDS patients, low-cost methods of monitoring disease status are underway.

More than 30 health technologies are currently at some point of development and another 20 are already commercialized and available on the market. Suggestions for new technologies are welcome. PATH's work in this area is supported by a wide variety of funders including the United States Agency for International Development under the HealthTech program, the Bill & Melinda Gates Foundation, UNICEF, and others. Not included in this booklet are descriptions of PATH's work on vaccine development and advancement.

For further information, please contact: [info@path.org](mailto:info@path.org)

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# Technology Solutions Portfolio at PATH

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**Technologies being developed and advanced at PATH  
address needs for:**

**Immunization and Safe Injection**

**Maternal and Child Health**

**Reproductive Health**

**Nutrition**

**Diagnostics for Infectious Diseases**

**Safe Water**



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# **Immunization and Safe Injection**





## Vaccines in Uniject

### Health need

The World Health Organization (WHO) estimates that in some countries the percentage of injections given with syringes or needles reused without sterilization is as high as 70 percent. At the same time, the use of multi-dose vials often leads to 50 percent of vaccine being wasted or children being turned away due to reluctance to open a vial for just one child.

### Technology solution

A decade ago, prefill syringes were too costly for use in developing-country public-sector health programs, and no prefilled syringe on the market offered an autodisable feature. In collaboration with USAID, WHO, and many others, PATH developed an autodisable, prefilled, single-use syringe known as the Uniject<sup>®</sup> device, initially for use with vaccines.

The Uniject device simplifies the act of giving an injection, makes the unsafe reuse of the syringe impossible, and reduces the burden on logistics systems by making medicament, needle, and syringe available at the same place and time. The device eliminates the wastage commonly associated with multidose vials. Today, the Uniject device is licensed to BD, the world's largest manufacturer of injection equipment, for commercial production and distribution. BD sells the empty Uniject devices to pharmaceutical and vaccine producers, who then fill their products into the devices and sell the finished, prefilled drug or vaccine in Uniject to public health programs.

### Current status and results

Today, BD produces Uniject devices in Singapore with a fully automated, high-volume production line and markets them globally to pharmaceutical companies. The first vaccine in the Uniject device, tetanus toxoid (TT), became available in 2000. Now, WHO has prequalified both TT and hepatitis B vaccine in the Uniject device.

Operational research to assess the potential of incorporating TT in the Uniject device into immunization programs was conducted in Afghanistan, Mali, and Ghana in 2003. Factors evaluated include safety, coverage, logistics, and cost. In 2003, several other countries introduced TT in the Uniject device into their immunization programs. By allowing traditional birth attendants to safely deliver injections the Uniject device is especially effective in reaching women who have not previously been immunized for various reasons.

*\*Uniject is a registered trademark of BD.*



UNICEF/HQ020263/Giacomo Pirozzi

**Prefilled, single-use injection device filled with vaccines.**

**"With Uniject anybody can inject the vaccine. An illiterate midwife who's never been trained in medicine or birthing can do an absolutely perfect job."**

Dr. Francois Gasse, UNICEF, *Reuter's Health*, July 2002.

### Availability

Uniject devices and the associated equipment for filling and packaging are available to vaccine and pharmaceutical companies from BD Pharmaceutical Systems, New Jersey, USA. Roderick Hausser, Tel: (201) 847-5185, Fax: (201) 847-4869. Hepatitis B vaccine and tetanus toxoid are available from manufacturers in India and Indonesia.

For more information regarding this project, contact Steve Brooke at [sbrooke@path.org](mailto:sbrooke@path.org).

### Donor support

Funding for this project has been provided by the **United States Agency for International Development** under PATH's HealthTech program.



## SoloShot

### Health need

Although sterile, disposable syringes and needles offer the best protection against transmission of bloodborne diseases, they are often reused in the developing world. Each year, more than 12 billion injections are administered worldwide; in the past in developing countries 50 percent of injections were estimated to be unsafe. A primary source of transmission of disease has been the reuse of contaminated needles and syringes. To be completely safe, single-use injection devices must be designed to automatically and irrevocably inactivate after a single cycle of filling and injection. The World Health Organization/Expanded Programme on Immunization (WHO/EPI) called for the design of such devices in 1987.

### Technology solution

In response to WHO's call, PATH designed one of the first feasible approaches to nonreusable syringes for immunizations: an autodisable (AD) syringe with a fixed needle that automatically locks after a single injection. When the syringe is filled to the preset 0.5-ml level, the plunger stops and cannot be pulled back further. After the vaccine is injected, the plunger automatically locks so that the syringe and needle cannot be reused. Known as the SoloShot syringe, this technology was licensed to and is now manufactured and marketed by BD, one of the world's leading syringe manufacturers. Third-party field validations of the device in Pakistan in the early 1990s demonstrated the acceptability and usability of the design. PATH also has assisted several other manufacturers of AD syringes to ensure a wide variety of products are available and to facilitate the lower pricing that accompanies increased competition and production volume.

### Current status and results

Since commercial introduction in 1992, 6 billion vaccinations have been delivered using SoloShot syringes by public health programs in more than 40 developing and emerging countries. United Nations Children's Fund—which has already distributed hundreds of millions of AD syringes to EPI programs—now provides only AD syringes to countries requesting disposable syringes, many of which are SoloShot syringes. BD continues to supply the syringes to national and international public health agencies at low cost. In fact, the syringe was one used in the recent PATH- and WHO-sponsored meningitis vaccine campaign in West Africa where millions of people were immunized. The price of AD syringes is dropping rapidly and is currently within two cents of the price of disposable syringes. PATH is also assisting USAID-supported family planning agencies with the introduction of a 1-ml AD syringe to be bundled with injectable contraceptives.

AD syringes are now routinely used in immunization programs throughout the world. They can be used safely by vaccinators regardless of past experience or training. The devices are quicker to use than a conventional syringe and are preferred over a conventional syringe by vaccinators due to the speed and ease with which a correct vaccine dose can be drawn.

*SoloShot is a trademark of BD.*



**An autodisable, single-use syringe.**

**“The autodisable syringe, which is now widely available at low cost, presents the lowest risk of person-to-person transmission of bloodborne pathogens.”**

*WHO-UNICEF-UNFPA Joint Statement, 2003.*

### Availability

This technology has been licensed and is available from BD Pharmaceutical Systems, New Jersey, USA, Michael Garrison [michael\\_garrison@bd.com](mailto:michael_garrison@bd.com).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program.





## Technologies for Immunization Safety

### Health need

Each year, more than 16 billion injections are administered worldwide. In some regions, 17 to 75 percent are estimated to be with reused, unsterilized injection equipment. It is estimated that unsafe reuse causes 20 million hepatitis B infections, 2 million hepatitis C infections, and 260,000 HIV infections annually. In addition, needlestick injury is estimated to cause 40 percent of hepatitis B, 40 percent of hepatitis C, and 2.5 percent of HIV/AIDS infection among the estimated 35 million health workers worldwide.

Immunization programs have been proactive in introducing technologies and practices for injection safety, notably with autodisable syringes, sharps disposal boxes, and needle-removal systems. Opportunities remain to further increase immunization safety by reducing the use of sharps and improving safety of other steps of vaccination. As new vaccines such as *Haemophilus influenzae* type b, human papillomavirus, pneumococcal, and rotavirus vaccines are rolled out in developing countries, children may be subjected to an increased number of injections. It is critical that immunization systems maintain a focus on safety to ensure that these children reap the maximum health benefits with minimal associated risks.

### Technology solution

There are a number of technologies available to improve injection safety in developing-country settings. Retractable-needle syringes have been used in industrialized countries for many years, but their relatively high cost has limited introduction in low-resource countries. As technology and market development lead to less-expensive options in this category, the value assessment is changing, and opportunities are growing for developing-country use. Needle removers separate the needle from the syringe immediately after giving an injection, containing the dangerous sharp waste in a small container for safe disposal. Syringe melters compact syringe waste volume, trap and disinfect needles, and facilitate recycling. Safety boxes, currently imported from Europe or Asia, may be able to be manufactured in Africa or other low-resource settings using innovative coatings and materials to meet international quality standards.

### Current status and results

PATH has been a leader in developing, identifying, and promoting appropriate solutions for safe injections and waste management. In 2008 PATH published a resource page on the web on the subject of medical waste, available at [http://www.path.org/projects/health\\_care\\_waste\\_resources.php](http://www.path.org/projects/health_care_waste_resources.php).

In 2009 the World Health Organization (WHO) published product specifications and a test protocol for needle cutters as part of their Performance, Quality, and Safety program. This established a standard for WHO prequalification which then facilitates procurement of quality devices by the United Nations Children's Fund and other international and national organizations.



Robert Maletta

**Needles and sharps waste are dangerous to the community.**

**"Recognizing the importance of needle-removal to improve the safety of sharps waste management, it is recommended that the process of assessment and introduction be accelerated in African countries."**

GAVI/Implementation task force workshop on the management of biomedical waste, Senegal, 2003.

### Availability

For more information regarding this project, contact Joanie Robertson at [jrobertson@path.org](mailto:jrobertson@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program and from the Bill & Melinda Gates Foundation.



## Vaccine Vial Monitors

### Health need

Vaccines require careful storage and transport to the point of use to avoid harmful heat exposure. In the past, there was no way to detect whether individual vials had been exposed to heat, so national immunization programs adopted conservative guidelines for vaccine handling and disposal of vaccines when heat exposure was suspected. In 1985, PATH launched a search for suitable technologies that could indicate exposure to heat. An appropriate technology used for the food industry was discovered; PATH worked with the manufacturer to adapt it for vaccines, resulting in a product known as the vaccine vial monitor (VVM).

### Technology solution

VVMs are small, circular indicators, printed directly on vial labels or adhered to the tops of vials. The inner square is chemically active and changes color irreversibly from light to dark with exposure to heat over time. By comparing the color of the inner square to the reference color, a health worker can determine whether the vaccine has been exposed to heat. Important decisions on whether to use or discard vaccine and which vials should be used first are now clear due to the VVM. VVMs can be manufactured for a variety of heat-exposure specifications suitable for use with any vaccine, including BCG, diphtheria, hepatitis B, Hib, HPV, measles, oral polio, pertussis, pneumococcal, rabies, rubella, tetanus, and yellow fever vaccines.

### Current status and results

Since introduction in 1996, VVMs have helped to ensure that only potent vaccine is used to immunize children and to extend the reach of services thus raising coverage. The presence of VVMs made it possible for the World Health Organization (WHO) to implement the "multi-dose vial policy" that allows health workers to use opened vials of some liquid vaccines for more than one day. This has markedly reduced vaccine wastage, saving millions of dollars in immunization programs throughout the world. VVMs are also used to help manage and improve vaccine distribution.

VVMs are manufactured by TEMPTIME Corporation in New Jersey under the product name HEATmarker™\* and are sold to vaccine producers throughout the world. WHO requires that all vaccine purchased through the United Nations Children's Fund (UNICEF) be labeled with VVMs. A new WHO/UNICEF joint policy statement urges all vaccine self-procuring countries, donor agencies, and international organizations to include VVMs among the minimum requirements for vaccine purchase agreements and donations. Since their introduction in 1996, over 3 billion VVMs have been used on vaccine vials. WHO and UNICEF estimate that the use of VVMs is saving the global health community at least US\$5 million per year.

\* HEATmarker is a trademark of TEMPTIME Corporation.



Labels on vaccine products to indicate heat exposure.

**"Used properly, this [vaccine vial monitors] can be a miracle tool to reduce wastage and prevent the use of heat damaged stock."**

Umit Kartoglu, WHO  
Department of Vaccine and  
Biologicals. *GAVI Immunization  
Focus*, July 2003.

### Availability

For more information on  
HEATmarker VVMs, contact  
TEMPTIME Corporation  
116 American Road  
Morris Plains, NJ 07950, USA  
Tel: (973) 984-6000  
Fax: (973) 984-1520  
website [www.temptimecorp.com](http://www.temptimecorp.com)  
e-mail [tedp@temptimecorp.com](mailto:tedp@temptimecorp.com).

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been provided by the United  
States Agency for International  
Development under PATH's  
HealthTech program.





## Mucosal Immunization Technologies

### Health need

AIDS, tuberculosis, acute respiratory-tract infections, and diarrheal diseases account for millions of deaths annually worldwide. All are caused by pathogens that enter the body via the mucosa, a mucous tissue lining found in the oral cavity as well as in reproductive and gastrointestinal tracts. These surfaces are home to key antibodies and specific cells that can be preferentially activated when relevant vaccines are administered directly to the mucosa. Mucosal vaccines face significant barriers to success, however, due to in situ dilution and dispersion, potential competition with replicating bacteria and viruses, interference from inert food and dust particles, enzymatic degradation, and low pH in the stomach. These factors can limit the ability of the vaccine to reach its target immune cells, resulting in a suboptimal immune response. To more effectively protect people from infection-causing pathogens that enter the body via the mucosa, new technological approaches are needed to address these challenges.

### Technology solution

PATH recently developed a mucosal immunization technology platform—viable in two formats—that builds on several proven formulation, adjuvant, and delivery technologies that enable the efficient sublingual administration of subunit vaccines. The first format is a liquid solution at room temperature that instantly transforms into a gel at human body temperature, enabling it to adhere to mucosal surfaces. Its gel matrix also protects the vaccine antigen from degradation caused by salivary enzymes. The second is a fast-dissolving tablet that disintegrates instantly in a small amount of saliva under the tongue, forming a solution or a viscous gel on the sublingual mucosa. Both formats contain a thermoresponsive polymer, a penetration enhancer, a muco-adhesive agent, and a safe as well as potent adjuvant that helps to prevent rapid clearance caused by salivation or swallowing. Furthermore, because each potential product presentation is needle-free, the mucosal immunization technology platform should help to improve the safety of vaccination.

### Current status and results

In vitro assays done at PATH demonstrated the thermoresponsive properties of the technology platform and its enhanced permeability of the epithelium barrier. Tests also revealed tolerability by cultured epithelium cells. Studies in animal models demonstrated a desirable spreading of gelatin and retention (>20 minutes) on the sublingual mucosa—maximizing the proportion of administered antigen gaining spatial access to the dendritic cells, which initiate immune response. Sublingual immunization of mice using tetanus toxoid vaccine elicited a high level of relevant antibodies in serum and in the secretions of the oral cavity as well as the gastrointestinal and reproductive tracts. Additional assessments are under way as PATH continues to research its two mucosal immunization formats as value-added product presentations for a number of existing and candidate vaccines in development.



PATH/Scott Arman

**Novel methods to induce mucosal immunity.**

**“The best defense against these predominantly mucosal pathogens would be vaccines, preferably mucosal vaccines capable of inducing both systemic and mucosal immunity.”**

van Ginkel F, Nguyen H, McGhee J. Vaccines for mucosal immunity to combat emerging infectious diseases. *Emerging Infectious Diseases*. March-April, 2000;6(2):123-132.

### Availability

For more information regarding this project, contact Dexiang Chen at [dchen@path.org](mailto:dchen@path.org).

### Donor support

Support for this project has been provided through funding from private foundations and individual donors to the **Health Innovation Portfolio** at PATH.

THE UNIVERSITY OF CHICAGO  
DEPARTMENT OF CHEMISTRY  
RESEARCH REPORT

1. The first part of the report describes the experimental work carried out during the year 1964. The results of the experiments are presented in the form of tables and graphs. The second part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

2. The third part of the report discusses the results of the experiments carried out during the year 1965. The results are presented in the form of tables and graphs. The fourth part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

3. The fifth part of the report discusses the results of the experiments carried out during the year 1966. The results are presented in the form of tables and graphs. The sixth part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

4. The seventh part of the report discusses the results of the experiments carried out during the year 1967. The results are presented in the form of tables and graphs. The eighth part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

5. The ninth part of the report discusses the results of the experiments carried out during the year 1968. The results are presented in the form of tables and graphs. The tenth part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

6. The eleventh part of the report discusses the results of the experiments carried out during the year 1969. The results are presented in the form of tables and graphs. The twelfth part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

7. The thirteenth part of the report discusses the results of the experiments carried out during the year 1970. The results are presented in the form of tables and graphs. The fourteenth part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

8. The fifteenth part of the report discusses the results of the experiments carried out during the year 1971. The results are presented in the form of tables and graphs. The sixteenth part of the report discusses the theoretical aspects of the problem and compares the experimental results with the theoretical predictions.

## Cold Chain Technologies

### Health need

Effective vaccine distribution and storage are critical to achieving immunization coverage and impact. As new and more expensive vaccines become available, greater capacity is needed in the cold chain to accommodate the new vaccines, and the loss of vaccine due to heat or freeze damage is becoming less tolerable due to greater financial risk. Innovative cold chain technologies can help improve the reliability of vaccine distribution, reduce unnecessary wastage of valuable vaccines, and help strengthen the overall immunization system.

### Technology solution

PATH is working to advance technologies that improve the cold chain; for example, "smart" refrigerators that keep vaccines cold without freezing, and lower-cost solar refrigerators without batteries that provide affordable refrigeration for more health clinics as well as facilitate immunization services in remote settings. PATH is also working on software solutions to update the management systems that underlie the cold chain infrastructure. A new tool is being developed for tracking country-wide inventories of cold chain equipment and improving the ability of managers to plan over multiple years to accommodate new vaccines.

### Current status and results

In 2008, PATH and the United Nations Children's Fund introduced the cold chain equipment management software (CCEM) version 1. Workshops were conducted in Seattle and Panama to train immunization managers and global experts. Version 2 is expected by mid-year 2009.

PATH is working to advance solar refrigerators that do not require traditional batteries for energy storage. Direct-drive solar refrigerators and new long-life batteries developed for the hybrid automobile market hold the promise of reducing operating costs while expanding the reach of vaccine refrigeration. In 2009 we will likely see the World Health Organization (WHO) prequalify the first device in the direct-drive class.

