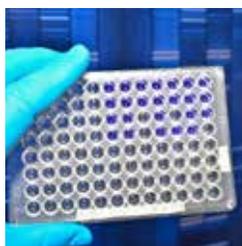


Innovate4Health

How Innovators Are Solving Global Health Challenges

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Innovate4Health: How Innovators Are Solving Global Health Challenges

Many of the world's biggest challenges are health challenges. The good news is that, more than ever, people are meeting these challenges with innovative solutions.

While we still face great difficulties, people all over the world live better than ever before thanks to innovation. New medicines prevent or alleviate disease. New devices diagnose problems, repair bodies, and overcome physical challenges. Still other inventions keep vaccines and medicines fresh and effective or ensure their authenticity. New business models help innovation to happen and ensure that it reaches those who need it.

Many of these innovations are secured by intellectual property rights, which support the ability of innovators to invent and bring solutions to market. Property rights, particularly intellectual property rights, foster the freedom of many hands and many minds to work on challenging problems. They put decisions in the hands of those closest to problems—innovators with knowledge of potential solutions and caregivers and consumers who understand their own needs best.

With just a bit of reflection, it becomes clear that innovation and the property rights that secure it are key to meeting global health problems. Sometimes, however, the blinding light of necessity makes it hard to see this fact. When people are in need, it is all too easy to grow impatient with the rights of innovators. When that happens, innovators get treated as an obstacle.

We think that better public policy would result from better understanding of how innovation can meet global health challenges. Our organizations, the Center for the Protection of Intellectual Property (CPIP) at George Mason University's Antonin Scalia Law School and the Information Technology and Innovation Foundation (ITIF), both non-profit, non-partisan research organizations, have teamed up to tell the exciting story of how innovation is making the world healthier.

Our Innovate4Health initiative culminates with this report, profiling 25 original case studies showcasing how innovators, many in developing countries, are tackling life-sciences/healthcare innovation in their nations and across the broader developing world. The 25 case studies are organized into the six following themes:

- Adapting healthcare interventions for environments where resources and infrastructure are challenging;
- Providing affordable and robust tests for diagnosing diseases;
- Improving HIV diagnosis and care;
- Affordable interventions to meet basic needs in challenging environments;
- Getting healthcare to the people in places where it's hard for people to come to the healthcare;
- Fostering health innovation in emerging economies.

Collectively the case studies tell a compelling and inspiring story of how entrepreneurs are creating IP-enabled life-sciences innovations that are helping to tackle some of the world's toughest health issues.

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Table of Contents

| | |
|--|-----------|
| Chapter 1: Introduction | 2 |
| Chapter 2: Challenge: Adapting Healthcare Interventions for Environments Where Resources and Infrastructure Are Challenging | 8 |
| Treating Neonatal Jaundice in the Developing World with D-Rev’s Brilliance | 8 |
| Embrace Infant Warmers Help Save Lives of Preterm Babies in Developing Countries..... | 10 |
| Intellectual Property Helps NephroPlus Improve Treatment for Chronic Kidney Disease in India..... | 13 |
| New Oxygen Machine Technology Confronts Blackouts in Emerging Nations..... | 15 |
| mPedigree Battles Counterfeit Drugs Through Innovative Verification System | 17 |
| Chapter 3: Challenge: Providing Affordable and Robust Tests for Diagnosing Diseases | 19 |
| Better Screening for HPV in Developing Countries | 19 |
| Miriam Bridges the Gap Between Developing-World Infrastructure and Cancer Detection..... | 22 |
| Nanobiosym’s Gene-RADAR Brings Real-Time Results for Zika Testing..... | 24 |
| Meeting the Needs of Rural Africa with Fyodor’s Point-of-Care Testing for Malaria | 27 |
| Chapter 4: Challenge: Improving HIV Diagnosis and Care | 29 |
| Point-of-Care Technology for HIV Diagnosis in Developing Countries | 29 |
| Daktari Diagnostics, Taking on Africa’s Healthcare Challenges One Diagnostic Device at a Time | 32 |
| DNAe Enhances HIV Treatment By Monitoring the Effectiveness of Antiretroviral Therapy..... | 34 |
| Chapter 5: Challenge: Affordable Interventions to Meet Basic Needs in Challenging Environments | 36 |
| Nutraset Uses Patents and Trademarks to Fight Severe Malnutrition Across the Globe..... | 36 |
| GRIT Leveraged Freedom Chair Brings Mobility to Developing World..... | 38 |
| Indian Startup Develops Nanomaterial Filter to Help Solve Global Drinking Water Crisis..... | 40 |
| Innovation Helps Solve Basic Sanitation Problems | 42 |
| Protecting Patients with VanishPoint Retractable Syringes..... | 45 |
| Nike’s Innovations Provide Comfort and Independence to People with Disabilities..... | 47 |
| Chapter 6: Challenge: Getting Healthcare to People in Places Where It’s Hard for People to Come to Healthcare Providers | 49 |
| Global Good’s “Arktek”: A Life-Saving Super-Thermos Vaccine Cooler | 49 |
| Eye Exams On-the-Go with PEEK..... | 51 |
| Zipline Enables Real-time Delivery of Essential Medical Supplies in Rwanda..... | 53 |
| The Handheld Cardio-Pad: Tackling Cardiovascular Disease in Africa Through Innovation | 55 |
| Proximie: Augmented Reality Technology Helps Bring Surgical Expertise to Conflict Zones and the Developing World..... | 57 |
| Chapter 7: Challenge: Fostering Health Innovation in Emerging Economies | 60 |
| Intellectual Property Helping to Drive Healthcare Innovations in India | 60 |
| How Strengthened IP Rights Unlocked the Potential of Biomedical Innovation in Brazil..... | 62 |
| Endnotes | 64 |
| About | 83 |

Chapter 1: Introduction

Many of the world's biggest challenges are health challenges, and there's widespread recognition that innovation is essential to improving public health. Nevertheless the potential of innovation to overcome global health challenges is, if anything, underappreciated. All too often, discussion about the role of innovation in international forums boils down to debates about how best to finance research and development (R&D) for new medicines in the laboratories of developed countries. This narrow view of healthcare innovation often fails to credit or recognize the extensive amount of health innovation occurring on the ground in developing countries.

To address this, we decided to spotlight how innovation can tackle global health challenges on the ground. This volume features 25 original case studies from throughout the world showcasing local and international actors working together to meet global health challenges by “innovating for health.” We focused particularly, but not exclusively, on innovation in developing countries as well as innovations occurring on the ground and closer to the point of delivery. As we did our research, admiring observers and passionate inventors directed us to more and more stories. This volume just scratches the surface of a large and exciting phenomenon.

We hope you'll appreciate this inspiring collection of stories about how entrepreneurs are meeting global health challenges with innovative solutions at all points in the healthcare system in both developed and developing countries.

Some Lessons Learned

Cumulatively, the case studies in this volume tell a heartening and inspiring story about the power of innovation to improve health outcomes. Several lessons emerged from the cases studies as highlights from the research:

Global health challenges are probably even more numerous and varied than most think—but people on the ground know what they are and have ingenious ideas about solving them. In one sense, this point is hardly surprising, since any detailed investigation into difficulties in delivering healthcare turns up new challenges. Still, studying how people solve problems in the field invites a renewed appreciation of how many problems there are yet to solve.

However, by approaching the subject as we did, we were encouraged to witness the problems as they are being solved. With the right resources and policy environment—and even sometimes without those conditions and against all odds—people apply their inventiveness and ingenuity to overcome the challenges they encounter in their own work and lives.

The people who understand health challenges best are those who work with them day-to-day, and it's these people who are most likely to invent an innovative approach or new solution. Regardless of how well-informed and effective an intergovernmental organization, non-governmental organization, or other large actor may be, understanding the true scope and nature of problems is a consistent challenge. Those closer to the problem have a better understanding of the most pressing issues and often the best insights for how to fix them. The key is to provide the right incentives and policy environment to support their work, as we discuss subsequently.

Among the diverse challenges addressed here are:

- Building medical devices for environments where power is unreliable or absent;
- Sorting real medicine from fake medicine in places where counterfeiting is overwhelming and regulators, police, and other authorities have limited resources;
- Providing quick, cheap point-of-care diagnoses of diseases;
- Providing cheap but intensive nutritional intervention;
- Providing sanitation and clean water where the infrastructure to deliver them does not exist and is not coming soon;
- Helping people who have limited resources overcome disabilities to live full lives in physically challenging environments;
- Getting health care to people who live in remote places; and
- Fostering innovation in emerging economies.

These challenges are incredibly diverse, but a common thread unites them: smart people working close to the problems are addressing them with clever, innovative solutions.

Healthcare challenges are indeed varied, and frankly, until humans achieve immortality, endless. Yet this means that there are tremendous opportunities to increase longevity and improve quality of life. As this report shows, these challenges are being met by innovation in the delivery of healthcare services, in more effective prevention and detection of diseases, and in novel therapies, treatment, and medicines.

Many of the biggest health challenges are practical, on-the-ground problems that are well suited to innovative solutions. As noted, discussions of innovation and public health often focus on R&D for new medicines, but innovation is just as relevant for the practical problems that bedevil healthcare delivery in much of the world. Certainly, the world's health challenges would often benefit from more attention and greater resources, but innovation allows people to do more with the same resources.

Innovation is the ultimate game changer. As economics teaches, without innovation we live in a world governed by the law of scarcity. Paul Samuelson, in his introductory economics textbook, once explained that “in the world as it is, children learn that ‘both’ is not an admissible answer to a choice of ‘which one?’” In fact, as one of us observed in previous work, the reason innovation is so important is that it helps overcome the ironclad law of scarcity.