PATH is assisting WHO in the development of new specifications for refrigerators and cold chain monitoring equipment that will encourage manufacturers to create innovative products that fit developing-country needs.

PATH continues to work on global policy that will help countries adopt new technologies and practices to preserve vaccine in the cold chain. For example, we are working with WHO to add specifications under their product qualification system that will allow new technologies, such as transport containers with new cooling technologies. We are also helping the global community study the possibility of removing some heat-stable vaccines from the cold chain in some locations.



PATH/Carib Nelson

**Appropriate and innovative technologies for vaccine cold chain.**

**"Vaccines are sensitive to heat and freezing and must be kept at the correct temperature from the time they are manufactured until they are used."**

*Immunization in Practice. A Practical Resource Guide for Health Workers. WHO, 2004.*

### Availability

For more information regarding this project, contact Joanie Robertson at [jrobertson@path.org](mailto:jrobertson@path.org).

### Donor support

Funding for this project has been provided by the **United States Agency for International Development** under PATH's HealthTech program and from the **Bill & Melinda Gates Foundation**.

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## Vaccine Stabilization

### Health need

Maintaining cold chains to store and transport vaccine is a challenging task in many developing countries. The potential for heat to damage vaccines is highest in areas where power outages or kerosene shortages prevent refrigerators from operating or where vaccine must be transported over long distances to reach remote populations. Vaccines containing an aluminum adjuvant are also sensitive to freezing. Accidental freezing can occur when vaccines are placed too close to the walls of ice-lined refrigerators, the evaporator in certain refrigerators, or the frozen ice packs inside insulated transport carriers. Inadvertent exposure of vaccines to damaging temperatures has been well documented in both developed and developing countries. When health workers suspect a vaccine is temperature-damaged, the vaccine is often discarded—at great cost to the immunization program. When temperature damage goes unnoticed, children may receive ineffective vaccine.

### Technology solution

Thermostable vaccines will improve the effectiveness and efficiency of immunizations by preventing temperature damage to vaccines, reducing vaccine wastage, and decreasing logistical and equipment requirements as well as the costs of vaccine transportation and storage, especially at the periphery of the cold chain. Thermostable vaccines will also facilitate coverage gains by enabling vaccine delivery in remote areas beyond the reach of the existing cold chain. Additional benefits, such as improved vaccine safety and superior product formats, are also possible depending on the stabilization methods used.

### Current status and results

PATH is researching several methods to improve the thermostability of vaccines of importance to developing countries such as vaccines for measles, hepatitis B, diphtheria-tetanus-pertussis (DTP), *Haemophilus influenzae* type B (Hib), *Shigella*, enterotoxigenic *Escherichia coli*, meningococcal A, and pandemic influenza. Research is being conducted in collaboration with vaccine producers, vaccine development projects, technology companies, laboratories, and universities. Recent achievements include:

- Development of a method to protect vaccines containing an aluminum adjuvant from freeze damage and advancing its application to pentavalent (DTP-hepatitis B-Hib) vaccine through formulation development, analytical method development, preclinical work, laboratory-scale production, and stability studies. PATH's vaccine freeze-protection technology is in the public domain so that vaccine manufacturers worldwide can use the approach.
- Identification of a technology to improve the heat stability of hepatitis B and Hib vaccines and demonstration of its compatibility with the above method to obtain a heat- and freeze-protected hepatitis B vaccine product.
- Marked improvements in the stability of hepatitis B and meningococcal A vaccines through reformulation involving glass-forming sugars plus other excipients and processing via spray drying.



Unit Kartoglu

**Thermostable vaccines improve vaccine effectiveness and ease logistics.**

**“...heat-stable vaccines and combination formulations can simplify and improve drug and vaccine delivery while expanding the reach of modern medicine to millions more who could benefit.”**

Daar AS, et al. Top 10 Biotechnologies for Improving Health in Developing Countries. *Nature Genetics*. 2002;32:37.

### Availability

For more information regarding this project, please visit our web site at <http://www.path.org/projects/vaccine-stabilization.php> or contact Debra Kristensen at [dkriste@path.org](mailto:dkriste@path.org).

### Donor support

Funding for this project has been provided by the Bill & Melinda Gates Foundation.



## Disposable-Syringe Jet Injection

### Health need

According to the World Health Organization (WHO), 16 billion injections are given each year, yet in developing countries at least 50 percent of injections given are unsafe.<sup>1</sup> Reuse of contaminated needles and syringes, needlestick injuries among health workers, and threats to the community from improperly disposed of and potentially contaminated needles and syringes are serious health risks, possibly spreading infection and diseases such as HIV and hepatitis.

### Technology solution

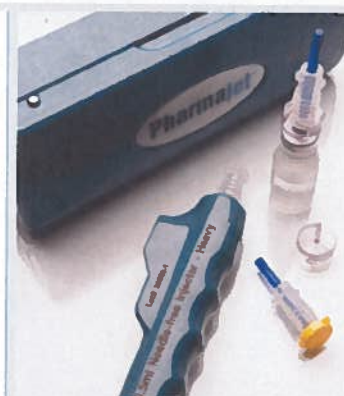
Jet injectors deliver vaccines and medicines without using needles; instead, jet injectors generate a pressurized liquid stream that pushes through the skin and delivers injections into the tissue. First introduced in the 1940s, early-model jet injectors were used to give millions of injections—even helping to eradicate smallpox. More recently, disposable-syringe jet injectors (DSJIs) have been developed to prevent cross-contamination between patients. This technology is currently the only available needle-free technology that can be used to deliver all injectable vaccines used in developing-country immunization programs, at all depths of delivery (intradermal, subcutaneous, and intramuscular). It also requires no change in vaccine formulation and can be filled from multi-dose and single-dose vials at the point of use.

PATH has worked with several developers on their respective DSJI technologies to advance designs that are affordable and adapted for routine immunization in low-infrastructure settings. In addition, PATH is exploring ways in which this technology could facilitate new vaccination strategies. For example, intradermal delivery offers the potential advantage of effective immunization with smaller doses, allowing for reduced costs of each vaccination and increased coverage for vaccines that are in short supply due to high cost or limited production capacity. PATH has identified potential benefits of using DSJIs for this type of vaccination.

### Current status and results

PATH is working with multiple device developers and global stakeholders, assisting with design, regulatory advances, economic analysis, and clinical research. PATH has conducted user assessments of device prototypes in the field (Brazil, China, and India) and suggested design adjustments based on user feedback. PATH helped to formalize a WHO Performance, Quality, and Safety specification and verification pathway for DSJI technology. Also PATH recently completed a clinical study where DSJIs were compared with traditional needles and syringes in delivering measles-mumps-rubella vaccine. PATH plans to continue to explore acceptability and sustainability of DSJIs, especially in terms of intradermal delivery in developing-country immunization programs.

<sup>1</sup> Simonsen L, Kane A, Lloyd J, Zaffran M, Kane M. Unsafe injections in the developing world and transmission of bloodborne pathogens: a review. *Bulletin of the World Health Organization*. 1999;77:789–800.



Scott Arman

Disposable-syringe jet injector.

**“Needle-free delivery systems offer an answer to the problem of sharps in the vaccination programs. That is why WHO is so interested in this technology. In addition, the intradermal administration of fractional doses of IPV [inactivated polio vaccine] could make this vaccine affordable for developing country use.”**

Dr. Roland Sutter of the World Health Organization and the Global Polio Eradication Initiative.

### Availability

For more information regarding this project, contact Darin Zehrung at [dzehrung@path.org](mailto:dzehrung@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development and the Bill & Melinda Gates Foundation.

# THE HISTORY OF THE

## REPUBLIC OF THE UNITED STATES

OF AMERICA

FROM THE FIRST SETTLEMENTS TO THE PRESENT TIME

BY

JOHN F. JOHNSON

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"The History of the United States of America"

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## Reconstitution Technologies

### Health need

Many obstacles must be overcome before a vaccine can be safely delivered to a child in a developing country. Delays in transit and uneven temperatures can spoil the vaccine. Some vaccines require reconstitution—mixing dry components with wet diluents—which can also cause challenges. Irregular supply chains can separate dried vaccines from their respective diluents. Even if everything arrives on time, together, and at the right temperature, poor lighting and outdated training can prevent a health worker from effectively administering the vaccine. In addition, the needles used to reconstitute vaccines represent a risk of transmitting infection and causing disease if used and disposed of improperly. All these contribute to inappropriate reconstitution and administration of vaccines—scenarios that have been connected to deaths and injuries around the world.

For reconstitution of critical vaccines to become safer and more economical, the process of reconstitution must be simple and must eliminate the adverse events and wastage that can occur with improper reconstitution. Technologies that keep a dried vaccine and its diluent together—ensuring that both are at the same temperature, are not separated, and have a simplified mixing process of the two parts—offer many advantages over current systems. Single-dose, prefilled reconstitution devices (SPRDs) can address these, representing a means of eliminating reconstitution errors, reducing supply wastage, and reducing the impact on the medical waste disposal system.

### Technology solution

Selective and strategic introduction of vaccines through low-cost SPRDs can reduce adverse events and wastage while improving vaccine effectiveness. PATH examined a variety of SPRDs to see if they were suitable for use in developing countries. Five devices were evaluated by health workers in Andhra Pradesh, India. Results were favorable: users felt they could deliver injections with more safety and less wastage with SPRDs. They also provided extensive input on the design and use of the devices.

### Current status and results

PATH continues to advocate for and support the development of low-cost SPRDs for use with spray-dried or lyophilized vaccines. PATH is also conducting additional research to assess how specific features of integrated reconstitution devices for vaccine delivery impact stakeholders all along the value chain. Our goal is to enable selective and strategic introduction of vaccines in a low-cost SPRD format to reduce mortality and morbidity associated with reconstitution-related adverse events. We facilitate interactions among users, device developers, vaccine manufacturers, and experts in research. At every point we aim to ensure that the technology is safe, affordable, and sustainable.



Scott Areman

**A simple, economical process for reconstitution of vaccines.**

**Single-dose, prefilled reconstitution devices (SPRDs) can make reconstitution of critical vaccines safer and more economical. SPRDs can help eliminate adverse events or wastage that can occur with improper reconstitution, which also reduces impact on the medical waste disposal system.**

### Availability

For more information regarding this project, contact Darin Zehrung at [dzehrung@path.org](mailto:dzehrung@path.org).

### Donor support

Support for this project was provided through funding from private foundations and individual donors to the **Health Innovation Portfolio** at PATH.



## Intradermal Adapter

### Health need

Rabies vaccine is expensive and often in short supply—approximately 20,000 people die of rabies each year in India, often because they were unable to access treatment. For rabies vaccine, the same or better protection can be achieved by delivering smaller amounts of vaccine intradermally (into the top layer of the skin), sparing valuable doses and stretching supplies to provide for more patients. Intradermal (ID) regimens for rabies vaccine have been adopted in many regions, protecting people who have been exposed to rabid animals, while saving costs and vaccine.

This approach is not yet universal, despite clear benefits, due in part to the difficulty of giving an ID injection correctly. The Mantoux technique, which uses a traditional needle and syringe for ID delivery, has historically been recognized as a difficult and inconsistently used technique. In many countries, only certain health care workers are able to perform ID injections, such as for rabies vaccine and Bacillus Calmette-Guérin or BCG, a vaccine given intradermally at birth to prevent tuberculosis. Smaller ID doses of other vaccines could also be effective. Such dose sparing could be particularly meaningful to immunization programs in low- and middle-income countries, as they could potentially reduce the amount of vaccine needed per patient, thereby cutting costs and overcoming vaccine shortages. However, concerns regarding the difficulty and a lack of reliability of conventional ID injections limit research in this field and introduction of this technique into immunization programs.

### Technology solution

The PATH intradermal adapter makes ID injections easier. It facilitates the procedure by standardizing injection depth and angle. It is anticipated that the ID adapter would expand the pool of health care workers capable of performing the procedure. This would have a particularly high impact in remote or underserved communities with more limited access to health care specialists.

### Current status and results

In partnership with SID Technologies of Newtown, Pennsylvania, PATH developed the ID adapter from the initial concept through manufacturing of clinic-ready devices. We modified and tested successive design prototypes, incorporating feedback from health care workers in the United States and India. Performance of the current model has been proven in preclinical testing, and will be demonstrated in a clinical trial with saline and ultrasound imaging in the United States in 2011. The ID adapter will then be used in a clinical trial with rabies vaccine in 2011.



PATH/Emily Griswold

**The intradermal adapter fits over a conventional needle and syringe.**

**“The use of reliable ID delivery devices for rabies vaccination and for other vaccines and drugs can have application in areas where health care workers are not used to, or confident with, ID delivery by the Mantoux technique.”**

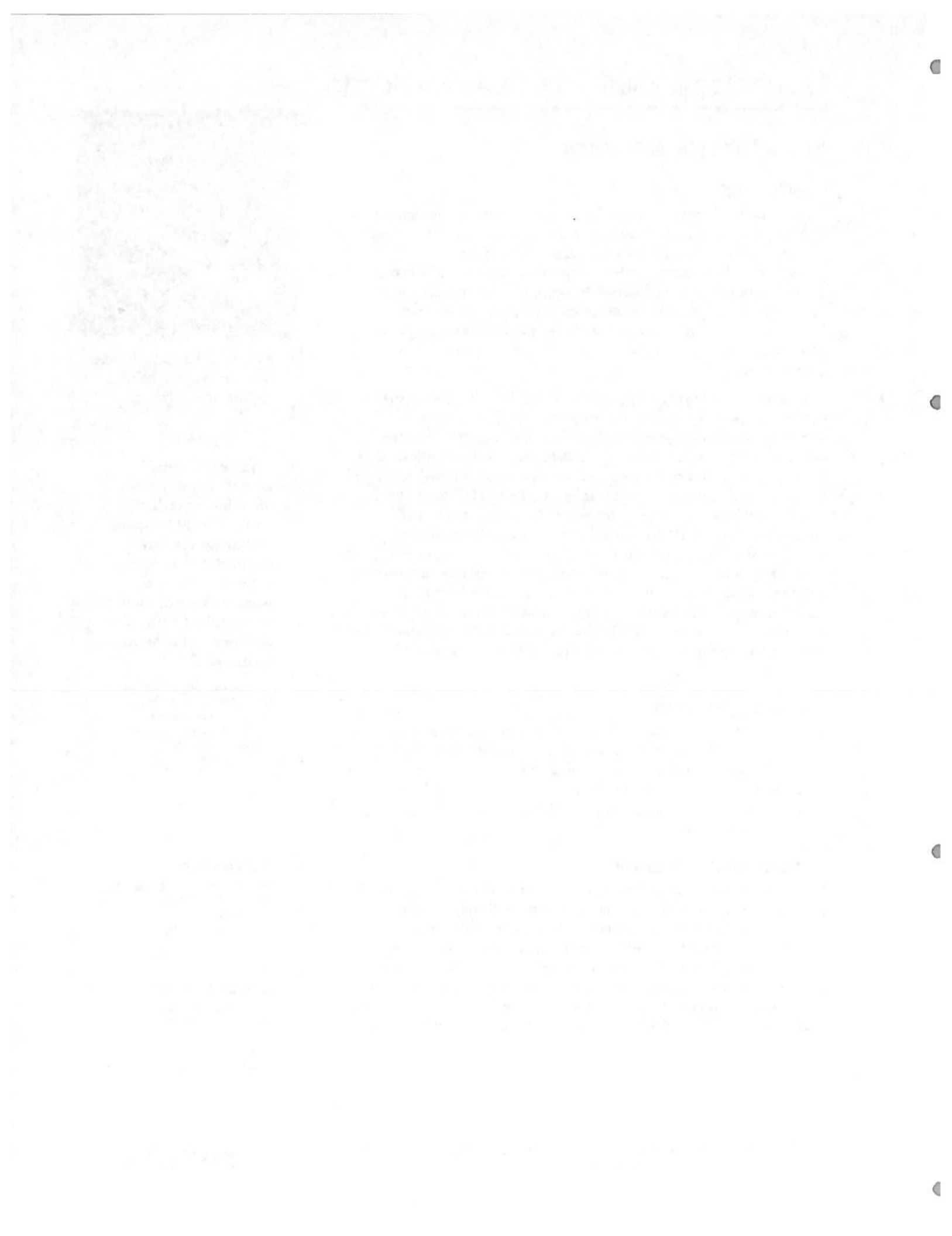
Recommendation of the World Health Organization/Bill & Melinda Gates Foundation Consultation, Annecy, France, October 7–9, 2009.

### Availability

For more information regarding this project, contact Darin Zehrung at [dzehrung@path.org](mailto:dzehrung@path.org).

### Donor support

Support for this project was provided through funding from private foundations and individual donors to the **Health Innovation Portfolio** at PATH.



## Microneedle Patches

### Health need

Some vaccines are too expensive for developing-country immunization programs. Others are subject to shortages or imperfect distribution systems. Any one of these factors can prevent people from accessing the vaccines that they need. PATH is exploring ways to bridge the gap.

A potential solution for some vaccines is intradermal (ID) delivery. The skin is an active player in the human immune system, particularly the shallow, upper layers. Delivering vaccines directly to these tissues can be very effective. Research shows that reduced-dosage of vaccine delivered intradermally can achieve the same results as an intramuscular or subcutaneous injection. ID delivery does so using up to 80 percent less vaccine—helping to optimize the capacity of the cold chain, lower the cost of each dose, and enable immunization programs to stretch their vaccine supplies across more patients.

This approach is not yet universal despite clear benefits. This is due, in part, to the difficulty of giving an ID injection correctly. The Mantoux technique, which uses a traditional needle and syringe for ID delivery, can be difficult to learn and impractical to use in many settings. Concerns regarding the difficulty and a lack of reliability of conventional ID injections limit research in this field and introduction of this technique into immunization programs.