Innovation allows people to do more with less, to do new things with old resources, and to create entirely new products and industries. As a result, output increases, job opportunities, wages and the economy grow, and people have wider choices. Innovation enables us to enjoy and do entirely new and different things. Its importance in promoting economic and social development cannot be overstated.¹

Yet the scarcer the resources, the greater the need for innovation.

Indeed, one of the biggest challenges we found innovators confronting again and again is scarcity—in access to trained professionals, in transportation, and in other infrastructure. For example, reports estimate that as many as 1 billion people lack access to essential health care because of a shortage of trained health professionals.² A 2014 World Health Organization (WHO) study estimated that a shortage of 7 million public healthcare workers exists today, with that number expected to rise to 13 million by 2035.³ More than 80 countries currently fail to meet the basic threshold of 23 skilled health professionals per 10,000 people.⁴ The challenge is even more daunting when it comes to specialists. For instance, Cameroon has fewer than 50 cardiologists supporting a population of over 23 million citizens.⁵ And Ethiopia, a country of some 90 million citizens, is served by a single radiation treatment center located in the capital of Addis Ababa.⁶

In other instances, people lack access to essential medicines, with their cost being a relatively small part of the problem. For instance, in 2014, researchers at the University of Utrecht in the Netherlands found that, on average, essential medicines are available in public sector facilities in developing countries only 40 percent of the time.⁷ If medicines cannot reach remote areas, patients are less able to access them. A 2009 survey of 36 countries found that 15 common generic medicines listed on the WHO Essential Medicines list are frequently unavailable in either the public or private sectors, with regional availability ranging from 29 percent in Africa to 54 percent in the Americas.⁸ Again, cost is only part of the problem. Indeed, the vast majority of drugs—at least 95 percent—on the World Health Organization's Essential Medicines list are off-patent, and thus potentially available in generic versions.⁹ The problem, in much larger part, stems from countries' underdeveloped health systems and the fact that many people live in rural areas, far from care. In fact, approximately 70 percent of the world's poor live in rural areas, where it becomes very difficult to cost-effectively deliver healthcare services and supplies.

What can be done if people lack physical access to trained professionals, key health equipment, and medical supplies? Innovators are addressing the problem by bringing healthcare to where people are. Several of the case studies show how innovative technologies can play key roles in helping tackle these challenges. For instance, the Arktek vaccine cooler keeps vaccines at a temperature between zero and eight degrees Celsius for 30 to 60 days. Dubbed the “keg of life” by Bill Gates, the Arktek can hold routine vaccinations for approximately 200 children or a village with a population of 6,000. It has played a transformational role in helping ensure medicines can reach patients in need throughout the developing world. Solutions like Arktek are helping to tackle the challenge that poor storage facilities and conditions cause significant wastage of pharmaceutical supplies each year. For instance, a recent study from India which followed a series of vaccine vials through the distribution process found that 76 percent failed quality testing because the vaccines they contained became frozen during the study period.¹⁰ Solutions that effectively get treatments to patients in the field can play a major part in tackling global health challenges.

Similarly, the Rwandan government has teamed with the startup Zipline to facilitate the real-time delivery of urgent medical supplies, such as blood or vaccines, to patients in remote locations via drones. Zipline's drones serve 21 Rwandan hospitals nationwide, providing instant access to life-saving blood products for over 8 million Rwandans, nearly two-thirds of the country's total population of 12 million. These examples highlight that, in many cases, requisite medicines and medical supplies already exist; the challenge lies in ensuring they can reach the patients who need them in the field.

Other case studies show how innovators are transforming medical equipment for use in the field. One example is the equipment used to test heart health and eyesight. In wealthy countries, people go to visit doctors who test both using bulky, expensive equipment. However, that model of delivery does not work as well in the developing world. Thus, Arthur Zang's Cardio-Pad was developed in Cameroon to monitor heart health in the field. The PEEK eye exam kit is a simple smartphone attachment that can do much of what would be done in an optometrist's office. Trained technicians can take this portable equipment to where people are and transmit the results back to doctors.

Similarly, the opportunity to prevent and detect illnesses before or as they are occurring also matters greatly. The case studies show how innovators are enabling earlier, more-accurate, and less-expensive methods for the detection of diseases such as cancer, HIV/AIDS, and Zika.

Innovation can happen anywhere, and flows both ways, between the global North and South, and between developed and developing countries. The human mind, with its infinite creativity and innovative capacity, is the one resource that exists everywhere. Sometimes, debates about innovation, intellectual property (IP), and public health that occur in places such as Geneva seem to forget this fact. They sometimes depict innovation as something that happens only in wealthy countries, with less-developed countries the passive recipients of such innovation. Nothing could be further from the truth.

Moreover, the world increasingly shares similar healthcare challenges. While many health problems in developing countries are certainly distinct, and while certainly there are unique infectious diseases such as malaria which particularly afflict developing countries, the maladies affecting the citizens of the developed and developing world are increasingly similar. For instance, by 2020, non-communicable diseases such as cardiovascular disease and diabetes will account for 70 percent of fatalities in developing countries.¹¹ Citizens of low- and middle-income countries bear 80 percent of the world's death burden from cardiovascular disease.¹² Forty-six percent of Africans over 25 suffer from hypertension, more than anywhere else in the world. Similarly, 85 percent of the disease burden of cervical cancer is borne by individuals living in low- and middle-income countries.¹³ Visual impairment strikes 253 million of the world's citizens, with 90 percent of visually impaired individuals residing in low-income countries.

All of the world's citizens benefit when innovative solutions are developed by scientists or entrepreneurs, whether they come from developed or developing nations. Indeed, innovative solutions such as the Cardio-Pad, which got its start in Cameroon, or the Embrace Infant Warmer are now being deployed in the developed world. Affordable diagnostics such as those described in our case studies have a place everywhere. We all benefit when many hands and many minds work on challenging problems.

Intellectual property rights matter and can foster economic growth and innovation in emerging economies. In almost every instance, the innovations in our case studies are secured by intellectual property rights, which support the ability of innovators to invent and bring solutions to market. Property rights, particularly intellectual property rights, put decisions in the hands of those closest to problems: innovators with knowledge of potential solutions and caregivers and consumers who understand their own needs best. They fund individual careers and industries dedicated to fixing health problems, as well as the businesses that get these solutions to individuals.

As the case studies here compellingly show, the ability to attain, protect, and enforce intellectual property is an indispensable, foundational catalyst for these life-sciences innovations to flourish. Put simply, intellectual property is a powerful enabler, not an inhibitor, of life-sciences innovation. For instance, Arthur Zang, the Cameroonian developer of the Cardio-Pad, noted that the ability to secure intellectual property rights was a vital impetus to begin—and to continue—innovating, pointing out that “patents enable you to protect yourself against rivals who simply want to copy your work.”¹⁴ The developers of the Embrace Infant Warmer, the PEEK system, and the Fyodor \$2 malaria-testing system also testify in these pages regarding the extent to which the ability to attain and protect IP rights were vital to both their innovations and their ability to establish and grow their companies.

Furthermore, the marriage of technology, intellectual property, and innovation isn't just bolstering quality of life in developing countries; it's contributing to economic growth and the development of regional high-tech clusters and ecosystems, which also support high-skill, high-wage jobs in these countries. For instance, Arthur Zang subsequently launched a company, Hi-More Medical, leveraging expertise gained with the development

of the Cardio-Pad into related medical devices such as electroencephalography (EEG) machines. The company, supported by one of a series of seed grants offered by the Cameroonian government and designed to bolster Cameroon's startup and innovation economy, hopes its low-cost medical device solutions may give rise to a vibrant medical diagnostics cluster centered in Cameroon but serving all of Central Africa.

With just a bit of reflection, it becomes clear that innovation and the property rights that secure it are key to meeting global health problems. Sometimes, however, the blinding light of necessity makes it hard to see this fact. When people are in need, it's all too easy to grow impatient with the rights of innovators. When that happens, innovators get treated as an obstacle. Unfortunately, that is what the previous United Nations (UN) Director General did when he convened the recent UN High-Level Access to Medicines Panel. Its mandate was greatly misguided when it charged panelists to “review and assess proposals and recommend solutions for remedying the policy incoherence between the justifiable [intellectual property] rights of inventors, international human rights law, trade rules, and public health in the context of health technologies.”¹⁵

Rather, as our case studies show, any inquiry into global health challenges that treats innovators and IP rights as part of the problem is out of touch and short-sighted. This report thus joins a growing body of work, including others such as the Organization for Economic Cooperation and Development's report “Trade and Innovation: Pharmaceuticals,” which attributes part of the success of emerging pharmaceutical sectors in Brazil and China to the introduction of patent protections.¹⁶ Moreover, that report demonstrates that stronger IP patent protection—alongside less stringent price controls—tends to encourage more or faster launches of drugs, while intellectual property rights lead to much greater introduction of foreign pharmaceutical products into developing markets and helps contribute to the globalization of clinical trials.¹⁷ IP and access to medicines at affordable prices are not incongruous. In fact, intellectual property fundamentally underpins innovation and the very existence of medicines that the access to medicines debate presupposes in the first place.

In conclusion, we believe that better public policy can result from a better understanding of how innovation is helping to meet global health challenges. We are pleased to bring you these exciting stories of how innovation is making the world healthier.

The case studies that follow are organized into six key global health challenges innovators are meeting with compelling new solutions:

- Adapting healthcare interventions for environments where resources and infrastructure are challenging;
- Providing affordable and robust tests for diagnosing diseases;
- Improving HIV diagnosis and care;
- Affordable interventions to meet basic needs in challenging environments;
- Getting healthcare to the people in places where it's hard for people to come to the healthcare;
- Fostering health innovation in emerging economies.