### Technology solution

Microneedles are a diverse field of delivery technologies designed to access the intradermal cells. Some microneedle patches consist of tiny needles coated with vaccine, while others use the skin's moisture to dissolve the vaccine into the intradermal layer. Hollow microneedles are a different type of device, using miniature needles attached to a regular syringe. Preclinical studies show great promise for these technologies, particularly with influenza and herpes simplex virus vaccines. Easy to use and intuitive, these devices could simultaneously make intradermal delivery easier and more effective.

### Current status and results

Building on earlier work under the Health Innovation Portfolio—where we tested herpes simplex virus, malaria, and hepatitis B vaccines with microneedles—PATH formed a collaboration with the Georgia Institute of Technology (Georgia Tech) and Emory University. This project aims to create a microneedle patch that allows people to self-administer influenza vaccine. PATH will evaluate the technology from a variety of angles, including medical, economic, social, and regulatory, and PATH will assist Georgia Tech in developing a strategy to address any issues. The team will also carry out a cost-effectiveness analysis to quantify the potential cost implications of a self-administered vaccine. Our work will assess the feasibility of this novel approach and help plan for the introduction of microneedles into clinical practice more effectively.



Scott Arman

One example of a microneedle patch.

**“If we can make it easier for people to be vaccinated and improve the effectiveness of the vaccine, we could significantly reduce the number of deaths caused every year by influenza.”**

Dr. Mark Prausnitz, Georgia Institute of Technology.

### Availability

For more information regarding this project, contact Darin Zehrung at [dzehrung@path.org](mailto:dzehrung@path.org).

### Donor support

Support for this project was provided through funding from private foundations and individual donors to the **Health Innovation Portfolio** at PATH, and from **National Institute of Biomedical Imaging and Bioengineering**.





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## **Maternal and Child Health**





## BIRTHweigh III

### Health need

Low birth weight is a well-known indicator of risk for newborn babies and is a major cause of infant mortality and morbidity in the developing world. Each year, millions of infants in developing countries are born underweight. Most babies are delivered outside of health facilities by nonliterate traditional birth attendants (TBAs) who may need appropriate tools to identify low birth weight newborns and follow up with appropriate care immediately.

### Technology solution

In the mid-1980s PATH conducted a needs assessment of TBAs in several African countries, which resulted in the concept of an easy-to-use, yes/no indicator of low birth weight that could be used by relatively untrained midwives and TBAs. BIRTHweigh I, developed and field-tested by PATH in several countries, was subsequently adopted for use in Indonesia. The device allowed nonliterate birth attendants to identify low birth weight newborns (<2,500 grams) and then follow up with special care. BIRTHweigh I was designed for low-resource, in-country production; local economic development; and regional distribution. United Nations Children's Fund (UNICEF) currently distributes a similar scale under the brand name BebeWey.

BIRTHweigh II, developed in the early 1990s, is a revised version designed for modern manufacturing methods and features a tactile as well as a visual indication of birth weight. This model performed successfully when included in a comparative evaluation of BIRTHweigh I, II, and BebeWey in Egypt. Nonetheless, interest among manufacturing and programmatic partners became scarce and project development was suspended.

More recently, PATH designed the BIRTHweigh III to meet the need for correctly dosing newborns with gentamicin to prevent serious bacterial infections. Using the same technological platform as the second scale, this scale permits nonliterate birth attendants and community health workers to categorize newborns into three different weight categories (normal birth weight:  $\geq 2,500$  grams; low birth weight: 2,000–2,499 grams; very low birth weight: <2,000 grams).

### Current status and results

Prototypes of BIRTHweigh III were built and field tested in collaboration with the Saving Newborn Lives Project in both Nepal and India in 2004. Results from both of these studies concluded that the BIRTHweigh III scale classified infants into weight categories with a high degree of consistency and accuracy and that the scale is extremely practical and useful for resource-poor settings, especially those with low levels of literacy. Even though the BIRTHweigh III scale is not yet commercially available, PATH continues to receive requests from programs in low-resource settings interested in using it. In 2006, PATH produced a report detailing feasible commercialization options to ensure availability and access of the BIRTHweigh III scale. PATH is making the report available to manufacturers interested in commercialization opportunities.



Hand-held, portable, plastic, spring scale for measuring low birth weight.

The scale will be very useful in settings where community health workers are dealing with decisions about identifying low birth weight newborns.

### Availability

For more information regarding this project, contact Patricia Coffey at [pcoffey@path.org](mailto:pcoffey@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program and by Save the Children.

THE UNIVERSITY OF CHICAGO

PHYSICS DEPARTMENT

CHICAGO, ILL.

Dear Sir:

I have the pleasure to inform you that your application for admission to the Ph.D. program in Physics has been accepted. You will be admitted to the program in the fall semester of 1964.

Sincerely,

Very truly yours,  
[Signature]

[Name]  
[Address]  
[City, State, Zip]

[Text]

[Text]

[Text]

[Text]

## Delivery Kit

### Health need

High rates of maternal and perinatal mortality in developing countries indicate a crucial need for new and innovative interventions for pregnancy and neonatal care. In developing countries most women have no access to maternity services due to distance, cost, and local customs; many give birth alone. High rates of neonatal and maternal tetanus and sepsis indicate a need for education and materials focused on clean birth practices.

### Technology solution

The basic delivery kit is an inexpensive, simple kit designed to help create a clean birthing environment, particularly for home births. The contents of the delivery kit include a clean razor blade, cord ties, a small bar of soap, a plastic delivery sheet, and pictorial instructions. The delivery kit is designed for use by skilled birth attendants, family members, and women who give birth unassisted in the home. Community health workers and traditional birth attendants are oriented to the kits so they can either provide it as part of their birth delivery services or encourage families to purchase the kit for home deliveries. The kits are also designed to be sold through retail distribution outlets. In 1994, PATH assisted a women's health small business in Nepal to design, develop, and market a locally appropriate kit. With the approval of the Ministry of Health (MOH) in Nepal, that kit is now being sold and used throughout the country. More than one million kits have been sold since 1994. Qualitative and quantitative evaluations have demonstrated its acceptability and effectiveness.

### Current status and results

To further demonstrate the health effects of kit use, PATH conducted the first cross-sectional study of single-use delivery kits in Africa. This major quantitative evaluation of the kit's impact on preventing cord infection and puerperal sepsis in Tanzania was carried out in collaboration with the National Institute for Medical Research and the MOH. A total of 3,262 women were enrolled in the study, which was completed in late 2004. Results show that the kit has significant impact in reducing rates of infection. Newborns of mothers who used the clean delivery kit were about 13 times less likely to develop cord infection than infants whose mothers did not use the kit. Women who used the kit were about 3 times less likely to develop puerperal sepsis than women who did not use the kit. The study results suggest that making clean delivery kits available through government health clinics, markets, private pharmacies, or other commercial channels could likely help reduce rates of infection. PATH continues to seek opportunities to promote the use of clean delivery kits and integrate their use into larger maternal and child health programming around the world. A manual describing how to set up a local production project is available from PATH.



**Inexpensive, simple, delivery kit for use in home births.**

**A recent PATH study in Tanzania demonstrates that clean delivery kits are an appropriate and acceptable technology that reduces rates of maternal and neonatal infection.**

### Availability

For use within Nepal, kits can be ordered from  
Maternal and Child Health  
Products Pvt., Ltd.,  
Purano, Baneshwor,  
P.O.B. 7136,  
Kathmandu, Nepal,  
Tel: 977-1-475-418,  
Fax: 977-1-410-375,  
email at [mch@ecomail.com.np](mailto:mch@ecomail.com.np).  
To purchase delivery kits from  
UNFPA, contact  
Procurement Services,  
Midtermolen 3, 2100  
Copenhagen, Denmark,  
email Ann Janssens at  
[janssens@unfpa.org](mailto:janssens@unfpa.org).  
For more information regarding  
this project, contact Siri Wood at  
[swood@path.org](mailto:swood@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program.





## Neonatal Resuscitator

### Health need

Birth asphyxia—when a baby does not breathe at birth—accounts for about 23 percent of the estimated 4 million neonatal deaths that occur annually worldwide. Approximately 904,000 newborns die every year due to intrapartum-related hypoxic events including intrapartum-related neonatal deaths and intrapartum stillbirths, and 99 percent of these deaths occur in low- and middle-income countries. Babies suffering from intrapartum-related events often do not breathe immediately at birth. Of the approximately 10 million babies who do not breathe immediately at birth, about 6 million require basic neonatal resuscitation. Sixty million home- or community-based births occur every year, but most do not have access to resuscitation resources.

### Technology solution

To address birth asphyxia, appropriate technology and neonatal resuscitation training should be available to all skilled birth attendants and to community-level health workers where skilled attendants are not available. According to the World Health Organization, basic newborn resuscitation requires a bag and a mask resuscitator for ventilation, a mucus extractor for suctioning, a source of warmth for thermal protection, and a clock. Neonatal resuscitation devices are also available in a tube-and-mask design. Recently, Laerdal Medical, a world-class manufacturer of resuscitation equipment, developed a low-cost, high-quality suite of neonatal resuscitation technologies for low-resource settings. Laerdal Medical collaborated with the American Academy of Pediatrics to develop a comprehensive set of training materials to teach evidence-based resuscitation skills in low-resource settings—the Helping Babies Breathe (HBB) program. The HBB materials and Laerdal equipment will be used to bring neonatal resuscitation skills and equipment to low-resource settings through a global development alliance. The estimated potential impact could be up to 1 million neonatal deaths averted.

### Current status and results

PATH's focus is to enhance availability of appropriate devices in low-resource settings, particularly Asia and Africa. Initially, PATH conducted a web-based survey to determine experts' practices and preferences related to neonatal resuscitators in developing countries, published an inventory of all neonatal resuscitation devices currently available worldwide, and conducted an evaluation of reusable, silicone bag-and-mask devices that cost less than US\$30 each. PATH also conducted a situation analysis of essential newborn care in selected states in India. To understand potential demand and supply and distribution channels of neonatal resuscitation devices, PATH conducted market assessment studies in two regions (southern Africa and West Africa). Results from both studies provide baseline information regarding availability, affordability, and use of current products in the region. Currently, PATH participates in the Global Development Alliance by providing assistance to strengthen logistics systems and create/increase demand for newborn resuscitation equipment and training.



PATH/Patrick McKern

**Neonatal resuscitator for use by birth attendants.**

**“Neonatal resuscitation is positively associated with lower newborn mortality, both asphyxia-related and all neonatal mortality.”**

From March 2008 consultation “Newborn Resuscitation: Strategies for Settings from the District Hospital to the Community in Washington, DC.”

### Availability

For more information regarding this project, contact Patricia Coffey at [pcoffey@path.org](mailto:pcoffey@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program and Atlantic Philanthropies under the Maternal and Neonatal Technology Initiative.



## Chlorhexidine for Umbilical Cord Care

### Health need

Omphalitis, an infection of the umbilical stump, is a common cause of morbidity and mortality in neonates in the developing world. Over 4 million neonatal deaths occur annually, of which 36% are attributed to neonatal infections. In some areas, this rate can be as high as 50%.

### Technology solution

Recent community-based randomized trials in rural areas in Bangladesh, Nepal, and Pakistan have shown that applying 4% chlorhexidine solution (CHX) to the umbilical cord stump prevents infection and saves newborn lives. These trials and concurrent research support cord cleansing with CHX as an efficacious, acceptable, feasible, and cost-effective newborn care intervention. CHX cord cleansing reduces the risk of death before 28 days by up to 23% and eliminates two-thirds to three-quarters of serious umbilical infections. Such findings suggest, for example, that widespread practice of CHX cord cleansing could prevent more than 200,000 newborn deaths each year in South Asia. CHX can be delivered through existing health services and initiatives such as antenatal and obstetric care and other essential newborn care activities. It can also be provided at large scale through retail outlets, including pharmacies, public facility- and community-based providers, and community health workers who have contact with women planning to give birth at home.

### Current status and results

PATH is developing and introducing CHX in low-resource settings beginning in Bangladesh and working towards global scale-up. PATH developed product specifications and transferred them to a Bangladeshi pharmaceutical company capable of manufacturing quality CHX at a reasonable cost. In parallel, PATH collaborated with a local market research firm to conduct a product attribute study that evaluated the preferences of potential users and service providers for containers and applicators. Study results were conveyed to the pharmaceutical company to develop a locally available CHX product. We assessed demand of CHX at multiple price points in two districts in Bangladesh using the contingent valuation method. PATH collaborated with the Projahnmo Study Group on operations research on training, behavior change, advocacy development, and distribution and also conducted stakeholder surveys to assess country readiness for product introduction. Findings from this research were incorporated into the final product design and go-to-market strategy. Policy dialogue and alignment is ongoing. The company will continue testing product stability and compatibility with the intent of seeking regulatory approval once policy alignment is achieved. At the global level, PATH submitted a successful application to the World Health Organization Essential Medicines List to include 4% CHX for umbilical cord care. PATH is implementing a global market development plan by coordinating a meeting to disseminate recent findings from randomized controlled trials to policymakers in the south Asia region, and conducting a manufacturer search for suitable industry partners in India.



PATH/Musumi Mettler

**A newborn treated with 4% chlorhexidine.**

**“We believe that the use of 4% chlorhexidine for topical cord antisepsis represents an important intervention with the potential for substantial effect on public health.”**

Mullany L, et al. Topical application of chlorhexidine to the umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: a community-based, cluster-randomised trial. *The Lancet*. 2006;367:910–918.

### Availability

For more information regarding this project, contact Patricia Coffey at [pcoffey@path.org](mailto:pcoffey@path.org).

### Donor support

Funding for this project has been provided by the **United States Agency for International Development** under PATH's HealthTech program.

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## Gentamicin in Uniject

### Health need

The World Health Organization estimates that at least four million neonatal deaths (i.e., death during the first 28 days of life) occur around the world every year. Newborn infections are responsible for approximately one-third of these estimated four million neonatal deaths. Case-fatality rates for severe bacterial infections are high in part due to not administering—or delaying the administration of—necessary antibiotics (including gentamicin). Treating infants in rural areas, where infrastructure is limited and where community health workers provide many essential services, presents a special challenge. To achieve maximum impact on neonatal sepsis rates, it is important that newborns with these infections receive immediate treatment.

### Technology solution

A prefilled, nonreusable syringe such as the Uniject<sup>®\*</sup> device can help ensure immediate delivery of the life-saving benefits of gentamicin in peripheral health care settings and homes. This prefilled, easy-to-use, injection-ready format ensures that an accurate, premeasured dose is given in a nonreusable, sterile device with minimal preparation and minimum waste. Administration can then occur when the signs of a neonatal infection are first detected. Community health workers and traditional birth attendants could be trained to use gentamicin in the Uniject device (gentamicin-Uniject) and a complementary antibiotic to extend accessibility and facilitate the administration of antibiotics. The dosing of the neonatal gentamicin course has traditionally been adjusted based on the neonate's weight. Since the Uniject device only delivers a fixed-dose, PATH collaborated in a recent study that identified safe and therapeutic fixed dosing intervals for treatment of neonates in common weight ranges using gentamicin-Uniject.

### Current status and results

Instituto Biologico Argentino (BIOL), an Argentine pharmaceutical manufacturer collaborating with PATH, is conducting the research and development and product registration necessary to make gentamicin-Uniject commercially available. PATH and BIOL have resolved stability issues encountered in previous efforts of filling the Uniject device with gentamicin. BIOL and PATH produced a clinical trial lot in 2007 and are initiating product registration in 2009. Also during 2009, PATH is collaborating with John Snow Incorporated to evaluate the first field use of gentamicin-Uniject in Nepal. Additional opportunities to evaluate the use of gentamicin-Uniject in the field are being explored.

*\*Uniject is a registered trademark of BD.*



Penny Dawson

**Prefilled, single-use injection device filled with gentamicin.**

**“...to further simplify the parenteral administration of gentamicin, the use of disposable syringes pre-filled with gentamicin, or a single-use simple Uniject device should be tested.”**

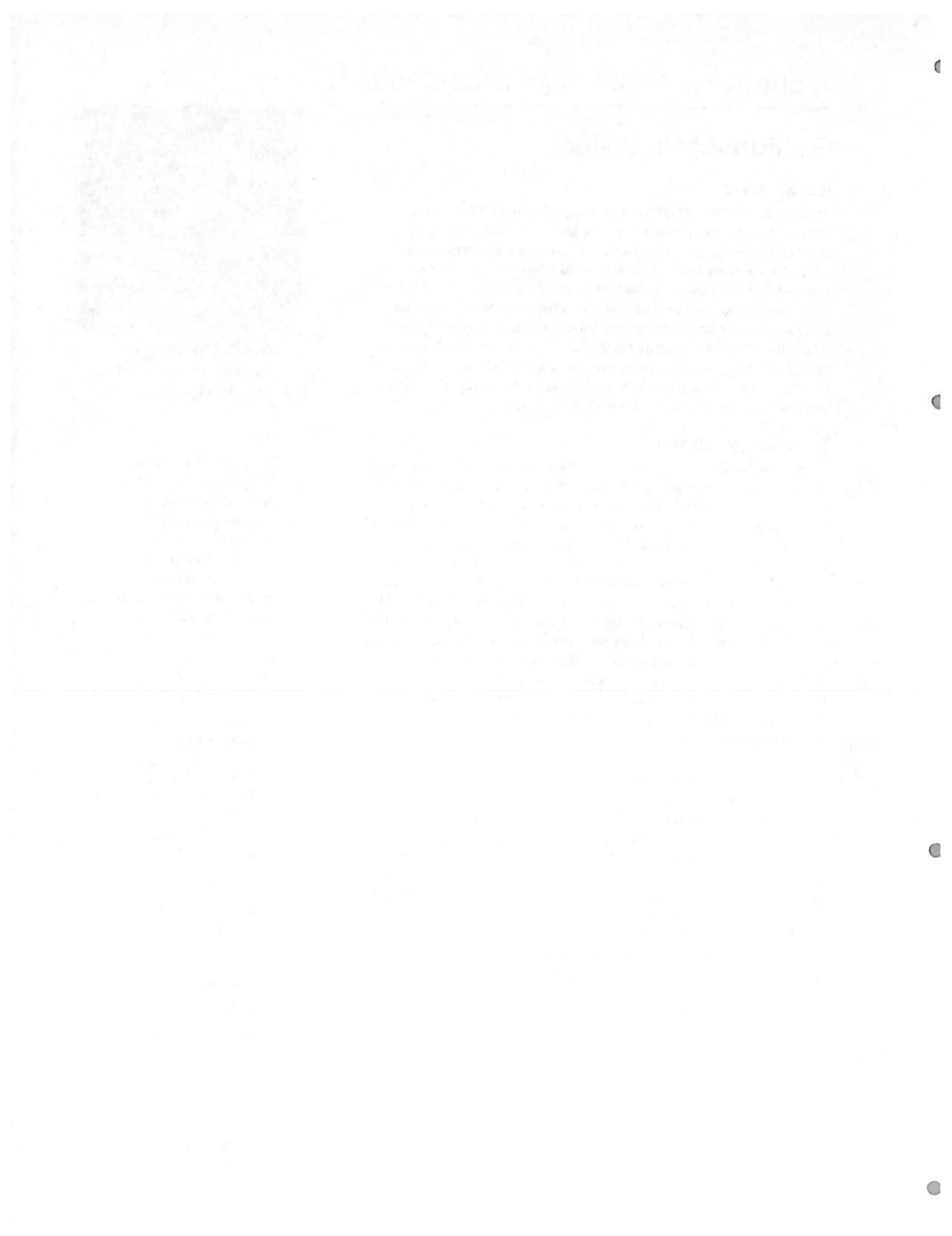
Bang AT, et al. Effect of home-based neonatal care and management of sepsis on neonatal mortality: Field trial in rural India. *The Lancet*. 1999;354:1955–1961.

### Availability

Uniject devices and the associated equipment for filling and packaging are available to vaccine and pharmaceutical companies from BD Pharmaceutical Systems, New Jersey, USA, Roderick Hausser, Tel: (201) 847-5185, Fax: (201) 847-4869. For more information regarding this project, contact Patricia Coffey at [pcoffey@path.org](mailto:pcoffey@path.org).

### Donor support

Funding for this project has been provided by the **United States Agency for International Development** under PATH's HealthTech program.



## Oxytocin in Uniject

### Health need

Postpartum hemorrhage is the leading cause of maternal mortality worldwide. Annually, approximately 130,000 women are known to die due to hemorrhage during childbirth. It is a particular problem in home deliveries of infants because the short response time required makes referral and transport to a health care facility impractical in most cases. The percentage of maternal deaths due to postpartum hemorrhage has been reported as 25 percent in sub-Saharan Africa, 27 percent in West Africa, and 45 percent in Indonesia. The use of oxytocin for routine management of the third stage of labor can significantly reduce the incidence of postpartum hemorrhage. The World Health Organization recommends use of a 10-IU dose of oxytocin given intramuscularly. To facilitate the recommended use of oxytocin in developing countries, particularly in peripheral health settings and in home deliveries (attended by a person with midwifery skills), a prefilled, easy-to-use, injection-ready dose of oxytocin would be ideal.

### Technology solution

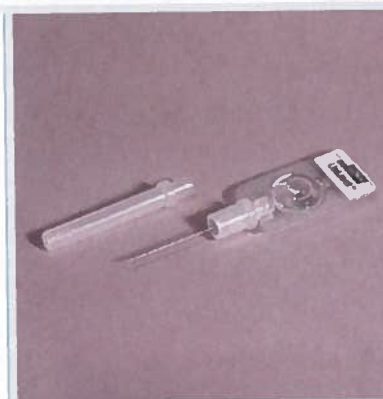
The Uniject<sup>®</sup> device is a prefilled, nonreusable syringe that offers delivery of the life-saving benefits of oxytocin to women in peripheral health care settings and homes. This easy-to-use, injection-ready format ensures an accurate dose in a nonreusable, sterile device with minimal preparation and minimum waste. These benefits can improve the ability of midwives and village health workers to administer oxytocin outside of health care facilities and in emergency situations or remote locations. Oxytocin can stand moderate heat exposure for some time, but substantial heat exposure reduces potency. Therefore, a time-temperature indicator can be included on the product package to help ensure that medication given to a woman is potent while allowing more flexibility for field transport and storage of oxytocin in the Uniject device (oxytocin-Uniject).

### Current status and results

Instituto Biologico Argentino, an Argentine pharmaceutical manufacturer collaborating with PATH, launched oxytocin-Uniject in the Argentine market in the fall of 2009. In addition to approval in Argentina and Guatemala, regulatory approvals are pending in 11 other Latin American countries. Gland Pharma, an Indian pharmaceutical manufacturer, has obtained regulatory approval in India. Pending completion of stability studies, Gland Pharma will begin applying for regulatory approval in other countries in late 2010.

A pilot introduction and evaluation in Guatemala was completed in 2009. Health workers found oxytocin-Uniject highly acceptable and easy to use. Pilot introductions and/or studies are planned in Ghana, India, Honduras, Nicaragua, and South Africa in 2010 (pending in-country approvals). PATH published a resource page online for countries and programs interested in using oxytocin-Uniject. This resource page is available at: <http://www.path.org/projects/uniject-oxytocin-resources.php>.

\* Uniject is a registered trademark of BD.



PATH/Glenn Austin

**Prefilled, single-use injection device filled with oxytocin.**

**“Uniject [with oxytocin] was well tolerated and offers an alternative for oxytocin administration.”**

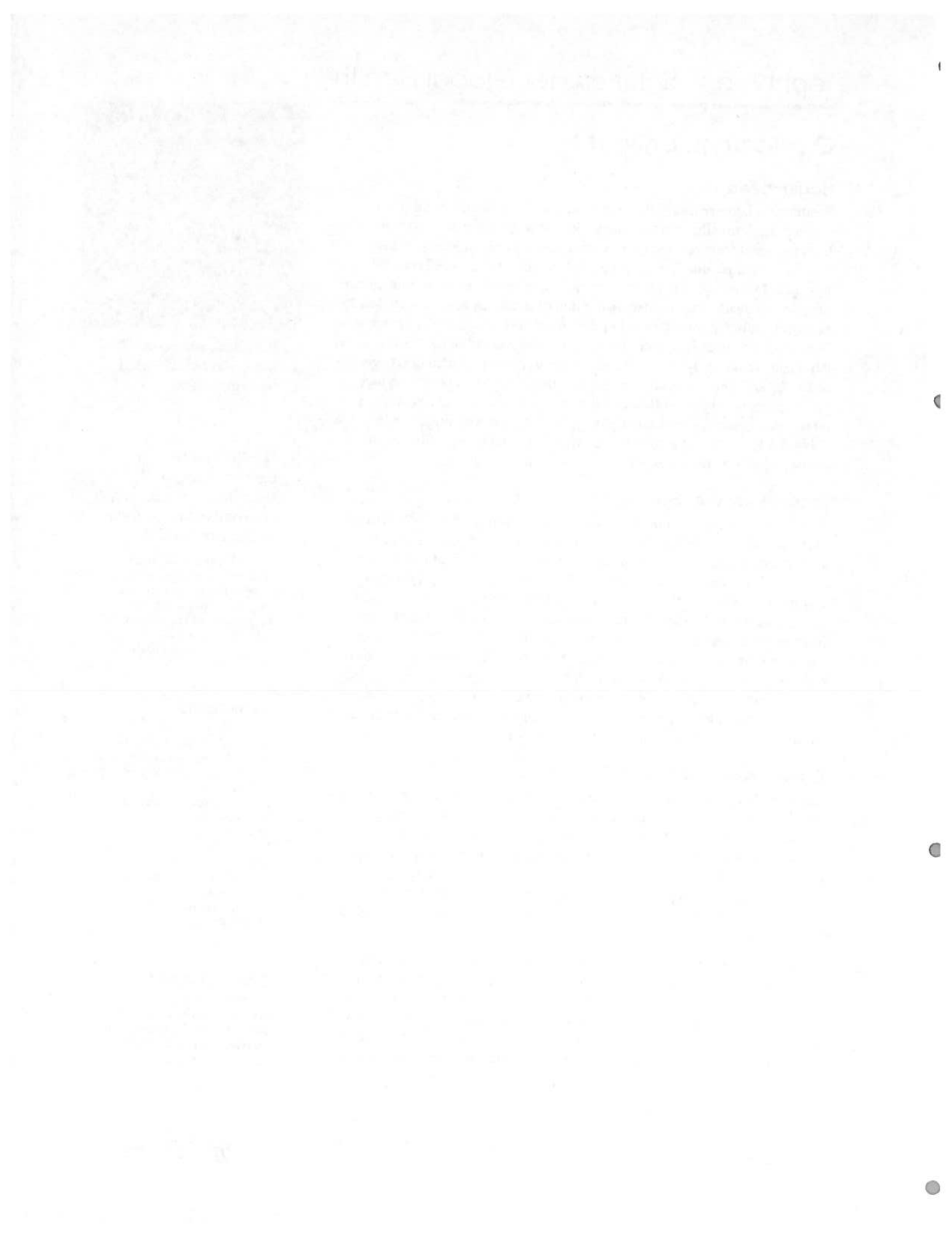
Strand RT, et al. Postpartum hemorrhage: A prospective, comparative study in Angola using a new disposable device for oxytocin administration. *Acta Obstetrica et Gynecologica Scandinavica*. 2005;84:260–265.

### Availability

Uniject devices and the associated equipment for filling and packaging are available to vaccine and pharmaceutical companies from BD Pharmaceutical Systems New Jersey, USA  
Roderick Hausser  
Tel: (201) 847-5185  
Fax: (201) 847-4869  
For more information regarding this project, contact Steve Brooke at [sbrooke@path.org](mailto:sbrooke@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program.





## Packaging Solutions for Nevirapine

### Health need

Clinical trials have shown single-dose nevirapine (NVP) to be a low-cost, efficacious therapy for prevention of mother-to-child transmission (PMTCT) of HIV-1. The single-dose therapy includes a 200-mg NVP tablet taken by the mother at the onset of labor and 0.6 ml of NVP oral suspension (NVP syrup) given to the infant within 72 hours of birth.

Achieving widespread use of NVP for infants in developing countries has been challenging because of the high prevalence of births outside the health care system, the required timing for the dose, and the limited reach of antenatal care and PMTCT services. Programs have begun giving the NVP tablets to HIV-positive pregnant women during antenatal visits to take home so they can have the tablet readily available. Fewer programs have been providing the infant dose of NVP syrup to take home, due in part to the lack of a simple, robust, and tamper-evident single-dose package.

### Technology solution

Improving single-dose packaging of NVP syrup for PMTCT programs is the primary objective of a public-private partnership among United States Agency for International Development, Boehringer Ingelheim (BI) (manufacturer of Viramune<sup>®</sup>\* brand NVP), and PATH. PATH has identified and evaluated the function and acceptability of numerous single-dose packaging candidates. BI has tested the physical compatibility of the candidates with their NVP syrup. USAID has provided funding as well as guidance on field needs.

The result was a simple yet elegant solution that has been successfully piloted and introduced in Kenya. PMTCT clinics are provided with supplies of two components—1-ml Exacta-Med<sup>®</sup>† dispensers (an oral-dosing syringe) and self-sealing foil laminate pouches designed by PATH to surround and protect the dispenser once the nurse fills it with the infant dose of NVP syrup. The pouch is also labeled with pictorial and expiry information that reminds the woman of proper use if she gives birth outside the health care system.

### Current status and results

PATH worked with the Elizabeth Glaser Pediatric AIDS Foundation, Family Health International, and the National HIV/AIDS and the Sexually Transmitted Disease Control Program of Kenya to evaluate the pouch and dispenser approach in PMTCT programs in Kenya. A pilot introduction was completed in July 2006. Results indicated high acceptability among health workers and HIV-positive mothers and confirmed the value of the approach. Country-wide introduction of the NVP infant-dose pouch is underway in Kenya. BI now makes the pouches available at no cost through its PMTCT Donations Program. PATH has developed a set of resources to support organizations considering introduction of the NVP infant-dose pouch which can be downloaded from PATH's website at [http://www.path.org/projects/nevirapine\\_pouch\\_resources.php](http://www.path.org/projects/nevirapine_pouch_resources.php).

\* Viramune is a registered trademark of Boehringer Ingelheim.

† Exacta-Med is a registered trademark of Baxa Corporation.



PATH/Patrick McKern

**Nevirapine packaging developed by PATH.**

**"Many babies will benefit...it will make a difference."**

Emily, Nurse at Vihiga District Hospital in Kenya.

### Availability

The NVP infant-dose pouch is currently available to qualifying programs at no cost through the PMTCT Donations Program along with the Exacta-Med Dispenser, manufactured by Baxa Ltd. For more information on how to receive the pouch, dispensers, and nevirapine, visit [www.pmtctdonations.org](http://www.pmtctdonations.org). For information regarding this project, contact Adriane Berman at [aberman@path.org](mailto:aberman@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program and the Sapling Foundation.

# THE HISTORY OF THE UNITED STATES

The history of the United States is a story of growth and change. From the first settlers to the present day, the nation has evolved through many challenges and triumphs. The early years were marked by exploration and the establishment of colonies. The American Revolution led to the birth of a new nation, and the subsequent years saw the expansion of territory and the development of a unique American identity.

The 19th century was a period of rapid change and growth. The Industrial Revolution brought about significant technological advancements, and the nation expanded its territory westward. The Civil War was a pivotal moment in the nation's history, leading to the abolition of slavery and the strengthening of the federal government. The 20th century has been characterized by global conflicts, social movements, and technological progress.

The United States has a rich and diverse heritage. The contributions of immigrants from various parts of the world have shaped the nation's culture and identity. The American dream, the pursuit of happiness, and the values of freedom and democracy are central to the nation's history. The future of the United States lies in the hands of its citizens, who must continue to uphold the principles that have made the nation great.

THE HISTORY OF THE UNITED STATES

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## Cryotherapy for Cervical Cancer Prevention

### Health need

Cervical cancer affects an estimated 490,000 women worldwide each year and leads to more than 270,000 deaths. About 85 percent of women who die from cervical cancer reside in developing countries. Cervical cancer can be prevented if precancerous lesions are identified early and treated promptly.

### Technology solution

Cryotherapy, a freezing treatment, is recognized as the most cost-effective and feasible approach to treating precancerous cervical lesions in these settings. It can also be used in a single visit screen-and-treat approach in primary care settings, an approach which has been demonstrated to increase rates of follow-up. Widespread availability of cryotherapy in developing-country settings is an essential component of an effective screening and treatment approach to cervical cancer prevention in these settings where it is needed most.

Cryotherapy uses a refrigerant gas to destroy abnormal cells. An important aspect of making cryotherapy readily available in developing-country settings is the ability to use carbon dioxide (CO<sub>2</sub>), the least expensive and most accessible type of gas, as the refrigerant.

### Current status and results

Recent bench testing of a range of cryotherapy devices has demonstrated that clogging or blockage of the device, previously thought to be associated with use of CO<sub>2</sub>, may only affect certain devices, suggesting that with an appropriate device, CO<sub>2</sub> could be used effectively.

One of the devices reaching unexpectedly warm temperatures in our bench testing was the LL100, (manufactured by Wallach Surgical Devices), the most commonly used equipment in low-resource settings. PATH shared these findings with representatives from Wallach Surgical Devices, and on September 19, 2009, Wallach took action. They issued a recall for the LL100 sold for use with CO<sub>2</sub>. The recall covers equipment that goes back 15 years and affects about 2,500 devices in use worldwide.

The integration of temperature-monitoring equipment into an upcoming clinical evaluation of cryotherapy will allow for assessment of the correlation between tip temperatures achieved and depth of necrosis—information critically needed in understanding whether CO<sub>2</sub> can be successfully used as the refrigerant gas for cryotherapy.



PATH/Jered Singleton

Cryotherapy device.