We hope that this report will contribute to a better understanding of the importance of IP-driven innovation in meeting global health challenges.

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Chapter 2: Challenge: Adapting Healthcare Interventions for Environments Where Resources and Infrastructure Are Challenging

Treating Neonatal Jaundice in the Developing World with D-Rev's Brilliance

By Nick Churchill



Severe neonatal jaundice kills over 100,000 newborn babies annually and causes severe brain damage to thousands more.¹ In most cases, the condition can be treated by simply shining a blue light on a baby's skin. However, each year more than 6 million infants worldwide do not receive adequate treatment. The problem is particularly severe in low-income countries, where many hospitals cannot afford the equipment to treat jaundice.

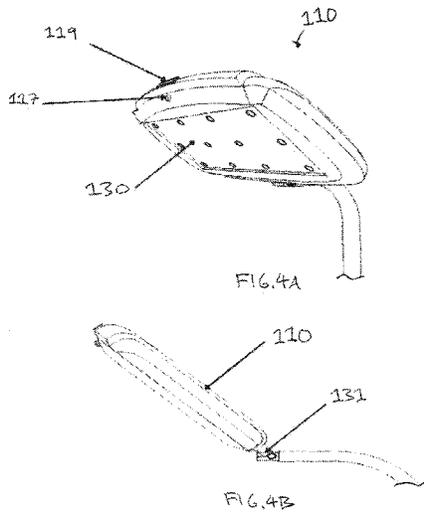
To address this global health problem, the innovators at D-Rev, a non-profit firm based in San Francisco, designed a high-performance, affordable device called Brilliance to treat severe neonatal jaundice.² Brilliance has been praised by users as "effective and user-friendly," and it was honored as the top innovation in the Health category of the 2016 Tech Awards.³ Since the introduction of the first Brilliance model in 2012, D-Rev estimates that the device has treated over 370,500 babies and has averted approximately 4,900 infant deaths and disabilities.⁴

Neonatal jaundice occurs when a newborn has elevated levels of bilirubin in the blood.⁵ Approximately 18 percent of babies have severely high levels of bilirubin, which, left untreated, can lead to brain damage, cerebral palsy, hearing loss, and even death.⁶ Severe jaundice can be treated with a process called phototherapy, which involves placing the baby under special blue lights.⁷ When the light is absorbed by the infant's skin, it helps break down bilirubin. Treated properly, severe jaundice usually does not cause lasting damage.

Phototherapy has long been recognized as a simple and effective treatment for severe neonatal jaundice; but at around \$3,000, traditional phototherapy devices are prohibitively expensive for many hospitals in developing countries.⁸ Hospitals that can obtain a traditional unit are often unable to afford the maintenance and repair

costs necessary to keep it running. The unreliable electrical systems in many developing countries can cause voltage spikes that damage device components. Commonly used fluorescent lamps require frequent replacement. As a result, phototherapy is unavailable to babies in many developing communities.

D-Rev is a product development company founded in 2007 to provide world-class, affordable healthcare technologies to people living on very low incomes. After learning that severe jaundice continues to cause brain damage in many parts of the world, D-Rev staff members visited hospitals in India and Nigeria to assess the availability of effective phototherapy and found that most of these hospitals did not have phototherapy devices that met standards for care. With the problem identified, D-Rev's design team got to work.

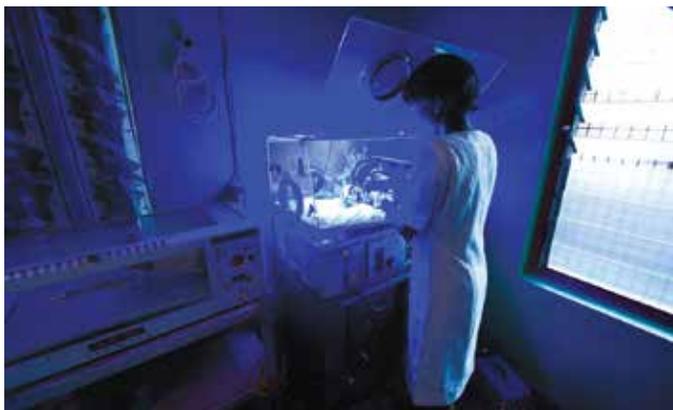


D-Rev's advanced devices, for which the developers are seeking a patent, use light-emitting diodes (LEDs) that last 60 times longer than fluorescent lamps, saving hospitals over \$240 per year on replacement bulbs.⁹ Brilliance is designed to withstand a range of power fluctuations without affecting performance and operates without cooling fans or filters, so there are fewer parts to maintain. The device is height-adjustable and can be integrated with the wide variety of other critical neonatal medical equipment found in hospitals serving low-income communities.

Importantly, D-Rev's devices are inexpensive to manufacture, which allows D-Rev to sell them for hundreds, instead of thousands, of dollars.¹⁰ The newest model incorporates the technology in their patent application, which ensures light intensity levels remain consistent across the treatment area at any angle of tilt. D-Rev also developed an integrated light meter to

help healthcare providers ensure that infants receive appropriate doses of light, something many low-income hospitals were previously unable to accomplish. Thus, the innovations developed by D-Rev are improving the technology and reducing the cost, making much-needed treatments more accessible throughout the developing world.

After successfully designing an affordable and effective phototherapy device, D-Rev's next challenge was finding a way to deliver Brilliance to the hospitals that needed it most. D-Rev's CEO, Krista Donaldson, recognized that the firm would need help to establish a sales and distribution network, noting, "We knew we needed to license in this case."¹¹ To achieve its goals, D-Rev needed to find a partner willing to manufacture its products and distribute them to hospitals and clinics in the poorest communities in the world.



D-Rev licensed its technology to Phoenix Medical Systems, a neonatal equipment firm based in India, which agreed to manufacture and distribute Brilliance while capping its price.¹² The licensing agreement was structured so that D-Rev would take a smaller royalty on sales to public and district hospitals, which tend to serve lower-income patients.¹³ In this way, D-Rev used its intellectual property rights to align the incentives of Phoenix's sales team with D-Rev's goal of reaching those patients most in need of affordable phototherapy.¹⁴

Donaldson has explained why D-Rev’s protection of its intellectual property “is a prerequisite to having the broadest possible impact.”¹⁵ First, intellectual property rights allow D-Rev to ensure that the quality of its products remains consistent. As Donaldson notes, a medical device “cannot fail the user, particularly a user in a vulnerable population.”¹⁶ Second, inconsistency erodes consumer trust, which limits the impact of a product. Third, D-Rev recognizes that designing an effective product does not necessarily solve the targeted problem. By retaining control of its intellectual property, D-Rev can ensure consistent manufacturing of its products, sustainable delivery to users who need it, and continued maintenance and support. Finally, D-Rev protects its intellectual property because the market is “the most economically sustainable and scalable way” of reaching their intended customers.¹⁷

D-Rev has demonstrated that the value of intellectual property goes beyond incentivizing life-saving innovations like Brilliance. Intellectual property rights empower innovators to increase their impact by partnering with market leaders such as Phoenix. As Donaldson concluded: “To succeed, serious partners (for-profit or non-profit) must also make an investment, and none are willing to do that with the threat of knock-offs.”¹⁸

Embrace Infant Warmers Help Save Lives of Preterm Babies in Developing Countries

By Gleb Savich



Preterm birth is the leading cause of death for children under five years old.¹⁹ An estimated 15 million babies are born before 37 weeks gestation each year, and nearly 1 million children under five die due to complications associated with such births.²⁰ Nearly three-quarters of them could be saved with current interventions.²¹ The disparity in survival rates of preterm babies based on a country’s wealth is startling.²² In high-income countries, almost all of the babies born after 32 weeks survive, but in low-income countries, only half survive.²³

Hypothermia is a significant factor contributing to the death of preterm babies. Preterm newborns are particularly vulnerable to hypothermia because they cannot generate enough heat to warm themselves on their own.²⁴ They also have less stored fat to insulate themselves against heat loss. Infant incubators are commonly used in neonatal care units to help preterm infants maintain safe body temperature. Such equipment costs thousands of dollars and requires a stable source of electricity to operate.²⁵

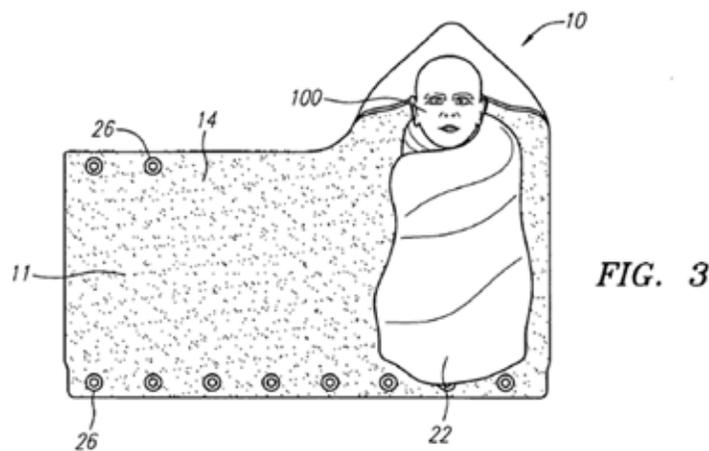
Healthcare interventions in the developing world often prove ineffective.²⁶ Expensive equipment donated to hospitals in developing countries is often useless because a stable electricity supply and replacement parts are unavailable. Despite long-term efforts of well-intentioned people, innovative solutions remain needed to meet these local challenges rather than more donations of existing technology.

Specifically, there has been a need to design infant incubators that address the unique challenges of the developing world. Embrace infant warmers, which were developed through a project class at Stanford University called Design for Extreme Affordability, were designed to meet these challenges.²⁷ Embrace infant warmers have won several awards, including the Economist Innovation Award and the TED Fellows award.²⁸

Projects start with developing-world challenges in mind, and students create innovative solutions that address problems using existing technology. An integral part of the course are need-finding trips, during which students learn about the needs of the target community while on location.²⁹ This enables the students to formulate an appropriate design process while also establishing deep connections with members of the local community.

The challenge leading to Embrace was to create a cheap infant incubator. The project team started by visiting hospitals in Nepal, and they quickly realized that most births occur in villages far away from hospitals with stable sources of electricity. Donated infant incubators were available, but they were left in storage because the birth facility lacked the infrastructure to use the machines.

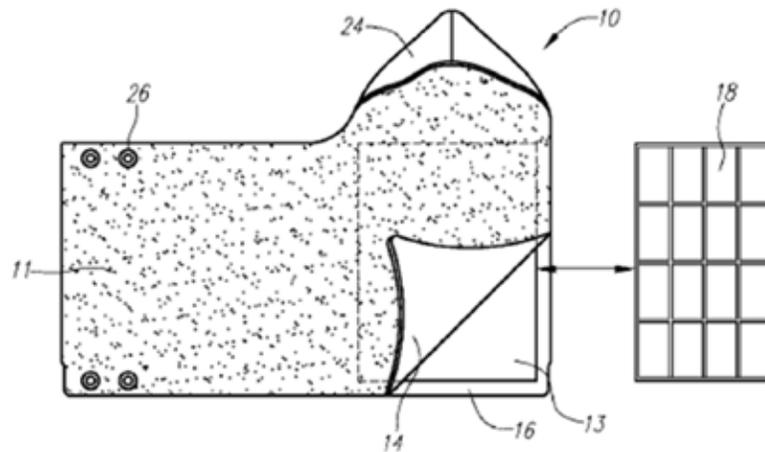
The team designed a portable device capable of maintaining the infant at approximately body temperature without having to be continuously connected to an electricity source. The device is able to do so by utilizing specialized temperature-regulating materials that keep a near-constant temperature despite gaining or losing heat energy.



These materials are called “phase-change materials” because they melt or solidify (in other words, they change phases) near body temperature. People normally think about the transfer of heat energy as making one thing warmer or another thing colder, but this is not true during a phase change. For example, during solidification, the material releases heat energy, which can be used to keep the infant warm, but it maintains its own temperature because the heat comes from the process of solidification rather than a loss of temperature.

Embrace infant warmers look like a swaddle or a tiny sleeping bag that cradles an infant. A temperature-regulating element is placed between the inner and outer fabric layers of the infant warmer. This element contains the phase-change material, chosen so that it melts or solidifies around normal human body temperature.

The temperature-regulating element can be heated or cooled to the desired temperature utilizing a recharging unit plugged into an electrical outlet or by placing the element into warm or cool water. Thus, no electricity is required to use the device. But even intermittent power sources can be beneficial because the unit can be charged when it's not in use. Once at the desired temperature, the temperature-changing element is inserted between the fabric layers of the infant warmer. One current version of the infant warmer maintains the desired temperature for at least four hours.³⁰



To further advance their invention, the team founded the Embrace Innovations company and have begun developing a strong patent portfolio.³¹ Secure and effective patent rights allow the enterprise to grow and adapt in furtherance of their mission. This includes adopting strategies such as providing products through for-profit and nonprofit mechanisms and contracting with third-party manufacturers to produce the devices. Income derived from the initial innovations can then be used for additional projects that will further benefit the developing world.

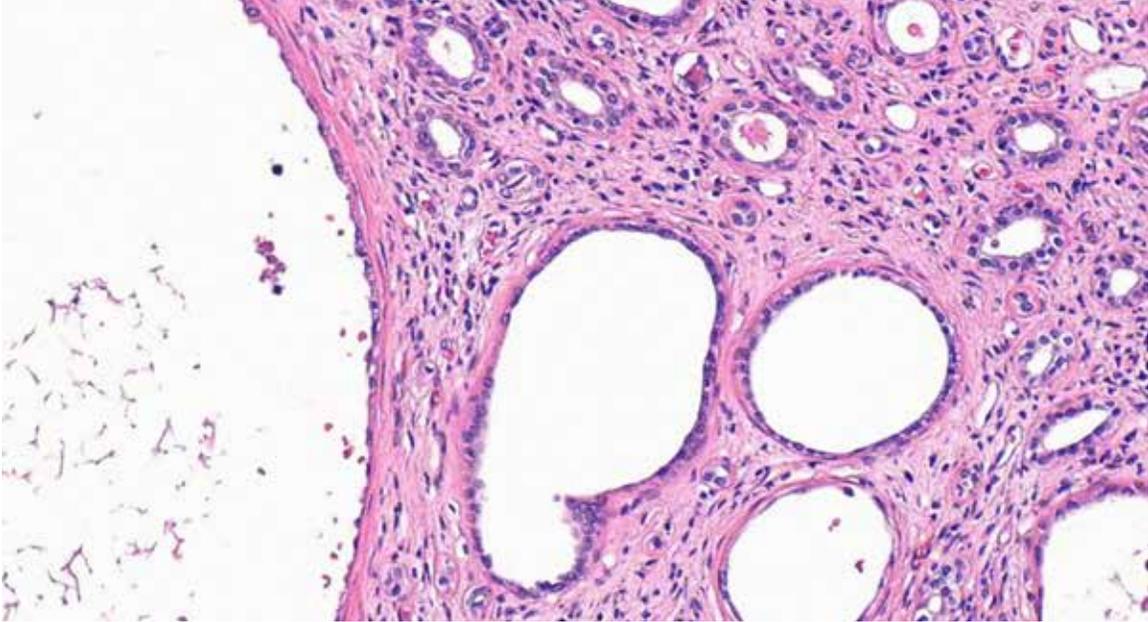
Today, Embrace infant warmers are manufactured by Phoenix Medical Systems in India and are available for a small fraction of the cost of standard incubators.³² The nonprofit arm of the company, Embrace Global,³³ is a part of Thrive Networks, an international NGO that utilizes evidence-based innovations to improve the lives of underserved populations in Southeast Asia.³⁴

The Embrace team has also gone on to develop other products: sleeping bags and swaddles for infants under the brand, Little Lotus.³⁵ Like Embrace infant warmers, these products utilize phase-change materials to ensure optimal sleeping temperature for babies. A portion of proceeds from every purchase of a Little Lotus product goes to providing access to Embrace infant warmers, showing how parallel projects can be used to benefit vulnerable populations in the developing world.

With the help of Embrace Global and its partners, Embrace infant warmers have been used to care for over 200,000 low birth weight and premature infants across 20 countries in the developing world.³⁶ This is the result of both the important innovation and the forward-thinking development that can only occur when inventors have control over the ideas they create.

Intellectual Property Helps NephroPlus Improve Treatment for Chronic Kidney Disease in India

By Nigel Cory



Chronic kidney disease, which causes people to lose their kidney function over time, affects an estimated 12 million people in India. With the increasing incidence of diabetes, the burden of such a chronic disease is only likely to increase. But one company—NephroPlus—uses a patent-pending process at the heart of its operations to provide safe, affordable, and effective treatment in a growing number of cities across the country. The company’s experience shows that service-focused intellectual property, not just patents for pharmaceuticals, can play a role in driving healthcare innovation in developing countries.

The problem in India is that more than 90 percent of the 230,000 Indians newly diagnosed with kidney disease each year die within months due to a lack of treatment.³⁷ There are many contributing factors—a lack of trained staff (India has less than a thousand nephrologists) and services that are fragmented, inefficient, potentially harmful, and largely available only in the big cities. Once kidney failure occurs, individuals require a kidney transplant or weekly dialysis treatment to stay alive. Kidney transplants—which can fail—are extremely limited due to stringent regulations, low kidney donation rates, and poor health infrastructure, which makes dialysis the most viable alternative.

Dialysis can keep one’s body in balance by removing waste, salt, and extra water to prevent these from building up in the body, maintaining a safe level of certain chemicals in the blood, and helping to control blood pressure. But poor-quality dialysis services have plagued India.³⁸ Negligent clinical processes, poor infection protocols, and insufficiently trained staff lead to cases where the blood of the donor isn’t properly screened or the dialysis units aren’t cleaned properly. Indicative of this, patients are at a high risk of cross infection—around 30 percent of patients in India who get dialysis for two years have a 30 percent chance they will be infected by hepatitis B or C or HIV.³⁹ So serious was the state of affairs in India that on November 26, 2014, India’s Supreme Court (in response to a public-interest legal case) sought a response from the federal and state governments on the status of dialysis and renal care infrastructure in the country.

In 2010, NephroPlus's founders, one of whom experienced chronic kidney disease, recognized the situation in India and set about identifying international best practices on clinical procedures to use at the heart of a new health-services company.⁴⁰ This led to the patent-pending "Zero Infection Point Kit," a 56-step process that allows the company to provide safe, effective, and affordable services to a growing number of Indians, especially low-income patients.⁴¹

The success of NephroPlus's intellectual property and business model is evident: in a few short years the company has become the largest private dialysis provider in the country.⁴² NephroPlus runs 78 centers across 53 cities in 15 states, some in large cities and others in underserved, smaller cities. NephroPlus's centers provide a complete range of healthcare services, such as hemodialysis, peritoneal dialysis, and kidney transplant services, along with counseling and diet-support services as part of a holistic focus on patient care. NephroPlus designs, builds, and operates low-cost centers to provide high quality and affordable dialysis services, either as standalone clinics or in partnerships with hospitals. NephroPlus does all of this at a better price than other providers: at \$25 per treatment, NephroPlus's services are 30 to 40 percent, sometimes 50 percent, lower than those of large hospitals in India.