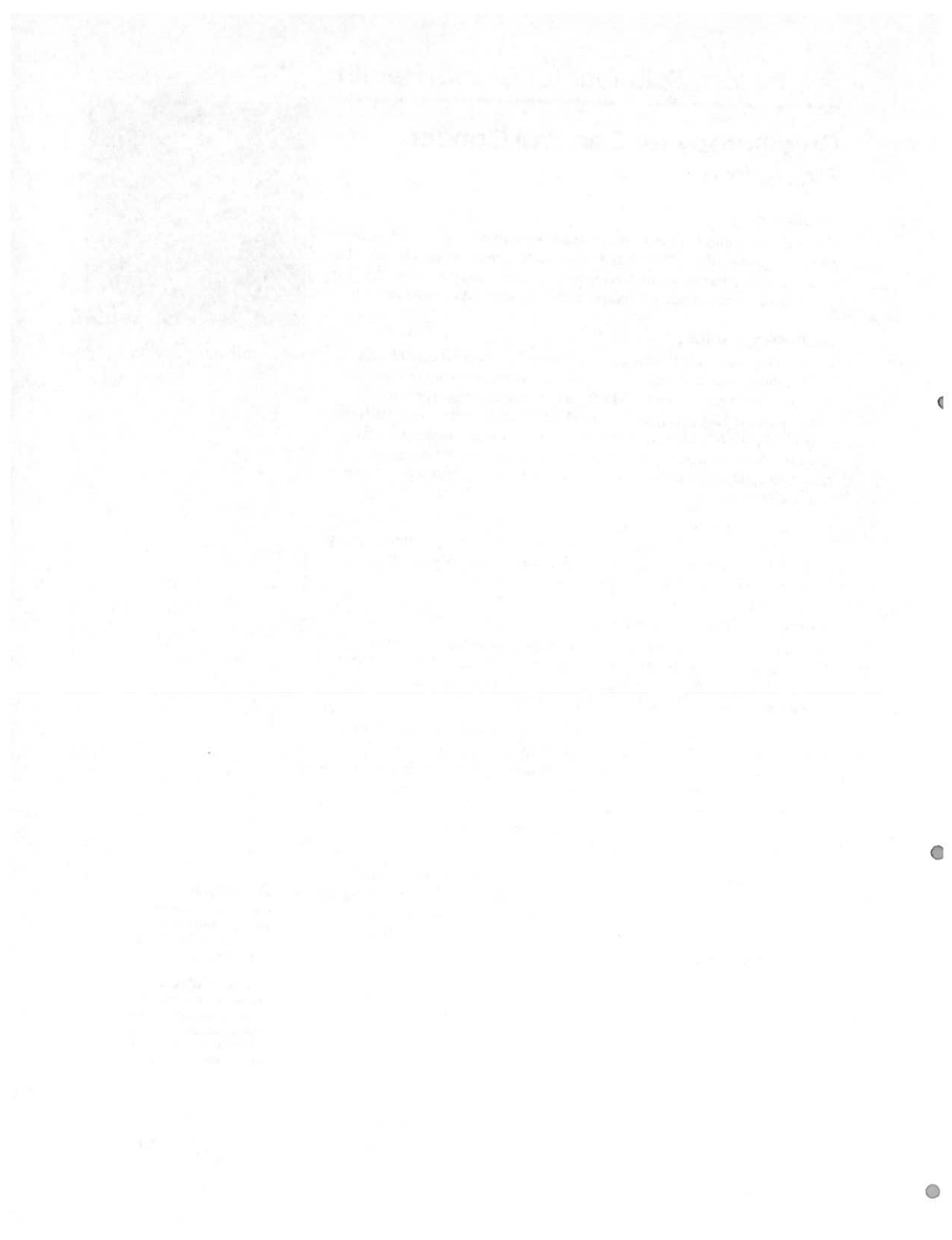
### Availability

For more information regarding this project, contact Jenny Winkler at [jwinkler@path.org](mailto:jwinkler@path.org).

### Donor support

Support for this project was provided through funding from private foundations and individual donors to the **Health Innovation Portfolio**.





## Lung Support for Newborns

### Health need

Without access to simple, inexpensive respiratory support devices, nearly one million babies die from birth asphyxia and prematurity worldwide each year. Ventilators are expensive to purchase; this limits availability in resource-limited countries. Even if the devices are donated, the need for highly trained personnel to operate, maintain, and repair the ventilators limits the use of modern ventilators. Practical methods for respiratory support of prematurely born infants could save hundreds of thousands of newborn lives each year. In low-resource settings there is a need for a simple, safe, inexpensive ventilator that is easy to operate.

### Technology solution

Through collaboration, PATH and Seattle Children's Research Institute are defining a clear strategy for developing, certifying, and commercializing low-cost devices that could dramatically reduce the risks of respiratory distress and long-term consequences or death associated with this condition. Seattle Children's developed two prototype devices that may meet these goals—a high-amplitude bubble continuous positive airway pressure (HAB-CPAP) device and the Hansen Ventilator.

Infants with lung disease have airways that tend to collapse due to fluid accumulation and inflammation. CPAP provides a constant distending pressure, keeping lungs open in spontaneously breathing infants. The HAB-CPAP is an inexpensive technology which takes advantage of the mechanical potential of water. It creates large airway pressure oscillations, at a lower frequency than conventional bubble CPAP (B-CPAP), allowing more gas to enter the lungs with each oscillation, thus improving ventilation.

The Hansen Ventilator is a simple ventilator design that uses the same principle as the HAB-CPAP to control gas exchange during exhalation. The ventilator, however, has a second tube placed deeper in the water column to control inflation pressures and a pinch valve controlling rate and duration of the breath. Combined with HAB-CPAP, the ventilator has the ability to provide the full range of respiratory support for infants experiencing different levels of disease severity and can be manufactured at a fraction of the cost of commercially available ventilators.

### Current status and results

Preclinical trials on the HAB-CPAP and the Hansen Ventilator generated exciting results. The HAB-CPAP provided the same level of respiratory support as a conventional ventilator in healthy subjects. In subjects with severe lung disease, the pressure rate product—an index of how hard a patient works while on a ventilator—was 50% lower during HAB-CPAP than with the conventional B-CPAP.<sup>1</sup> In another study, the Hansen Ventilator, combined with HAB-CPAP during exhalation, provided greater ventilation when compared with a conventional ventilator. Development continues with the goals of obtaining an US Food and Drug Administration approval and a CE mark.

<sup>1</sup>DiBlasi RM, Zignego JC, Tang DM, Hildebrandt J, Smith CV, Hansen TN, Richardson CP. Noninvasive respiratory support of juvenile rabbits by high-amplitude bubble continuous positive airway pressure. *Pediatric Research*. June 2010;67(6):624–629.



Seattle Children's Research Institute

The Hansen Ventilator.

**Practical methods for respiratory support of prematurely born infants could save hundreds of thousands of newborn lives each year.**

### Availability

For more information regarding this project, contact Darin Zehrung at [dzehrung@path.org](mailto:dzehrung@path.org).

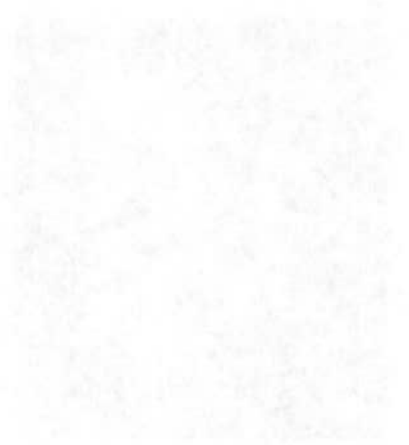
### Donor support

Support for this project was provided through funding from private foundations and individual donors to the **Health Innovation Portfolio**.

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## Developing an Affordable Sanitary Pad

### Health need

Girls as well as women in the developing world suffer from lack of adequate solutions to manage menstruation. Imported pads are prohibitively expensive for low-income families. Research conducted in Uganda indicates that about 90 percent of the urban poor women and girls cannot afford off-the-shelf sanitary pads and instead improvise with materials such as grass, leaves, old newspapers, and pieces of cloth. These materials, however, have been linked to certain reproductive tract infections. They also have limited absorbency and make it difficult for girls to participate in school during their periods. The United Nations Children's Fund estimates that 1 in 10 school-age African girls either skips school during menstruation or drops out entirely because of lack of menstrual hygiene solutions. Numerous studies have confirmed that educating girls is associated with significant development and health benefits to the girls, their families, and society. These benefits include protecting girls from HIV/AIDS, abuse, and exploitation; reducing subsequent child and maternal mortality; improving child nutrition and health; decreasing fertility rates; enhancing women's domestic role and their political participation; and improving economic productivity.

### Technology solution

PATH's solution is to develop and advance low-cost menstrual management options for girls and women in low-resource settings. Our finding from focus group discussions and literature reviews indicated that girls and women are interested in disposable products that offer better absorbency and have a cheaper price tag than available options. There are also reusable options (cloth pads and menstrual cups) that can last for several years, but they require a higher up-front cost, access to clean water and soap, and thorough drying—resources that aren't always available in poor communities. We are currently exploring a hybrid concept (i.e., a combination of a reusable surround with a disposable, absorbent core) to address the growing challenge of disposing of plastic-lined pads and to reduce the cost. This hybrid option could also offer girls and women the flexibility of using a variety of absorbent materials that are available to them.

### Current status and results

Our effort to develop a hybrid approach is underway. We collected and tested a range of disposable pads currently on the market worldwide, as well as pads made from local agricultural waste, for absorbency and their ability to retain fluid. From this process, we learned that many of the pads made locally in low-resource communities work as well as the imported pads. Based on our findings, we are developing the target product descriptions. As the next step, using target product profiles, we will collect data systematically from key stakeholders, including girls and women, through interviews and focus group discussions to define product specifications. We will also seek opportunities to assist small sanitary pad producers to improve their production and distribution mechanisms.



PATH/Jesse Schubert

**Absorbent fluff pulp made from banana fiber (left) and wheat straw (right).**

**The Kasiisi Project Girls Support Program in Uganda found a 30% decrease in absenteeism and an improvement in grades when sanitary pads and underwear were provided to primary school girls.**

[http://www.globalgiving.com/pfil/2700/Affordable\\_Sanitary\\_Pads.pdf](http://www.globalgiving.com/pfil/2700/Affordable_Sanitary_Pads.pdf)

### Availability

For more information regarding this project, contact Nancy Muller at [nmuller@path.org](mailto:nmuller@path.org).

### Donor support

Support for this project was provided through funding from private foundations and individual donors to the **Health Innovation Portfolio**.

# THE HISTORY OF THE UNITED STATES

The history of the United States is a story of growth and change. It begins with the first people who lived on this land, and continues through the years of exploration, settlement, and the struggle for independence. The story is one of a people who have built a great nation, and who are still building it today.

The first people who lived on this land were the Indians. They were here long before the Europeans came. They lived in small groups, and they were very skilled at hunting and farming. They were the first to teach the Europeans how to live in this land.

The Europeans came to this land in the 15th century. They were looking for new places to settle, and they found this land. They were very interested in the land, and they began to settle here. They brought with them many new things, and they taught the Indians how to live in a different way.

The Indians and the Europeans lived together for many years. They learned from each other, and they grew to love each other. But in the 17th century, the Europeans began to fight with the Indians. They wanted more land, and they wanted to control the land. The Indians fought back, and there was a long and hard war.

The war ended in 1763. The Europeans won, and they took all the land. The Indians were forced to move to a small area of land. They were very sad, and they were angry. They wanted their land back, and they wanted to live in peace.

The Europeans lived in the land for many years. They built a great nation, and they became very powerful. They fought many wars, and they won. They were very proud of their nation, and they loved it very much.

The Indians lived in the land for many years. They were very happy, and they loved their land. They were very skilled at hunting and farming, and they were very brave. They were the first to teach the Europeans how to live in this land.

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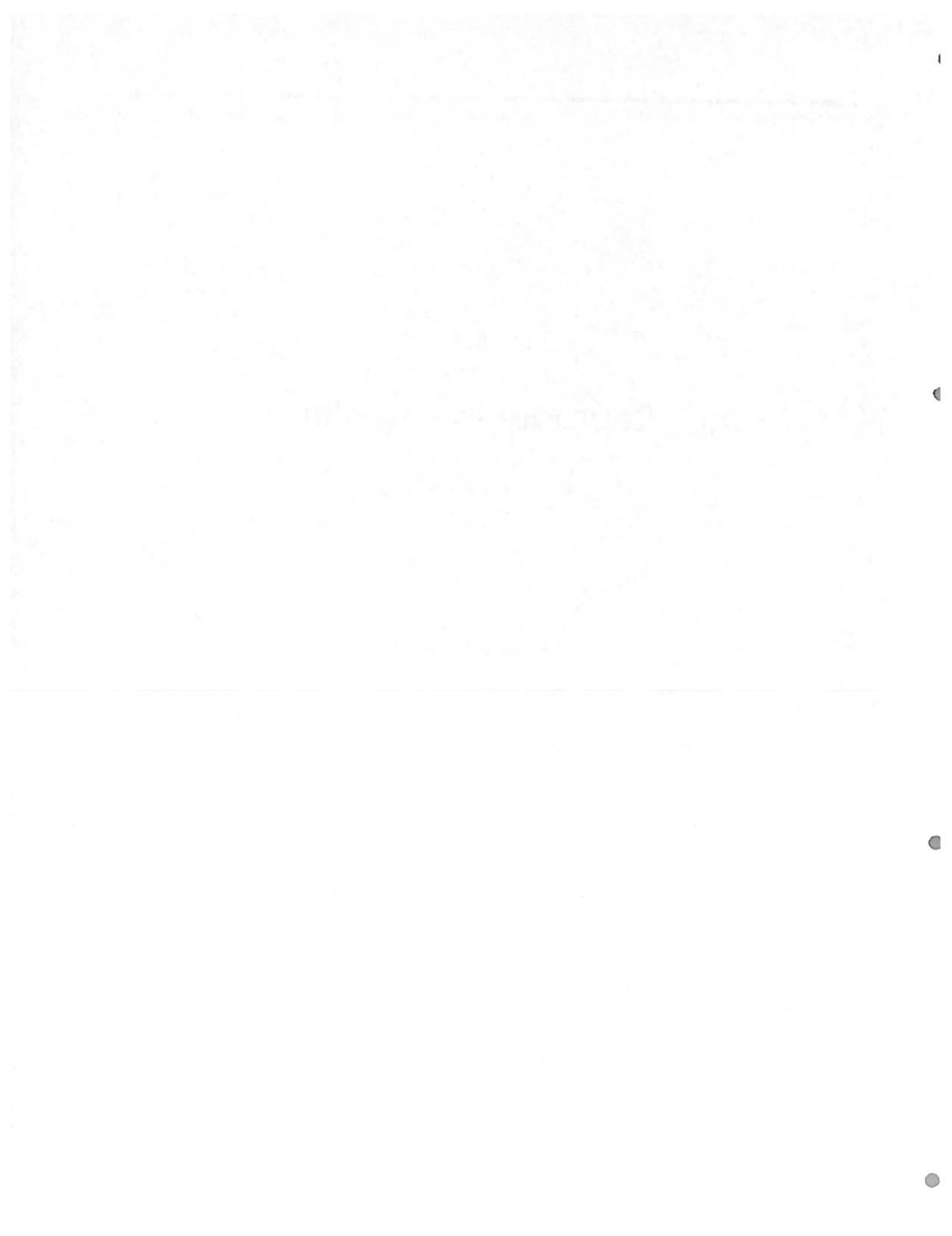
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# Reproductive Health

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## Injectable Contraceptives in Uniject

### Health need

The World Health Organization (WHO) estimates that annually the reuse of injection devices may cause 20 million infections with hepatitis B virus, 2 million infections with hepatitis C virus, and 250,000 infections with HIV worldwide. International development and family planning agencies have been seeking feasible and affordable methods to reduce unsafe injection practices that could lead to the spread of bloodborne diseases. This is true for vaccines and medicines as well as injectable contraceptives that are becoming increasingly popular around the globe as women search for safe, highly effective, reversible methods of contraception that do not require compliance with a daily regimen.

Depot medroxyprogesterone acetate (DMPA, also known as Depo-provera) is administered by injection once every three months, making it highly convenient. While provision of sterile needles and syringes with every dose of contraceptive is the current standard, the risk of reuse still exists. Autodisable (AD) syringes prevent reuse, but like disposable syringes they can be diverted to other uses during the distribution process.

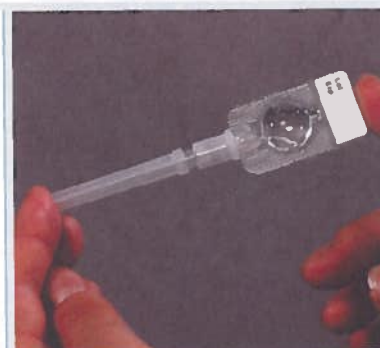
### Technology solution

With guidance from WHO and a multitude of other collaborators, PATH developed an AD, prefilled syringe known as the Uniject<sup>®</sup> device. Today, the Uniject device, which is licensed to BD, prevents reuse, simplifies matching of syringes and supplies, ensures dose accuracy, and is simple to use in both clinic and community settings. Use of the Uniject device as a means of helping to increase safe community access to injectable contraceptives in developing countries has been a long-term goal at PATH, the United States Agency for International Development (USAID), and other international agencies.

### Current status and results

BD has invested significant funds to develop large-scale manufacturing operations so it can supply empty Uniject devices to pharmaceutical companies in large quantities at reasonable prices. Pfizer is currently proceeding with a European Medicines Agency submission of depo-subQ provera 104 in the Uniject device (depo-subQ in Uniject) for regulatory approval. PATH is playing an increasingly large role in both global and country-level introduction planning for depo-subQ in Uniject and is coordinating planning activities of a range of external stakeholders on behalf of USAID. Activities by PATH and external partners are building the evidence base and country-level preparedness for eventual product introduction and scale-up. These activities include an acceptability study in Malawi, as well as demand modeling, logistics research, and detailed introduction planning for five countries: Kenya, Malawi, Pakistan, Rwanda, and Senegal.