Even with a focus on lean and efficient operations, NephroPlus knew that to make its services more affordable and accessible it needed to do more given the large number of poor patients in India. So the company began to register its centers with the government, thereby allowing patients to pay via public insurance plans. As of 2015, approximately 25 percent of NephroPlus patients used public insurance to cover their costs. This figure is expected to grow to 30 percent by 2020. This has helped the company treat more of the poorest people. As testament to this, a 2016 study found that 67 percent of NephroPlus's patients were considered to be living at the base of the income pyramid in India.

Along these lines, NephroPlus acted as an agent for change within India's hospital system—both public and private—which had failed to supply the growing need for high-quality treatment of chronic kidney disease. First, NephroPlus entered into revenue-sharing agreements with private hospitals to split revenue, also allowing lead nephrologists to become minority investors in the partnership.⁴³ Second, NephroPlus bid for government contracts to build dialysis centers in public hospitals. Again, being flexible on how it leveraged its core competitiveness—the patented treatment process—while also being mindful of the interests of diverse stakeholders allowed the company to expand its services.

NephroPlus's success has attracted significant financial backing—the company raised \$10 million from the International Finance Corporation and \$3 million from a private venture capital fund.⁴⁴ Over the next five years, NephroPlus aims to reach over 40,000 patients and to help create 10,000 skilled jobs, including doctors, nurses, and dialysis technicians. The company is planning to establish one clinic in every district of the country by 2018. Half of its future centers will be located in smaller cities to make dialysis services more accessible to lower-income patients. NephroPlus is also looking to go international and expand to five countries in Africa and Asia by 2020.

NephroPlus's success has coincided with much-needed government reforms, including changes in funding. In November 2016, India's Health Minister stated that the government aimed to open 4,000 dialysis centers across the country. While there hasn't been a separate allocation of funding for kidney disease treatment, the government is now providing funding through India's National Health Mission for state-driven public-private partnerships (PPPs), which 30 states have used for dialysis projects.⁴⁵ The governments pay these centers on a per-treatment basis. In this, the state and district hospitals can offer space to private service providers who bid to secure a contract for the space. As of March 2017, India's Health Ministry has approved 519 such PPP proposals, including those from NephroPlus.⁴⁶

Nephroplus's success relies on its ability to leverage its intellectual property as part of a business model that is efficient, profitable, and adaptable. It has certainly benefited from the Indian Government's growing attention to the issue and reforms to funding, health insurance, and operational policies. This underscores how access to healthcare is a complex subject that involves many different issues and stakeholders, which in this case, has changed in recent years to vastly improve access to better and more-affordable treatment for chronic kidney disease.

NephroPlus's story highlights the need for a broader focus on the barriers to healthcare, rather than accusing intellectual property of being the main culprit, as many involved in the debate regarding improving access to healthcare in developing countries have done, such as in the misguided report by the United Nations High Level Panel on Access to Medicines. This blinkered approach is not only wrong, but damaging, as it distracts from the need for broader discussions about the wide range of barriers to healthcare in any given country.

New Oxygen Machine Technology Confronts Blackouts in Emerging Nations

By Andrew B. Levey



Oxygen therapy, in which supplemental oxygen is used as a medical treatment, is vital to children with pneumonia.⁴⁷ Rolling blackouts in Uganda and other developing nations, which can last for hours at a time, are stopping oxygen concentrators—machines that concentrate oxygen from the ambient air—from providing this vital therapy.⁴⁸ Problems are worse in more remote places that lack an electricity infrastructure in the first place. As a result, children already vulnerable to pneumonia are denied effective treatment. Currently, pneumonia accounts for at least 18 percent of all deaths of children under five years old.

The World Health Organization (WHO) has stated that methods for providing oxygen are needed in low-resource settings to combat poor energy infrastructure and theft of needed supplies.⁴⁹ Through their FREO2 Foundation, Professors Roger Rassool and Jim Black of the University of Melbourne are tackling this problem with the FREO2—Siphon.⁵⁰

FREO2 has improved upon existing oxygen concentrator technology by locally storing oxygen at low pressure, making it available when needed to supplement a disconnection of energy to the machine.⁵¹ While developing a new approach to the technology, the team managed to keep costs low and produce a product suitable for remote relocations vulnerable to blackouts.⁵² Lack of reliable electricity has been addressed in other ways, but those methods are only sufficient for larger, more-established medical facilities.⁵³ More remote and desolate clinics needed a different solution.

Professors Rassool and Black developed a concentrator which utilizes running stream water to create a low-pressure vacuum, which can be used to separate oxygen from the air in the environment.⁵⁴ The team determined that the central issue isn't specifically energy related, but a matter of creating a difference in air pressure to

create air flow. The final product is cost efficient, easy to use, and simple to operate. Taking a step back and re-imagining the basic concepts of an oxygen concentrator allowed the team to arrive at the conclusion that electricity was not needed. A working prototype is already operating in Gippsland, Australia, with planned expansion to other countries. Professor Rassool is conducting operational and field work studies in Uganda to begin implementation of the device where it is needed most.



FREO2’s patent application describes the foundational innovation. Concentrating oxygen from the atmosphere involves passing air over a “molecular sieve,” which removes nitrogen and leaves primarily oxygen behind.⁵⁵ The energy to move the air across the sieve in older technology came from electricity creating high pressure to push air into the sieve. Figure 2, from the patent application, shows how a siphon operating between two levels of water can accomplish the same goal by pulling the air instead of pushing it. The water flowing through the siphon will draw in air, shown in typical patent fashion with a number (13) and a line. Drawing in air creates a vacuum that can be used to pull air into the sieve and concentrate the oxygen.

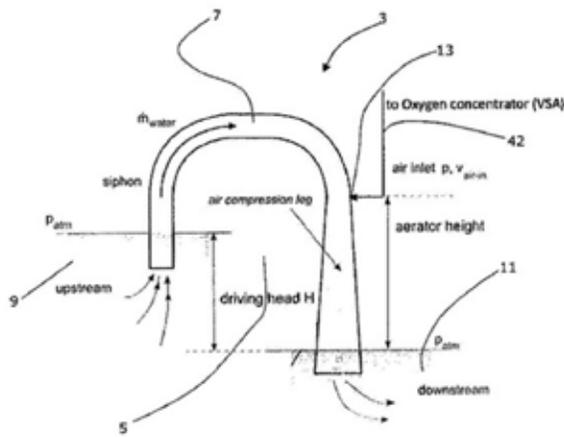


FIG. 2

The Bill & Melinda Gates Foundation and numerous others have recognized the value of the innovation, awarding the inventors funding to continue research, development, and deployment of their invention.⁵⁶ FREO2 is poised to continue its research and manufacturing into the near future. Ultimately, the inventors hope to bring their startup to Australia, where they want to establish a network within the community and potentially form manufacturing capabilities for future deployments. As the inventors note, they have a long road ahead but the rewards to be reaped are great.

The FREO2 device will save lives. As the inventors emphasize, the innovative technology allows remote clinics to keep oxygen concentrators performing by simply utilizing available water sources, which will support their primary mission—saving lives. And the benefits of IP protection will help ensure that they fulfill their mission.

mPedigree Battles Counterfeit Drugs Through Innovative Verification System

By Kevin Madigan



Counterfeit medicines sold under a product name without proper authorization are a serious threat to global public health. Classified by the World Health Organization as substandard, spurious, falsely labelled, falsified and counterfeit (SSFFC) medical products, counterfeit drugs are regularly designed to appear identical to genuine products.⁵⁷ However, they fail to effectively treat the disease or condition for which they are intended, and in some instances, they can cause adverse reactions or death.

A recent BBC investigation revealed a multi-billion-dollar global trade in counterfeit drugs resulting in 120,000 deaths a year in Africa alone.⁵⁸ And though counterfeit drugs affect economies, health care systems, and patients worldwide, developing nations are most at risk, with an estimated counterfeit rate of 10 to 30 percent of medicines sold.⁵⁹ The prevalence of unauthorized drugs in countries with less-advanced healthcare systems has created a dangerous pharmaceutical market with few resources to help consumers distinguish between a drug that could potentially save their life and something that might kill them.

In 2007, Ghanaian tech entrepreneur Bright Simons set out to address this troubling threat to public welfare by creating a way to quickly confirm the legitimacy of a pharmaceutical.⁶⁰ Realizing that low literacy and technical capacity were limiting the efficacy of existing consumer-targeted controls such as holograms and bar codes, Simons wanted to create a user-friendly system that would help consumers instantly check the authenticity of a drug using their mobile device. Simons envisioned a verification mechanism that would not only enable consumers to protect themselves against dangerous counterfeits, but also help pharmaceutical manufacturers defend their brands and shield shopkeepers from the liability of selling fake drugs.