*\*Uniject is a registered trademark of BD.*



**Prefilled, single-use injection device filled with injectable contraceptives.**

**"The Uniject device has gone all the way from the drawing board to realization."**

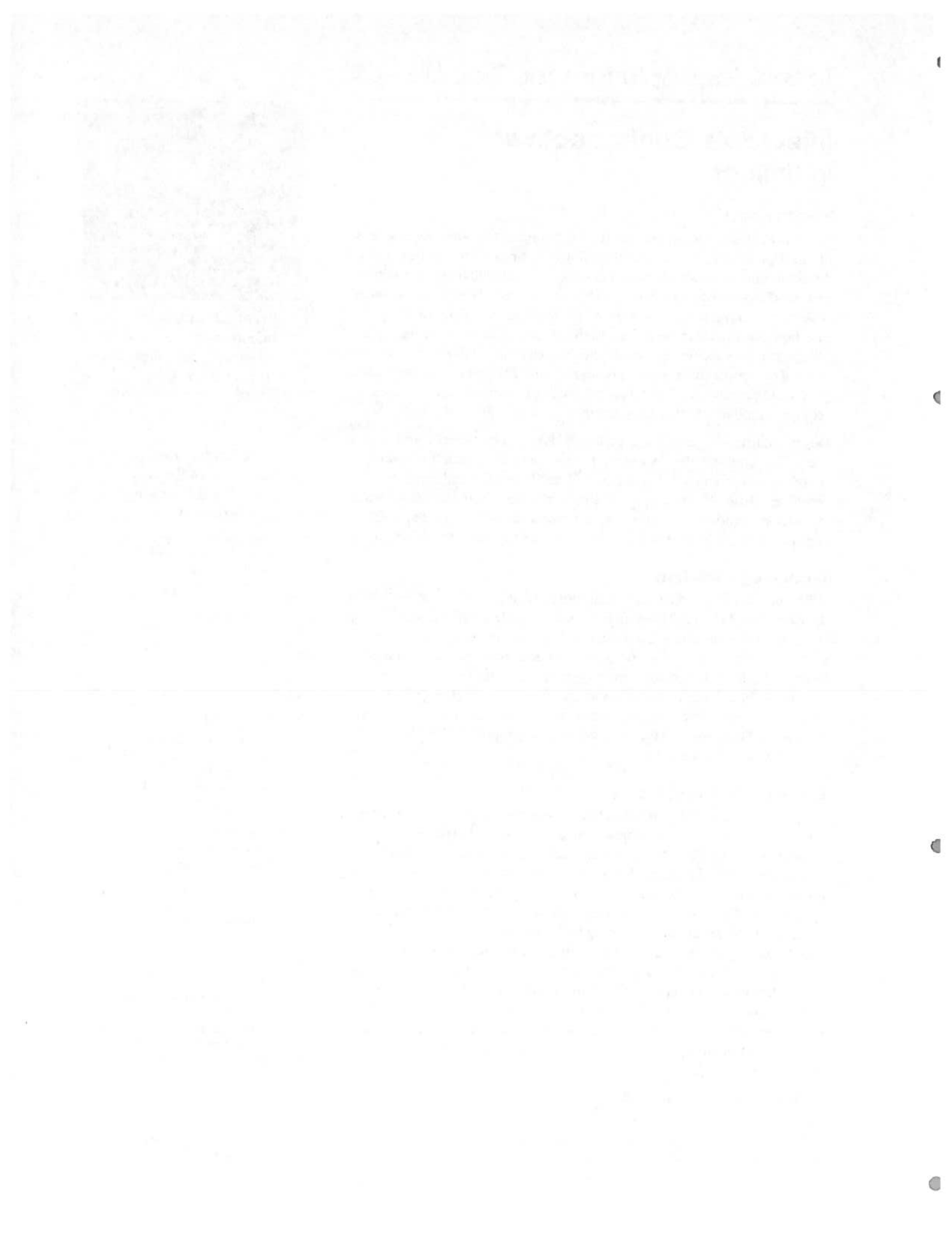
*Craig Stephens, Judge for Tech Museum Award given to PATH for Uniject in 2003.*

### Availability

Uniject devices and the associated equipment for filling and packaging are available to vaccine and pharmaceutical companies from BD Pharmaceutical Systems New Jersey, USA  
Roderick Hausser  
Tel: (201) 847-5185  
Fax: (201) 847-4869  
For more information regarding this project, contact Steve Brooke at [sbrooke@path.org](mailto:sbrooke@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program.



## SILCS Diaphragm

### Health need

Access to family planning has helped millions of women plan and space births resulting in improved health outcomes. Despite these successes, an estimated 215 million women worldwide who want to avoid pregnancy lack access to modern contraceptives. In developing countries alone, approximately 80 million pregnancies that occur are unintended. An estimated 385,000 women die every year from complications associated with pregnancy and childbirth, with unsafe abortion accounts for a high percentage of maternal deaths. Almost all these deaths are preventable. In addition, women represent more than 50 percent of people living with AIDS; and sexually transmitted infections, excluding HIV/AIDS, are the second most important cause of loss of health in women, especially young women. Women want and need more female-initiated methods that can protect against pregnancy and sexually transmitted infections. Diaphragms could help meet this need, but some characteristics of traditional diaphragms limit their use and acceptability.

### Technology solution

PATH responded to the call for simple-to-use, female barrier protection by developing the SILCS Diaphragm, a single-size, reusable device with a contoured rim that allows the SILCS Diaphragm to fit most women with improved comfort. Design and development of the SILCS Diaphragm began in 1994, and user-centered evaluations of over 200 prototype designs resulted in refined performance and features. The single-size design will simplify the logistics of supply and provision. PATH used stakeholder assessments to ensure that comfort, ease of handling, and acceptability were built into the product. As a result, the SILCS Diaphragm directly addresses user and programmatic needs which will lead to improved access and acceptability. Acceptability studies among naïve users in South Africa and Thailand found that women were able to learn to use the device easily and that women and men found the SILCS Diaphragm acceptable during use. In a comparative crossover study of the SILCS Diaphragm with a traditional diaphragm in the Dominican Republic, 19 of 20 women reported preferring the SILCS Diaphragm device after short-term use. Eventually, the single-size device could be provided over the counter or outside the clinic-based system where regulatory authority and clinical practice allow.

### Current status and results

The SILCS Diaphragm design was patented by PATH in 1998; a second patent on a spring modification has been filed and granted in several countries. Clinical validation is nearly complete. Applications for regulatory approval are planned for 2011 and will include a regulatory application for market approval in Europe and an application to the United States Food and Drug Administration as a contraceptive. PATH also is evaluating the SILCS Diaphragm as a microbicide delivery system. PATH licensed the technology of a commercialization partner in 2010. In addition, PATH is actively seeking regional partners to distribute and introduce this new diaphragm through both private- and public-sector markets in selected countries.



PATH/Mike Wang

**The SILCS Diaphragm, an intravaginal barrier contraceptive.**

**“A significant advantage [of the SILCS Diaphragm] for resource-poor settings is that it is a reusable method that women can control with little dependence on the health care system.”**

*W. Holmes editorial in Sexual Health, May 2010.*

### Availability

For more information regarding this project, contact Maggie Kilbourne-Brook at [mkilbou@path.org](mailto:mkilbou@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development through CONRAD, the Bill & Melinda Gates Foundation, and other donors.

# THE HISTORY OF THE CITY OF BOSTON

FROM THE FIRST SETTLEMENT  
TO THE PRESENT TIME  
BY  
JOHN H. COLEMAN  
OF THE CITY OF BOSTON

BOSTON:  
PUBLISHED BY  
J. B. LEECH, 15 NASSAU ST.  
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## Woman's Condom

### Health need

According to 2011 estimates, women represent more than half of the 33 million HIV infections worldwide, with heterosexual contact as one of the primary modes of transmission. In developing countries alone, approximately 80 million pregnancies that occur are unintended. An estimated 356,000 women die every year from complications associated with pregnancy and childbirth, with unsafe abortion accounting for a high percentage of maternal deaths. Many women lack power over sexual decisions; they are not in a position to ask their partners to abstain from sex with others or to use male condoms. An estimated 215 million women wish to delay or space their pregnancies but do not have access to modern contraceptives.<sup>1</sup>

### Technology solution

A female condom can protect against sexually transmitted infections, including HIV, as well as pregnancy. Experience with currently marketed female condoms has shown that women and men are interested in and will use these barrier devices if they are acceptable and easy to use. With user input from several countries, PATH designed the Woman's Condom to be more acceptable to use for both partners. Couples evaluated prototypes and offered design suggestions to improve acceptability, thus making it more likely that the barrier will be used consistently and properly. The Woman's Condom is comfortable and easy to use. Its unique design features enable easy insertion, secure fit during use, good sensation, and easy removal.

### Current status and results

In 2008, PATH transferred production of the Woman's Condom to the Dahua Medical Apparatus Company (Dahua) in Shanghai, China. Results from a contraceptive effectiveness trial currently being conducted by the Eunice Shriver National Institute of Child Health and Development (NICHD), with CONRAD acting as the regulatory sponsor, will be used to apply for United States Food and Drug Administration clearance in 2014.

The Woman's Condom was granted CE Mark approval in December 2010, which certifies the device meets consumer safety standards and can be marketed in countries in the European Union. In addition, an application to the Shanghai Food and Drug Administration for clearance to market the Woman's Condom in China is pending; we expect a response in mid-2011. The Woman's Condom is currently under review by the World Health Organization/United Nations Population Fund Technical Review Committee; approval by this committee could lead to bulk public-sector purchase by United Nations agencies.

PATH received funding in January 2011 from the Netherlands Ministry of Foreign Affairs to support the Protection Options for Women (POW) product development partnership. Through the POW, PATH, along with Dahua, CONRAD, and the Eunice Shriver NICHD is coordinating efforts to raise awareness of and demand for the Woman's Condom and promote female condoms worldwide.

<sup>1</sup> Guttmacher Institute. *Facts on Investing in Family Planning and Maternal and Newborn Health*. New York: Guttmacher Institute; 2010.



PATH/Glenn Austin

**A next-generation female condom.**

**“The participants rated the Woman's Condom better than two [other products] in terms of appearance, ease of use and overall fit, and better than [another product] in terms of feel.”**

*Joanis C, Beksinska M, Hart C, Tweedy K, Linda J, Smit J. Three new female condoms: which do South-African women prefer? Contraception. 2011;83:248–254.*

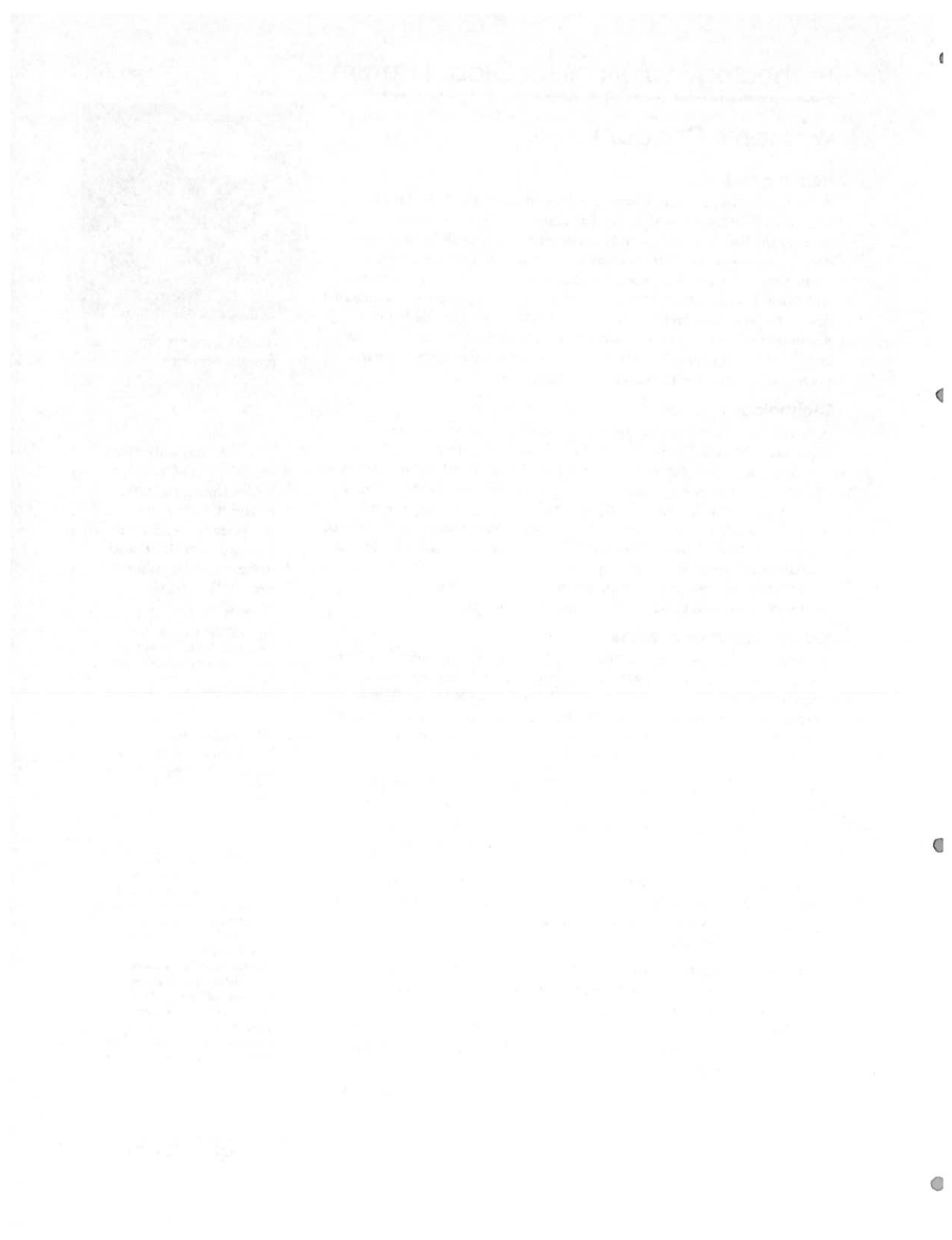
### Availability

For more information regarding this project, contact Patricia Coffey at [pcoffey@path.org](mailto:pcoffey@path.org).

### Donor support

Funding for this project has been provided by the **United States Agency for International Development** under the CONRAD program and the PATH HealthTech program, **The Bill & Melinda Gates Foundation**, the **Netherlands Ministry of Foreign Affairs**, **Universal Access to Female Condoms**, the **Lemelson Foundation**, **William and Flora Hewlett Foundation**, and others.





## Microbicide Delivery

### Health need

In the midst of the growing AIDS pandemic, microbicides could provide urgently needed options for women and men seeking protection from HIV and other sexually transmitted infections. With numerous microbicide products in preclinical or clinical trials, most research has focused on the safety and effectiveness of candidate products, with much less research targeted on devices for delivering these products.

### Technology solution

Microbicide delivery devices will be critical in ensuring safe and effective use of microbicide products. The device impacts the product's overall safety (relationship with product purity and stability, avoidance of local trauma associated with insertion or use), efficacy (consistent delivery of the required amount of product in the intended location), and acceptability (comfort, ease of use, disposability). PATH's goal is to ensure that safe, acceptable, and appropriate delivery devices are available for introduction and use with microbicides in low-resource settings. Since 2003, PATH has conducted a wide range of activities to inform and advance the development of new microbicide delivery methods including stakeholder research, clinical and acceptability research, bench testing, commercialization activities, regulatory work, and product development.

### Current status and results

In collaboration with microbicide sponsors, researchers, device manufacturers, design companies, and universities, PATH is currently advancing several novel microbicide delivery methods to help reduce cost, ensure microbicide efficacy, and increase user acceptability. Methods include:

- **SILCS Diaphragm:** We are evaluating the feasibility of the SILCS Diaphragm as a controlled-release delivery method for long-term use. This combination of barrier method and microbicide could enable prevention of both pregnancy and disease.
- **SILCS Diaphragm:** We are evaluating the SILCS Diaphragm as a delivery system for microbicide gel. Two studies were recently completed. One study assessed gel retention and distribution in the vagina comparing SILCS Diaphragm single-sided and double-sided gel delivery to a vaginal applicator. The second study used the same three gel application modes and evaluated couples' use acceptability.
- **Paper applicator with dosage stop:** This user-filled applicator is low cost, easily disposed of, and prevents over-filling, making it an important option for microbicide gel delivery in low-resource settings. We are currently evaluating it with Tenofovir 1% gel.
- **Rectal applicator:** This applicator has been designed specifically for the rectal delivery of microbicide products.



PATH/Jesse Schubert

**Microbicide in a tube with applicator.**

**Devices used to deliver microbicide products must be acceptable, affordable, and appropriate for women and men around the world to ensure optimum access and use of microbicides.**

### Availability

For more information regarding this project, contact Jessica Cohen at [jcohen@path.org](mailto:jcohen@path.org).

### Donor support

Funding for this project has been provided from private foundations and individual donors to the **Health Innovation Portfolio** at PATH, by the **United States Agency for International Development** under PATH's HealthTech program, and from the **Foundation for AIDS Research**.



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# Nutrition



## Retinol Binding Protein Enzyme Immunoassay (RBP-EIA)

### Health need

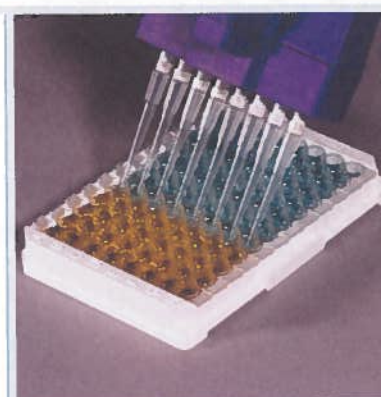
For almost 50 years, researchers have known that administering oral doses of vitamin A could prevent the consequences of severe vitamin A deficiency (VAD)—including blindness and death. Analysis of over 150,000 children between the ages of six months and five years from several countries in which VAD is a concern indicate that almost one-quarter of early childhood deaths, especially related to diarrhea and measles, could be prevented by vitamin A (retinol) supplementation. Public health planners and researchers need easier, less expensive ways to assess the extent of VAD among populations to inform public policies and promote well-targeted supplementation programs. Strategies for controlling VAD aim to provide adequate intake through dietary improvement, fortification, and supplementation. To identify the optimal mix of strategies and to monitor progress, reliable information on the magnitude and distribution of VAD in populations is needed. The current tools to do so are expensive and require external assistance; simpler, less-expensive, field-appropriate tools are needed.