Simons partnered with drug companies and other stakeholders to upload pedigree information from individual packs of medicine into a central registry using standard mass-serialization methods similar to those employed in the radio-frequency identification (RFID) barcode system familiar in the United States and other developed countries. Calling his company mPedigree, Simons built a mobile verification service that enables consumers to text a product code that is then checked against the registry of authentic medicines, instantly verifying that the medicine they've acquired is legitimate and safe.⁶¹

Since forming mPedigree in 2009, Simons has brought his system to Nigeria, Kenya, and India, with pilot programs in Uganda, Tanzania, South Africa, and Bangladesh.⁶² In 2015, mPedigree codes appeared on over 500 million drug packets from clients such as AstraZeneca, Roche, and Sanofi, and its verification network has been essential in combating a serious counterfeit antimalarial drug scheme that was putting thousands of Africans at risk.⁶³

Though mPedigree is best known for its work with pharmaceutical certification, Simons has expanded its verification system to address counterfeits in other industries through his development of the cutting-edge supply-chain transformation technologies, EarlySensor and Goldkeys.

mPedigree's EarlySensor technology offers a proactive solution to companies plagued by unauthorized imitations by identifying patterns in counterfeiting activity and alerting partner government agencies of suspicious trends.⁶⁴ The project "scans large pools of authentication, traceability, supply chain & logistical referencing, and user-generated data to mine insights and plot evolving patterns" to empower both manufacturers and consumers to predict counterfeiting activity before it occurs.⁶⁵ EarlySensor technology is currently used by three major pharmaceutical and cosmetic companies in Nigeria, and empirical analysis has shown a 65 percent reduction in the circulation of counterfeit versions of their brands.⁶⁶

With Goldkeys, mPedigree has developed a set of web tools to provide brand owners with "complete, real-time, control of key events in their supply chain."⁶⁷ The technology enables companies to manage distribution networks and retail-point integration, as well as track end-consumer activity through web applications and cloud computing. Goldkeys also allows consumers to "call in" their product by voice call or text on a mobile device to ensure authenticity and receive consumer support.

Through the combination of EarlySensor and Goldkeys, mPedigree's innovative technology is facilitating the protection of both brand owners and consumers and ensuring that data collection and authentication mechanisms are leading to the safer distribution of medicines, cosmetics, seeds, and other essential products.

As a company dedicated to helping others protect their product reputation and brand, mPedigree understands the importance of effective IP rights and has utilized patent, copyright, and trademark protection in the development and commercialization of its own brands and services. In the early days of the company, as it formed partnerships with tech and pharmaceutical industry giants, mPedigree was careful to retain the rights to its creations, with Simons stating in a recent interview that, "[w]e had one interest to protect: our intellectual property."⁶⁸



By providing a dynamic link between consumers and manufacturers, mPedigree is making communications at the point of purchase routine and creating value for consumers, manufacturers, regulatory agencies, and sellers. A project 10 years in the making, mPedigree is built on the recognition that protecting intellectual property—both mPedigree's and its clients—can save lives.

Bright Simons' vision and dedication to fighting the counterfeit drug epidemic in Africa and beyond through pharmaceutical verification is a testament to the vital role innovation and technology play in confronting global challenges, and as its motto states, mPedigree is indeed "bringing quality to life."

Chapter 3: Challenge: Providing Affordable and Robust Tests for Diagnosing Diseases

Better Screening for HPV in Developing Countries

By Nigel Cory



Cervical cancer is a completely preventable disease, yet it remains the leading cause of cancer-related death and morbidity among women in the developing world, with approximately 85 percent of the disease burden occurring in low- and middle-income countries.⁶⁹ To address this challenge, countries need to use testing as part of population-based screening for human papillomavirus (HPV), which is the principal cause of cervical cancer.⁷⁰ Screening for HPV is particularly important in developing countries given the large number of people with HIV/AIDS, who are more susceptible to HPV due to their weakened immune systems. Previously, there were few HPV tests well suited for developing countries, but a new product—Xpert HPV—changes this by offering an accurate, real-time, self-contained, and easy-to-use molecular testing mechanism that can be used at the point-of-care.

Developing countries face a number of unique challenges in screening and testing for cervical cancer. Pap smear (cytology) screening has been successful in reducing the rates of cervical cancer in developed countries; however, logistical and resource requirements (such as a lack of trained personnel) make this difficult for developing countries.⁷¹ In contrast, “see-and-treat” screenings using visual tests are simple, affordable, and scalable to primary healthcare facilities in developing countries. However, this comes with the disadvantage of the higher potential for false-positive results.

The World Health Organization recommends testing for high-risk HPV (hrHPV) infection be incorporated into cervical screening programs worldwide. Large-scale studies have shown the efficacy of molecular tests for hrHPV, leading to recommendations in Europe, Australia, the United States, and elsewhere to incorporate hrHPV DNA tests into population-based screening programs.⁷² Molecular cervical cancer screening—the detection of HPV DNA, RNA, or oncoproteins—has the potential to overcome the shortcomings of visual

inspection. However, molecular testing was initially thought to be cost- and resource-prohibitive for developing countries, but newer tests such as Xpert HPV are cheaper, simpler, and more accessible for use at the point of care.

The Xpert HPV test is a rapid (around 60 minutes), fully automated, and easy-to-use test for hrHPV infections that is as accurate as laboratory-based testing.⁷³ Xpert HPV was developed as molecular tests are more sensitive than existing detection methods for high-grade cervical intraepithelial neoplasia (a precancerous condition on the uterus). Xpert HPV uses disposable cartridges to hold the reagents, primers, and probes for the simultaneous detection of 14 hrHPVs, including HPV types 16, 18, and 45. Detecting HPV genotypes 16 and 18 is critical as they are associated with approximately 71 percent of all cases of cervical cancer, while HPV genotype 45 is associated with approximately 6 percent of additional cases of cervical cancer.⁷⁴ Quick and accurate testing allows for same-day screening and treatment, which has advantages for patients and providers by reducing attrition of care (a particular problem with non-communicable diseases) and by reducing healthcare costs for patients and providers (given the costs associated with multiple visits).⁷⁵

Xpert potentially makes screening and treatment more accessible as it has proven to be an effective point-of-care HPV DNA test, while using patient-provided specimens (as compared to clinician-provided). A 2016 study in Papua New Guinea (PNG) was the first to use a point-of-care hrHPV test for clinical cervical cancer screening in a high-burden, low-income country.⁷⁶ The study showed that Xpert HPV worked well and that patient-collected specimens for the detection of hrHPV are comparable to clinician-collected specimens. Low-income countries may be able to use this feature (patient-provided samples and easy to use technology) to expand cervical screening, as a similar program that relies on clinician-collected samples will require substantially more resources. PNG is a good test for Xpert HPV: PNG has among the world's highest estimated burdens of cervical cancer (incidence rates 6.3 times higher than those of Australia and New Zealand and a mortality rate that's 13.5 times higher), with cervical cancer being the most common cancer among women in PNG.⁷⁷

Another study in Zambia—which has the world's second-highest annual cervical cancer incidence and mortality rate—showed that Xpert HPV matched or exceeded traditional visual identification methods.⁷⁸ The study took place at the Cervical Cancer Prevention Program (CCPPZ) in Lusaka, Zambia and included 200 women. The results of this study supported existing research which showed that Xpert HPV performs well with women with HIV. Incorporating it into a clinic like the CCPPZ shows the potential for its broad impact as CCPPZ, since its inception in 2006, has played a major role in Zambia's efforts to screen and treat people with HIV as part of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) program.

Cepheid, which developed Xpert HPV, is a leading molecular diagnostics company based in the United States.⁷⁹ The development of Xpert HPV is typical of the time, money, and effort needed to improve healthcare in developed and developing countries alike. In the early- to mid-2000s, Cepheid invested hundreds of millions to research and develop the foundational technology behind the GeneXpert system (which Xpert HPV is part of) and cartridges.⁸⁰ This came in addition to supplementary funding provided through public-private partnerships with the National Institute of Allergy and Infectious Diseases and other organizations.

Cepheid has relied on intellectual property to secure patents for its GeneXpert platforms and cartridges and to protect its proprietary chemistry and manufacturing processes.⁸¹ It now holds an extensive patent portfolio.⁸² Cepheid is able to reap the rewards from its intellectual property portfolio and re-invest earnings in new technology that will be critical to improving healthcare in developing countries, such as the Xpert HPV.

Cepheid is ideally placed to help developing countries fight cervical cancer as it has the largest installed base of molecular detection systems (as compared to other HPV DNA tests) in developing countries. Cepheid's GeneXpert platform is widely used for the diagnosis of tuberculosis (TB) and TB drug resistance in developing

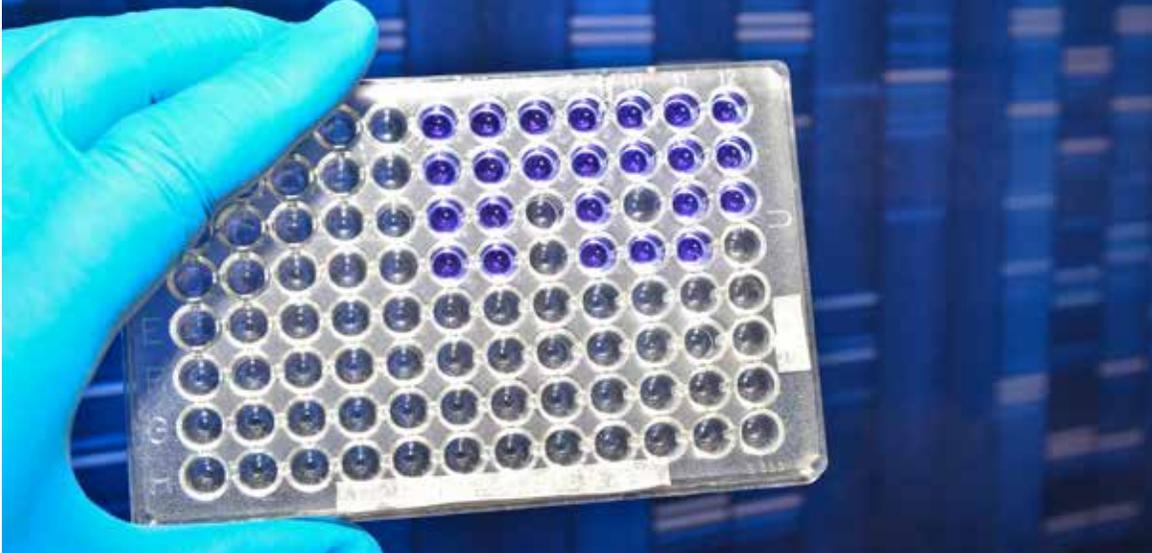
countries around the world. Cepheid could potentially integrate the Xpert HPV test as part of its Infinity system, which includes dozens of individual tests in a single automated system. In a 2013 presentation on Xpert HPV, Philip Castle, chairperson and CEO of the Global Coalition Against Cervical Cancer and executive director of the Global Cancer Initiative, highlighted this potential: “The excitement [around] this is [that] where there is TB, there are undoubtedly higher rates of cervical cancer....The fact that GeneXpert is placed in many of these high-burden, high-risk populations offers the opportunity to deliver cervical cancer prevention in these places ... One can imagine almost a field kit at the smallest configuration [of the GeneXpert] ... [as well as] high-throughput, centralized testing.”⁸³