### Technology solution

RBP has been shown to be a surrogate indicator for retinol, an accepted indicator of vitamin A status. The RBP-EIA was developed by PATH as an easy way to detect and quantify RBP using human plasma or serum. The test is rapid; results are available within 40 minutes. It can be read on a standard or portable EIA reader, and the results are calculated based on values from calibrator control sera provided with the kit. The RBP-EIA has been designed to produce data rapidly; to reduce reliance on costly, centralized laboratory facilities; and to provide an effective tool for field monitoring of VAD in at-risk populations. Laboratory validation has shown a strong correlation between the results obtained by the RBP-EIA and retinol, as determined by high-performance liquid chromatography (HPLC), when serum is used. The RBP-EIA has also demonstrated a strong correlation to HPLC using samples collected from a population of children at risk of VAD. The RBP-EIA predicted a VAD prevalence of 20.2 percent, while the use of HPLC determined the prevalence to be 20.4 percent. A 2004 field evaluation conducted in Thailand demonstrated that RBP is a good surrogate of retinol in both venous and capillary blood samples to estimate VAD in preschool children. Results from experiments using dried blood spots as a sample for the RBP-EIA demonstrated a positive correlation.

### Current status and results

PATH successfully licensed its RBP-EIA technology to Scimedix, a US diagnostic device manufacturer, for introduction to commercial markets. As of 2011, over 700 test kits had been distributed to support the assessment of nearly 30,000 samples through the Demographic Health Surveys in Uganda, Tanzania, and other academic research institutions. Scimedix continues to support RBP-EIA availability as part of their commercial strategy to stock and supply test kits for orders requiring relatively small quantities for specialized use in diagnostic or surveillance activities.



**Simple, less-expensive  
test for vitamin A  
deficiency.**

**“The potential for  
local assessment of  
vitamin A serum  
concentrations through  
RBP determination is  
promising. This would  
bring an accurate  
and simple vitamin A  
assessment methodology  
into the ‘toolbox’ of local  
public health workers.”**

Tanumihardjo SA, Blaner WS, Jiang T. Dried blood spot retinol and retinol-binding protein concentrations using enzyme immunoassay as surrogates of serum retinol concentrations. *MOST Technical Report*, June 2002.

### Availability

Tests can be ordered from Caryn Shapiro, Scimedix, New Jersey, [cshapiro@scimedix.com](mailto:cshapiro@scimedix.com). For more information regarding this project, contact Ralph Schneideman at [rschneideman@path.org](mailto:rschneideman@path.org).

### Donor support

Funding for this project has been provided by the **United States Agency for International Development** under PATH's HealthTech program.





## Ultra Rice®

### Health need

Billions of people suffer from micronutrient malnutrition—a factor that substantially contributes to the global burden of disease, affects the development of young children, and dramatically reduces the productivity of entire populations.

### Technology solution

PATH's Ultra Rice technology is a culturally appropriate and cost-effective micronutrient delivery system that packs vitamins and minerals into extruded rice grains made from rice flour. Ultra Rice resembles milled rice in size, shape, and color. When it is blended with milled rice, typically at a 1:100 ratio, the resulting fortified rice is nearly identical to traditional rice in smell, taste, and texture. Since the micronutrients are inside the grains, they are less vulnerable to nutrient loss during preparation and cooking. The Ultra Rice formulation can carry a range of micronutrients, including vitamin A, iron, zinc, thiamin, and folic acid.

### Current status and results

PATH's Ultra Rice project is focused on expanding its evidence base, developing markets, and broadening product adoption.

### Market development

In **India**, PATH transferred the Ultra Rice technology to Swagat Foods in early 2008. PATH also has license agreements with Christy Friedgram Industry and Sirius Overseas Private Limited. In August 2010, Akshaya Patra, the world's largest school lunch program, incorporated Ultra Rice into its centralized kitchens in Rajasthan, where rice fortified with multiple micronutrients is now served daily to 185,000 schoolchildren. In 2009, PATH and the Naandi Foundation pursued a similar pilot, reaching 60,000 schoolchildren daily in Andhra Pradesh.

In **Brazil**, PATH transferred the Ultra Rice technology to Adorella Alimentos in 2009. Select municipalities in Mato Grosso do Sul, São Paulo, and Ceará now serve Ultra Rice grains in school lunch programs that collectively reach 55,000 schoolchildren daily. In addition, PATH is helping to establish several state-level alliances and a technical center of excellence at the Federal University of Viçosa.

In **Burundi**, PATH—in partnership with World Vision—will soon distribute fortified rice to 15,000 children daily through a school meal program supported by the World Food Programme (WFP). PATH aims to improve the micronutrient status of children served by the program and generate further operational and biological impact data—expanding the evidence base for Ultra Rice and helping to build the case for its inclusion on the approved commodity lists of the two largest food aid suppliers, the US Government and the WFP.

### Affordability

It costs about US\$0.43 to \$0.56 per child per school year to integrate Ultra Rice into rice-based lunches, delivering one-third to one-half the recommended daily intake of iron, folic acid, zinc, and thiamin in one serving of rice.

*\*Ultra Rice is a registered trademark in the United States of Bon Dente International, Inc.*



Savir Mahotra

### Ultra Rice addresses micronutrient deficiency.

### Research highlights

- Iron-containing Ultra Rice was more effective than iron drop supplements at improving the iron status of children aged 6 to 24 months in a southwest region of Brazil.
- Schoolchildren aged 5 to 12 years consuming Ultra Rice in India had a significant increase in iron stores, as well as a significant reduction in the incidence of morbidities compared to a control group.
- The prevalence of anemia among women in Mexico consuming Ultra Rice decreased by 80 percent, resulting in a significant decrease relative to a control group.

### Availability

For more information regarding this project, contact Dipika Matthias at [dmatthias@path.org](mailto:dmatthias@path.org).

### Donor support

This project is funded by the Bill & Melinda Gates Foundation and the United States Department of Agriculture National Institute of Food and Agriculture.



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Street Address: 2201 Westlake Ave Suite 200 Seattle, WA 98121 USA  
Tel: (206) 285-3500 Fax: (206) 285-6619 [www.path.org](http://www.path.org)

# THE HISTORY OF THE

REPUBLIC OF THE

UNITED STATES OF AMERICA

FROM 1776 TO 1863

BY

JOHN P. FULTON

NEW YORK

1863

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# **Diagnostics for Infectious Diseases**



## HIV Dipstick

### Health need

The spread of HIV by parenteral infection via blood or blood products has been largely eliminated in the developed world through the routine screening of blood. However, blood supplies may still not be routinely screened in developing countries, where the current cost of test kits and equipment is prohibitively high or where access to appropriate tests is low. In addition, there are continual needs for low-cost, highly accurate HIV tests to supplement available diagnostic-test algorithms for research purposes and for field surveillance and epidemiology.

### Technology solution

In the early 1990s, PATH developed a rapid, inexpensive method for detection of antibodies to HIV-1 and HIV-2. The HIV dipstick was developed with the primary goal of providing an accurate, simple, HIV screening method for small- to medium-sized blood banks in developing countries. The cost per test from manufacturers was initially lower than the cost of other commercially available rapid tests. The assay takes approximately 20 minutes to perform and requires no special equipment.

The affordability and ease of use of the HIV dipstick make it suitable for low-volume HIV testing where more sophisticated, automated methods are neither cost-effective nor appropriate. The HIV dipstick is currently being used in blood banks and public health laboratories for diagnosis of HIV and also as a screening tool in HIV surveillance studies. A study by the World Health Organization (WHO) in Burkina Faso demonstrated that using the HIV dipstick in combination with another commercial test is an accurate and cost-effective method of serodiagnosis of HIV.

### Current status and results

The HIV dipstick test was evaluated in the laboratory as well as under field conditions using over 10,000 serum samples, and has consistently demonstrated a sensitivity of over 99%, while retaining a specificity of 98% or more. An independent evaluation by WHO of the HIV-1 version of the test was completed in 1990. The dipstick was subsequently optimized for combined detection of HIV-1 and HIV-2 in 1992, and has now been evaluated in 17 different countries.

PATH transferred the technology for production to local firms in Argentina, India, Indonesia, and Thailand. Kits from these producers were evaluated by WHO's Global Programme on AIDS in 1995 and 1998 and received high marks for accuracy, ease of use, and suitability. HIV tests from three of the manufacturers were added to the WHO/UNICEF bulk procurement list for HIV tests in 1997. Since the initial technology transfers, total sales of the HIV dipstick to both public- and private-sector buyers have exceeded 19 million tests. In 2004, the licensees worked together to reengineer and upgrade the product. One major outcome of the development of the technology was the lowering of the cost and increased availability of rapid HIV tests from multiple companies, resulting in much more affordable HIV testing throughout the developing world.



**First low-cost, rapid HIV-1 and HIV-2 test on the market.**

**“The availability of the dipstick and other quick, easy tests has enabled countries in the South to develop effective, on-site diagnostic testing procedures and provide same-day results.”**

*From the International Development Research Centre website.*

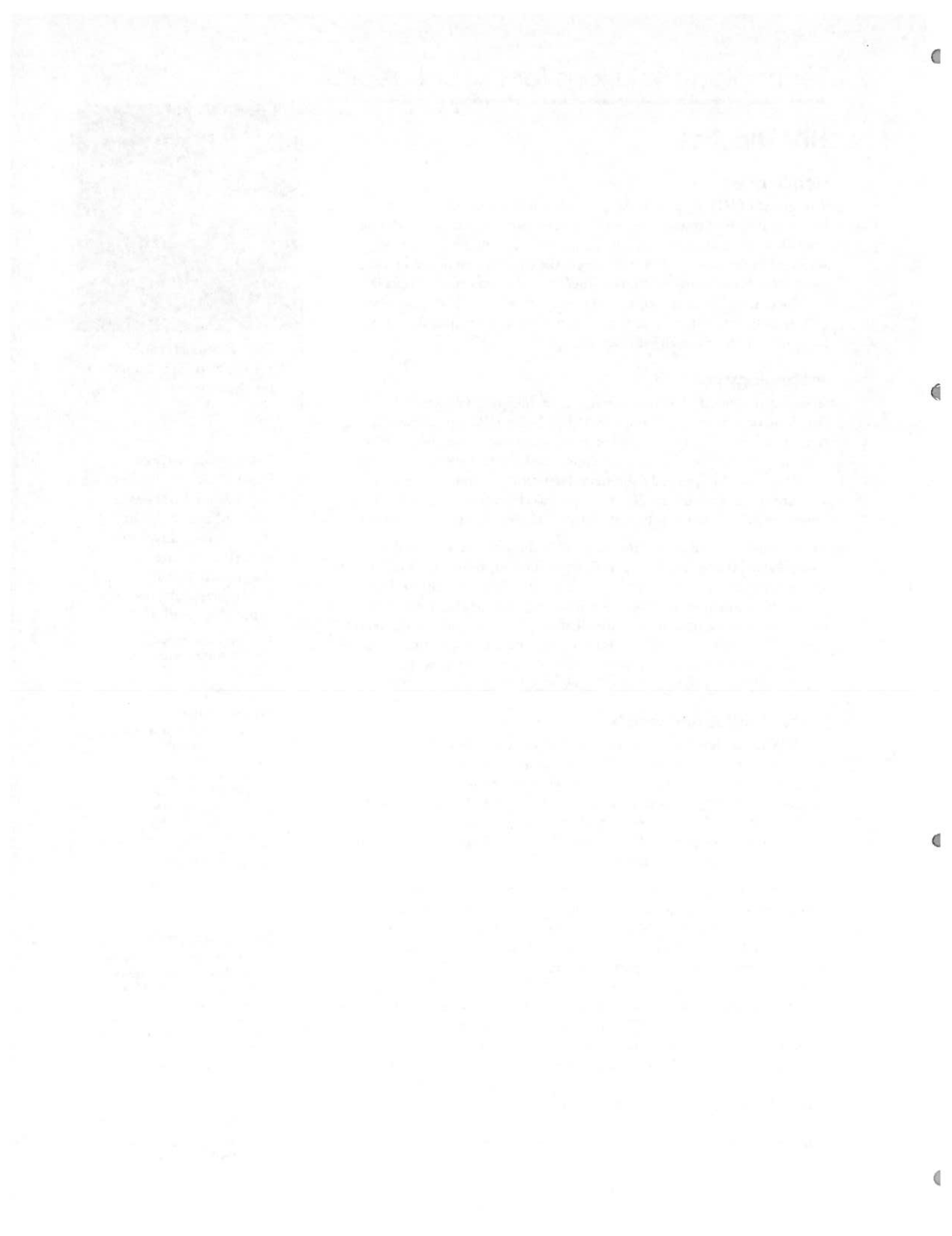
### Availability

For more information regarding this product, contact Joachim Oehler, The Concept Foundation, 111 Paholyothin Road, Thailand Science Park, Klong 1, Klong Luang, Pathumthani 1212, Thailand, Tel: 662-564-8021, Fax: 662-564-8024, joehler@conceptfoundation.org.

### Donor support

Funding for this project has been provided by the International Development Research Centre of Canada, the Rockefeller Foundation, and by the United States Agency for International Development under PATH's HealthTech program.





## PATH Chagas Immunochromatographic Strip Test

### Health need

Chagas disease (American trypanosomiasis), caused by the parasite *Trypanosoma cruzi*, is one of the most significant neglected diseases in the developing world. It is found throughout Latin America and is primarily transmitted by insects native to this region. Untreated chronic Chagas disease can lead to serious cardiac and digestive complications, resulting in loss of productivity and ultimately death. An estimated 10 million people are infected with *T. cruzi* worldwide, and more than 25 million are at risk of being infected every year according to the World Health Organization. Adding to the burden, the highest incidence of Chagas disease is found in poor and rural settings, where a tremendous diversity of parasite reservoirs and vectors combine with inadequate housing conditions to greatly facilitate disease transmission. As such, Chagas disease dramatically and disproportionately impacts the poorest and most disadvantaged populations.

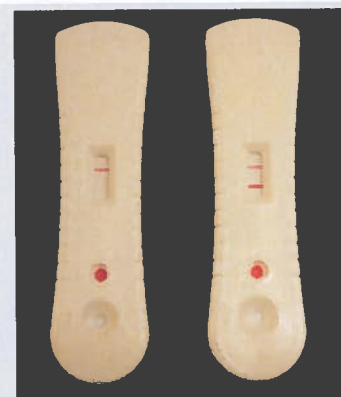
The use of two or more diagnostic tests is currently recommended for confirmation of infection. However, the diagnostic tests most commonly used—enzyme-linked immunosorbent assays (ELISA) and immunohemagglutination assays (IHA)—require well-equipped laboratories, skilled technicians, and/or refrigeration, making it difficult for these tests to be used in low-resource settings.

### Technology solution

The PATH Chagas Immunochromatographic Strip (ICS) Test has the potential to become an effective and appropriate tool for detection of Chagas disease because ICS tests offer many advantages for use in low-resource settings. They provide test results quickly and require neither sophisticated laboratories nor extensive training. The successful use of ICS tests by trained community health workers is widely recognized as evidenced by the use of ICS tests in HIV and malaria clinical management throughout resource-poor communities around the globe.

### Current status and results

PATH has conducted an evaluation of the PATH Chagas ICS Test in our laboratory using 375 previously characterized clinical specimens from a Chagas endemic region. These analyses showed that the PATH Chagas ICS Test had a sensitivity of 99.5% and specificity of 96.8%. The results to date are promising, and we will soon begin a field evaluation of test performance with whole blood specimens. Simultaneously, we are working to establish partners who will manufacture and distribute the PATH Chagas ICS Test at a price lower than other point-of-care tests.



Prototype PATH Chagas ICS Test, positive (right) and negative (left) results.

PATH/Rebecca Barney

**The need for an affordable, accurate Chagas diagnostic has been reiterated by every Chagas regional initiative. To address this need PATH is developing a rapid test for Chagas disease that combines a well-accepted and inexpensive format ICS test, with a *T. cruzi* antigen that is proprietary to a private company in Argentina.**

### Availability

For more information regarding this project, contact Cori Barfield at [cbarfield@path.org](mailto:cbarfield@path.org).

### Donor support

Funding for this project has been provided from private foundations and individual donors to the **Health Innovation Portfolio** at PATH.



## Rapid Tests for Cervical Cancer

### Health need

Cervical cancer is a preventable disease that strikes an estimated 470,000 women each year and kills more than 270,000 of them. While the industrialized world has made good progress in preventing the disease, about 85 percent of cervical cancer deaths occur in developing countries where it is a leading cause of cancer mortality among women. The lack of effective cervical cancer screening and treatment programs in poorer countries, including lack of accurate, easy-to-use, and affordable screening tests that provide rapid results, is the main cause of inequity.

### Technology solution

In 2003, PATH began assessing the scientific and economic feasibility of providing new screening tests for the types of human papillomavirus (HPV) that cause most cervical cancers. PATH entered into collaborations with private-sector partners—QIAGEN Inc. (formerly Digene Corporation) and Arbor Vita Corporation—to develop two different rapid tests that would be safe, accurate, affordable, simple, and acceptable to women in low-resource settings. If development of such tests is successful, women would then have highly sensitive alternatives to Pap smear testing and would be able to get test results more quickly. If rapid-results testing revealed that a woman is infected with a high-risk type of HPV, she could receive medical management on the same day, which would greatly reduce her risk of developing cervical cancer.

By 2008, while PATH continued to advance a rapid HPV strip test with Arbor Vita, PATH and QIAGEN had jointly developed an HPV DNA molecular test, called careHPV™. This test processes dozens of samples in approximately 2.5 hours. The test was evaluated in Shanxi, China, where 2,500 rural women were screened using vaginal and cervical samples, and it yielded good results.