Cepheid also engages with developing countries as part of a specific program to help them use its products to improve healthcare services. In 2013, Cepheid sold 5,509 GeneXpert systems, with around 1,800 of these being in the company’s high-burden developing country program, where the company subsidizes the placement of thousands of GeneXpert systems and cartridges in various non-profit NGOs (mainly to test tuberculosis and TB drug resistance).⁸⁴ Furthermore, Cepheid licenses its intellectual property with particular partners to minimize or in some cases eliminate royalty payments associated with its GeneXpert platforms in developing countries. Intellectual property allows companies like Cepheid the flexibility and control to pursue a strategy of price and market entry differentiation depending on the individual market.

Xpert holds the potential to greatly improve the number of people being screened for HPV in developing countries. But again, as in previous Innovate for Health cases studies, the technology behind Xpert HPV (and the intellectual property embedded in it) is addressing only one part of the broader policy environment that affects healthcare outcomes in developing countries.⁸⁵ Cervical cancer screening illustrates this, as despite numerous demonstration projects showing that simple and cost-effective methods for prevention (particularly visual inspection with acetic acid and immediate cryotherapy) are viable and effective, screening coverage rates remain very low in developing countries.⁸⁶ This has been known for some time, yet rarely have such methods been adopted and scaled up by governments in developing countries.⁸⁷ Xpert HPV offers a potentially better tool for improving screening in the future, but this highlights the underlying point that Xpert HPV’s impact will ultimately depend upon the broader healthcare system it’s used in.

Miriam Bridges the Gap Between Developing-World Infrastructure and Cancer Detection

By Alex Summerton



Originally a disease diagnosed predominantly in developed countries, cancer is now a leading cause of death in the developing world, which reports over half of all new cases annually.⁸⁸ The rise in cancer in the developing world is attributed to improving technological, medical, and socioeconomic conditions. People are living longer due to reducing other causes of mortality such as infectious disease, unsanitary conditions, and maternal and infant mortality. The result is populations living long enough to begin seeing end-of-life diseases such as cancer.⁸⁹

However, the advances leading to the higher detection of cancer in the developing world have not been accompanied by the advances to fight it. Treatment costs remain prohibitively high.⁹⁰ Detection usually occurs late during the disease's progression, generally after symptoms begin to present and chances of survival decrease. Underdeveloped infrastructure makes accessibility to screening and treatment difficult. Doctors' offices can be remote and crowded, and trained oncologists are few and far between, leaving necessary expertise inaccessible to patients.

The overall effect is a developed-world disease outstripping developing-world technology and infrastructure.

Miroculus aims to combat the challenges of cancer screening, in both the developed and developing world, by providing accurate, low-cost, and accessible technologies that can be easily deployed at the earliest stages when treatment is cheaper and more effective.⁹¹ Founded by Alejandro Tocigl, Foteini Christodoulou, and Jorge Soto, Miroculus is developing a method of screening for cancers via microRNA.

The flagship product of Miroculus is Miriam, a cancer-detection platform enabling accurate, early screening of cancer. Debuted at TEDGlobal in 2014, Miriam is a non-invasive tool that can rapidly screen for a wide range of cancers.⁹² Its design means it can be deployed during routine health examinations, rather than as part of cancer testing once symptoms have presented. Miriam works by assaying blood for the presence of microRNAs. Miroculus's team has shown that certain microRNAs in a patient's blood are correlated with specific types of cancer.⁹³ So far, Miroculus has proven the concept of enabling Miriam to detect pancreatic, lung, breast, and hepatic cancer.

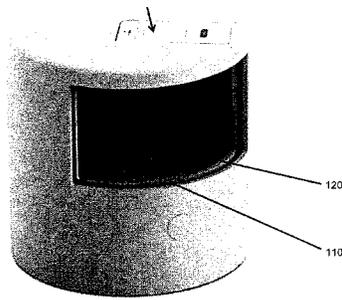


FIG. 11D



FIG. 25

Miriam achieves its goals through a simple yet elegant construction, requiring only a camera, computer, and testing substrate in a standard well plate. Each well contains a reactant keyed to a specific microRNA.⁹⁴ A patient's sample is added to each well and tested for the presence of microRNA. When the particular microRNA in the well is present in the patient's sample, the reaction produces a luminescent effect. Miriam's camera monitors these reactions by recording the change in luminosity of the wells during testing, sending these images via Miriam's computer to Miroculus's cloud computer. Miroculus then analyzes the pattern to determine which microRNAs are present and whether the patient has cancer.

Miriam's advantageous three-piece construction provides low-cost implementation while remaining clinically effective. Driven by Miroculus's objective to democratize cancer-screening technology, a Miriam testing platform can be created using cheap and readily available technologies found throughout the developing world. During Miriam's first debut, one of the founders showed the technology being deployed via a 3D-printed test chamber and a smartphone. Both 3D printing and smartphones are viewed as platforms for bringing developed-world medical technologies to the developing world.⁹⁵ Combining innovative biological science and versatile technology such as 3D printing and smartphones allows Miriam to substitute for complex specialized equipment requiring far more training and resources to implement.

Miroculus is employing a blend of IP protections in the distribution of Miriam. It's combining an open source release of how to construct the Miriam platform, including copyrighted design plans for making the 3D printed device, with patent protection over its microRNA-based testing method. Choosing to use this dual IP protection allows Miroculus to ensure a quality product in real world use with sufficient income to both run the company and develop the next generation of technologies.

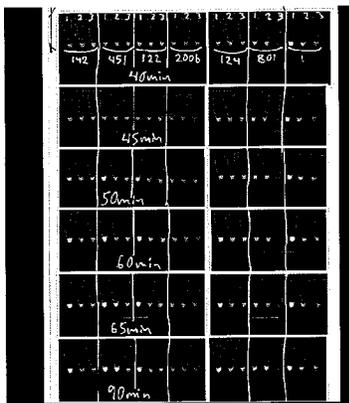


FIG. 3

To test the deployment and efficacy of Miriam, Miroculus has elected to employ open source distribution of Miriam. Instructions for building a fully functional Miriam are currently available on GitHub, including 3D printing instructions and software, firmware, and hardware instructions for a testing computer implemented on Arduino.⁹⁶ These documents and code are published under open-source licenses. This owner-driven free exercise of rights provides Miroculus with two major advantages. First, Miroculus can enjoy open collaboration and improvement on Miriam's design and software.⁹⁷ Second, making Miriam open source can encourage the adoption of the technology leading to additional economies of scale and providing Miroculus reputational benefits in the marketplace.

Miroculus is also utilizing patent protection for aspects of Miriam that require technical sophistication beyond having access to a 3D printer.⁹⁸ It is globally seeking patents for testing wells and the detection system. By patenting the disposable wells, Miroculus can secure a return on its research and investment into Miriam. Because Miroculus views supplying the testing wells as the best income strategy for the technology, with revenue from supplying platforms being only incidental, Miroculus will be able to leverage the low-cost adoption of Miriam afforded by delivering an open-source platform.

Miriam is a story of modern technology being used to bridge the gap between the developed and developing world. Miroculus has a goal of enabling cheap, routine screenings for a wide range of cancers to lower the costs, both economic and human, of the disease. By making its testing device easily available, Miroculus aims to reach its goal of accessibility. And by securing patent protection for its testing wells, Miroculus will be able to ensure a return on its technology. This will allow further development and democratization of the necessary technology for combating the world's most pressing diseases.

Nanobiosym's Gene-RADAR Brings Real-Time Results for Zika Testing

By Gabrielle Eriquez



Because there is currently no preventative vaccine for Zika, a mosquito-borne virus known to cause severe birth defects in pregnant women, the ability to obtain a fast and accurate diagnosis is critical.⁹⁹ However, especially in the developing world where Zika's presence is greatest, there are significant issues with current diagnostic tests: they are in extremely high demand, especially during the summer months, and, accordingly, are very costly.¹⁰⁰

Enter Nanobiosym's Gene-RADAR: a tablet-sized device which can detect Zika RNA from human serum.¹⁰¹ Though it's currently only authorized for Zika testing pursuant to an FDA Emergency Use Authorization, this device has the potential to facilitate the availability of faster, cheaper Zika testing worldwide.¹⁰²

Due to the scale of the disease, getting tested for Zika is not as simple as a quick trip to a local clinic. Testing criteria prioritize pregnant women who have possibly been exposed to the virus.¹⁰³ These criteria result in many others who are not pregnant, but still may have been exposed, being turned away from getting tested.