### Current status and results

PATH is currently conducting demonstration projects with careHPV™ within public-sector facilities in India, Nicaragua, and Uganda. The results from these projects will be used to inform ministries of health and other key stakeholders about the feasibility, effectiveness, and acceptability of careHPV™. A prototype of Arbor Vita's AVC AVantage™ HPV E6 test was completed, and it is being evaluated in China to determine its performance. The results from both the demonstration projects and field testing will become available by the end of 2012.

In addition, in order to facilitate the establishment of health services that are ready to incorporate the new tests, PATH is working closely with Jhpiego and the Peruvian Cancer Institute to establish regional centers to train service providers in triage and treatment techniques necessary for follow-up with HPV-positive women. PATH and Jhpiego also are collaborating closely with regional and global health organizations in order to mobilize support from international and developing-country-based champions of alternative screening and treatment technologies.



Lab technician working with the careHPV™ test, Shanxi, China.

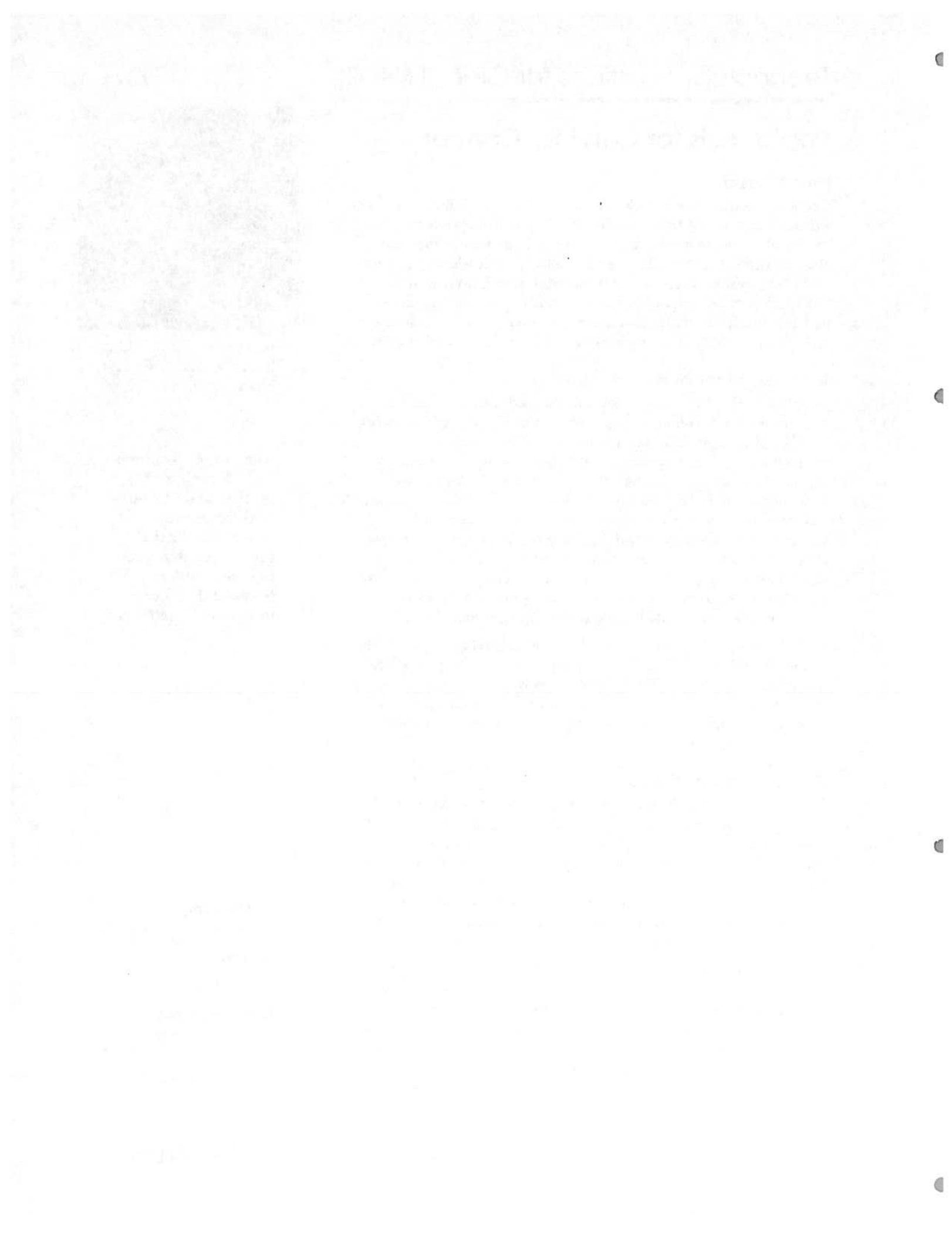
**Safe, simple, accurate, and affordable biochemical screening tests for cervical cancer may be the breakthrough needed to reduce suffering due to cervical cancer in low-resource settings.**

### Availability

For more information regarding this project contact [start@path.org](mailto:start@path.org).

### Donor support

Funding for this project has been provided by the **Bill & Melinda Gates Foundation** and by the **National Institute of Allergy and Infectious Diseases**.



## Simple and Affordable Testing for Multidrug-Resistant Tuberculosis (TB)

### Health need

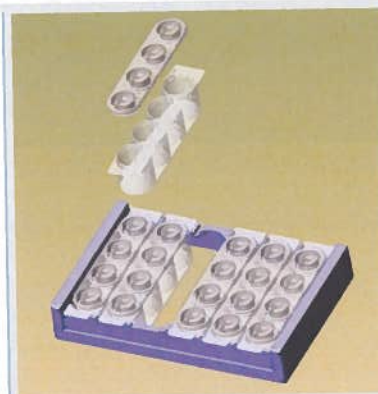
Tuberculosis, a bacterial disease caused by *Mycobacterium tuberculosis*, is a major health problem in developing countries and is reemerging as a major health threat in the developed world. High prevalence in some developing countries is associated with HIV infection and AIDS. World Health Organization (WHO) statistics indicate there are 20 million cases of active TB worldwide, and approximately 8 million new cases occur each year. TB has the highest mortality rate of any infectious disease in the world and results in approximately 3 million deaths annually. TB is a highly contagious disease that can be difficult to identify and diagnose accurately. Since it is curable with a course of antibiotic therapy, early diagnosis and treatment can curtail the spread of the disease within the general population.

### Technology solution

PATH has undertaken several different approaches to providing a solution to this problem over the years. Currently, PATH is working with collaborators in Peru (from the Wellcome Trust and Imperial College in the UK) and India (Lepra Society) to adapt the Microscopically Observed Drug Susceptibility (MODS) platform to resource-limited laboratory settings. MODS is a liquid culture-based method for determining TB positivity and resistance to first line antibiotic therapies (isoniazid and rifampicin). This test uses a simple and inexpensive tissue culture plate and commonly available culture media to determine these outcomes. The original platform has been validated in five countries with extremely high sensitivity and specificity and a rapid turnaround from specimen collection to results dissemination (usually within seven days).

### Current status and results

Field-based evaluations of MODS have demonstrated that poor biosafety of the tissue culture plate system and complicated aliquoting of assay reagents are potential obstacles to widespread uptake of the platform. PATH is engaged in three parallel activities in development of the MODS platform. First, we are developing a biosafe containment cap for the tissue culture plate that will ensure that assay reagents and biohazardous sputum specimen do not leak from the culture plate. Second, we hope to reduce assay steps for users by creating a system for inserting premeasured dry reagents into each sample well. Thus, users will only have to add decontaminated sputum and water to the specimen well prior to incubation. Third, we are soliciting commercial manufacturers in the developing world to eventually manufacture the MODS platform as a "kit" for sale to providers and laboratories.



Representation of the biosafe MODS plate design.

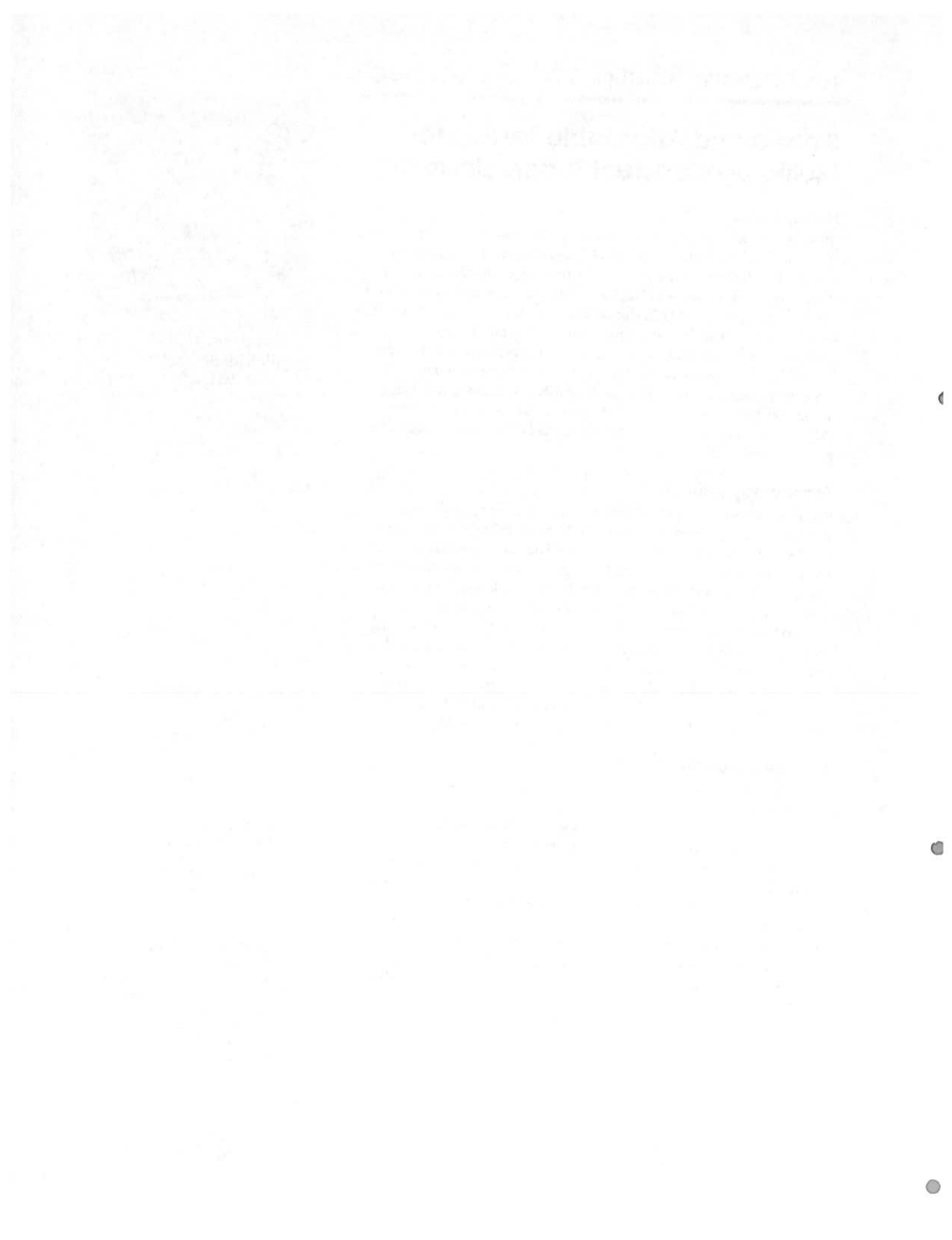
### Availability

For more information regarding this project, contact Matthew Steele at [msteele@path.org](mailto:msteele@path.org).

### Donor support

Funding for this project has been provided by the United States Agency for International Development under PATH's HealthTech program and from the Bill & Melinda Gates Foundation.





## Rapid Strip Test for Malaria

### Health need

Despite intensive public health efforts, more than 300 million new cases of malaria occur each year, resulting in more than a million deaths worldwide. Microscopy is still the standard method for diagnosis in many parts of the developing world, but it is time consuming, labor intensive, and can only be performed by expert microscopists in specialty clinics or higher levels of the health care system. It is impractical whenever large numbers of samples must be examined. An alternative test method was urgently needed for the rapid and accurate identification of falciparum malaria infection in smaller clinics and rural hospitals.

### Technology solution

The malaria immunochromatographic strip (ICS) test developed by PATH under HealthTech utilizes relatively inexpensive, off-the-shelf components and is formatted to identify *Plasmodium falciparum* in whole blood. A test can be completed in less than 20 minutes using a single drop of finger-stick blood. It can be performed and the results interpreted by technicians with minimal training. The strips are stable for months at ambient temperatures when appropriately sealed in foil pouches, and built-in procedural controls indicate whether each strip performs correctly.

### Current status and results

The malaria ICS test has been evaluated in the laboratory as well as under field conditions in the developing world in collaboration with the Centers for Disease Control and Prevention and USAID in Peru and Malawi. The evaluations demonstrated a sensitivity of over 96%, and a specificity of 93% or more. Ease-of-use studies have also concluded that the test is extremely easy to interpret. PATH then licensed the manufacturing know-how to two companies, one in Germany and one in India. Reported sales of the test by spring 2005 were 300,000 tests. PATH has also provided technical assistance to two other commercial manufacturers for development of their own falciparum malaria ICS tests; sales have been in the range of 40,000,000 worldwide.

The simple, rapid ICS technologies allow testing for falciparum malaria in rural or small clinics or hospitals in the developing world so that accurate results can be returned the same day, allowing effective patient follow-up and prescription of appropriate therapeutic drugs. This is especially important since WHO now recommends artemisinin combined therapy, a relatively expensive treatment, because the falciparum malaria organism is resistant to chloroquine. Epidemiological surveillance teams can also use the test to gather baseline data or to assess the effect of public health interventions. The tests can supplement or confirm infection in conjunction with microscopic diagnosis of malaria at central reference facilities. In lower-volume blood banks or transfusion centers, the test can be used to rapidly test donated blood before storage and subsequent transfusion.



**A rapid, easy-to-read, low-cost test for malaria.**

**A study of the PATH-developed rapid test for malaria diagnosis found that in areas where microscopy expertise is lacking and laboratory capacity limited, the rapid test is considered useful.**

Parkes R, et al. Comparison of a nested polymerase chain reaction-restriction fragment length polymorphism method, the PATH antigen detection method, and microscopy for the detection and identification of malaria parasites. *Canadian Journal of Microbiology*. 2001;47(10):903-907.

### Availability

The test has been transferred to companies in Germany and India and is available from: Human GmbH, Tel: 49-6122-9988-275, Fax: 49-6122-9988-100 or Span Diagnostics, Tel: 91-261-8677211, Fax: 91-261-8679319.

### Donor support

Funding for this project has been provided by the **United States Agency for International Development** under PATH's HealthTech program.

# THE HISTORY OF THE

The history of the world is a story of the human race, of its struggles, its triumphs, its failures, and its progress. It is a story of the human mind, of its power, its limitations, and its growth. It is a story of the human heart, of its love, its hate, its hope, and its despair. It is a story of the human spirit, of its courage, its faith, its doubt, and its redemption.

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## Safe Water



## Safe Water: A Market-Based Approach

### Health need

Safe drinking water is essential to good health. However, in resource-poor settings, water often comes from unsafe sources and carries deadly pathogens. The World Health Organization estimates that 1.1 billion people lack access to improved water supplies, and 1.8 million people—including nearly 5,000 children a day—die each year from preventable diarrheal diseases; many of these deaths are attributed to unsafe water.

Various products exist today to treat and safely store water. Yet, according to international experts, less than 1% of those without access to improved water supplies are being reached with current efforts to promote household water treatment and storage. Clearly, the scale of the problem is far beyond what current efforts can handle.

### Technology solution

Commercial markets currently supply low-income consumers in the developing world with household goods such as soap, food items, and basic commodities. PATH understands that household water treatment and safe storage (HWTS) products can be successfully marketed and sold to these consumers in a similar way for positive health outcomes.

Market-based solutions offer a number of potential advantages. In general, the private sector is more nimble and innovative, has greater resources, is more responsive to consumer preferences, and has the potential for sustainability and scalability without ongoing subsidies. Through the Safe Water Project, PATH has worked to catalyze and facilitate new partnerships and approaches to selling HWTS to low-income consumers. By providing incentives and reducing risks for commercial partners, PATH works to launch them in new directions, serving a low-income market. The goal is that partners can take these initiatives to scale—independent of PATH—and the marketplace will make them sustainable, ultimately leading to a greater overall impact on health.

### Current status and results

PATH's strategy is to invest in activities that advance the household water treatment category and benefit all organizations that seek to increase access to water treatment products to low-income populations. PATH and our partners have developed and are currently testing market models in India, Southeast Asia, and Eastern Africa.

In India, users were engaged as co-designers to inform the creation of product design guidelines for companies developing new products for low-resource settings. Four PATH-improved products are being carried forward by private-sector partners, including two water treatment elements and two HWTS gravity-fed devices. One improved HWTS device is already being sold in Cambodia. PATH is implementing pilot projects in a number of countries to test four market-based distribution models. PATH also continues to refine tools to support our distribution partners around sales recruiting and training, active monitoring, and encouragement of sound enterprise operating principles.



PATH/Glenn Austin

**A young girl collects water to use in the home.**

**“Current efforts in household water treatment and storage are reaching only 7-8 million people, or less than 1% of those without access to safe water.”**

Thomas Clasen, London School of Hygiene & Tropical Medicine.

### Availability

For more information regarding this project, contact Glenn Austin at [gaustin@path.org](mailto:gaustin@path.org).

### Donor support

Funding for this project is provided by the Bill & Melinda Gates Foundation.



# THE HISTORY OF THE CITY OF BOSTON

FROM THE FIRST SETTLEMENT  
TO THE PRESENT TIME  
BY  
JOSEPH NEALE

VOLUME I  
FROM THE FIRST SETTLEMENT  
TO THE YEAR 1630

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