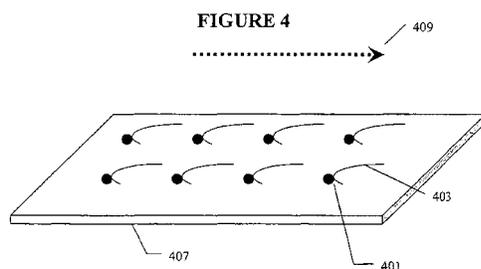
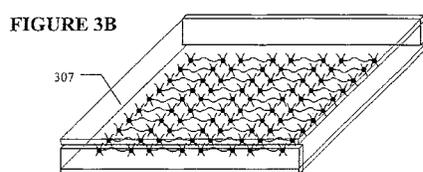
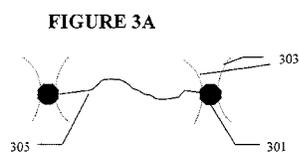
The problem is even greater in developing countries in Latin America.¹⁰⁴ Poor areas lacking adequate sanitation and air conditioning are favorable breeding grounds for mosquitoes. The only advice that many of these countries give to women to combat Zika is to avoid pregnancy; however, these countries have the world's highest proportion of unintended pregnancies.¹⁰⁵

The difficulties in preventing and combating Zika that impoverished people in Brazil face have been well documented.¹⁰⁶ For those living in more affluent areas, Zika testing is available even for patients who are not pregnant. But at free public clinics in poorer neighborhoods (where it's easier to contract Zika), lines are out the door. Symptomatic patients spend hours waiting, only to receive saline for dehydration and to still have to return if their symptoms persist.

The lack of available testing for many patients in developing countries is influenced by cost. Tests typically cost hundreds of dollars.¹⁰⁷ For those who can't even afford window screens or insect repellent, affording a Zika test at this price is next to impossible.¹⁰⁸

Timing is the other likely factor contributing to this issue. Dr. Anita Goel, CEO and founder of Nanobiosym, noted that even in Florida, testing was back-logged due to medical centers having to ship patients' samples to outside labs.¹⁰⁹ Results could take up to five weeks to come back.

Outside the United States, 4 billion people don't even have access to this basic, albeit inefficient, centralized testing mechanism.¹¹⁰ "[In developing countries], clinical testing is offered by the occasional network of unregistered laboratories operating without regulatory oversight. Services might be of too poor quality to be of any worth in medical decision-making."¹¹¹ Timing is obviously crucial for pregnant women, but it's also important for any other potentially infected person, since Zika can be transmitted sexually whether or not symptoms are present.¹¹²



Gene-RADAR has the potential to remedy these issues by decentralizing and mobilizing testing, thus lowering cost and wait times.¹¹³ Gene-RADAR employs nanobiophysics to diagnose, in real-time, diseases that contain DNA or RNA.

This foundational technology is not limited to Zika. The mobile device was an award nominee for Saving Lives at Birth's 2015 Grand Challenge for Development for utilizing the platform to detect early HIV in infants in Rwanda.¹¹⁴ It was also presented in the same year as a diagnostic solution for other global pandemics such as Ebola.¹¹⁵

Centralized lab platforms can run from several hundred thousand to one million dollars.¹¹⁶ Though Gene-RADAR's cost is still being optimized, the goal is to make it affordable even to the poorest areas of the globe. In terms of wait time, Gene-RADAR should be able to return results in about an hour, eliminating the back-log problem that comes with centralized testing mechanisms.¹¹⁷

Gene-RADAR is patented and does not require running water, constant electricity, or highly trained personnel to operate.¹¹⁸ The patented improvements over previous technologies both result in a smaller machine and improvements in the accuracy of testing.¹¹⁹

The device's footprint is much smaller than that of large, centralized testing machines.¹²⁰ Gene-RADAR is tablet-sized and only 3.5 pounds, versus 50-plus-pound platforms that are certainly not mobile and likely do rely on having constant electricity (which is not always available).

Gene-RADAR diagnosis is also more accurate than that of the other Zika tests currently available.¹²¹ Current testing methods that look for Zika-specific antibodies have a high proportion of false positives. Other tests, like Gene-RADAR, look for DNA or RNA. But these other tests also result in false positives by confusing a sequence with that of another Zika-like virus, such as Dengue. The advances in Gene-RADAR improve accuracy to solve these problems by detecting a virus's precise RNA sequence.

From a public health perspective, testing as many people as possible in at-risk areas will help contain the virus. If people know quickly whether they're infected, there's less of a chance of infecting others. Through multiple global initiatives, Nanobiosym's next step is to increase production and distribution where the need is greatest.

According to Dr. Goel, patent protection via the Nanobiosym incubator has allowed this revolutionary technology to expand beyond the research labs. "Our incubator focuses on bringing together a holistic approach using physics, medicine, nanotechnology, and information technology to create new science or technology, then incubate it all into different products and spin-off companies that can transform how we solve some of the world's greatest challenges."¹²²

The innovative technology that is Gene-RADAR is a prime example of innovation working to promote groundbreaking solutions to real-world challenges. For Zika (and other diseases with genetic footprints), this means the potential for cheaper, faster, and more readily available testing that would undoubtedly benefit global health.

Meeting the Needs of Rural Africa with Fyodor's Point-of-Care Testing for Malaria

By Jaci Arthur



Every year, more than 200 million cases of malaria are reported worldwide. It can often be mistaken for a less serious malady, as symptoms include “fever, chills, and flu-like illness.”¹²³ If quickly identified, the disease is treatable. Yet more than 445,000 people, mostly children in sub-Saharan Africa, died from malaria in 2016.¹²⁴

Expeditious diagnosis of the disease can result in faster treatment and lower mortality rates. The patented Urine Malaria Test (UMT) developed by Dr. David Sullivan, a Johns Hopkins Bloomberg School of Public Health professor and microbiologist, addresses this global challenge by offering a rapid, accurate, more convenient, and less expensive alternative to traditional laboratory testing.¹²⁵ The UMT is also the first point-of-care (POC) test for malaria that does not require the use of trained personnel or a blood sample.

Ninety percent of all malaria-related deaths in 2015 occurred on the African continent.¹²⁶ Much of this can be attributed to a lack of access to health services and personnel due to poverty, remoteness, and a general lack of healthcare infrastructure.¹²⁷ According to a 2011 report, about 31 percent of Ethiopians live on less than \$1.25 a day.¹²⁸ Even when health services are free of charge, trips to medical facilities are quite costly for the average, rural African because patients will often have to take an entire day off from work to travel.

In Niger, a patient may have to walk more than four hours to receive medical treatment at an overcrowded, ill-equipped facility.¹²⁹ Many people turn to presumptive diagnosis or self-medication at the first sign of a fever, resulting in widespread drug resistance and more expensive treatments.¹³⁰ Meanwhile, others gamble on the chance it's simply a virus that will pass, never seeking diagnosis or treatment.

On average, there are 1.15 health workers for every 1,000 people in sub-Saharan Africa, with numbers as low as 0.4 physicians for every 10,000 people in countries like Chad.¹³¹ The few laboratories in rural areas that can identify diseases such as malaria are underfunded, short-staffed, and ill-equipped.¹³² Although there are several POC tests for malaria, most of them require trained personnel taking a blood sample.¹³³ Having a

proper diagnosis within 24 hours of the onset of symptoms can reduce the mortality rate, but such diagnosis is difficult for most Africans. All these factors lead to a deadly combination, especially for those in rural Africa.¹³⁴

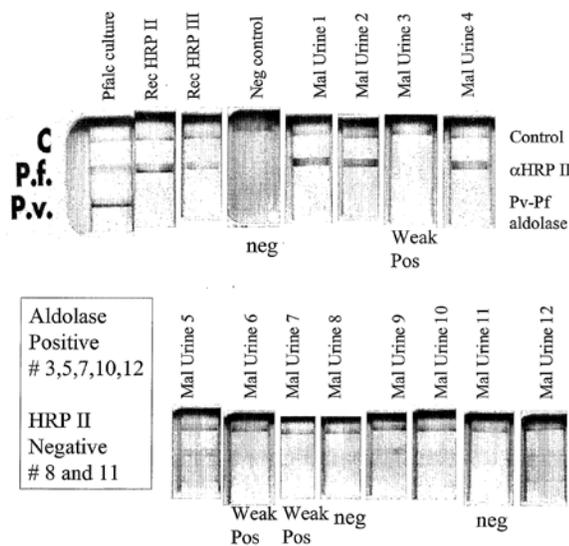
Maryland-based Fyodor Biotechnologies was founded in 2008 by Nigerian biotechnologist Eddy Agbo specifically to address these problems.¹³⁵ In 2009, the company was granted an exclusive worldwide license from Johns Hopkins University to research, develop, and commercialize the UMT.¹³⁶

As its name suggests, the UMT tests a patient’s urine, rather than blood, for “novel Plasmodium proteins,” and it provides results in less than 25 minutes, thus abating fears, eliminating the need for presumptive diagnosis, and reducing costly, lengthy, and unnecessary trips.¹³⁷ Unlike other tests for malaria, the UMT can be taken at home and is as easy to use as an at-home pregnancy test. The UMT is currently priced at about 2 each; however, Dr. Agbo intends to reduce the price once production increases.¹³⁸

Preclinical studies were conducted by researchers at Johns Hopkins University, and the UMT is currently in clinical validation.¹³⁹ Fyodor intends to seek concurrent regulatory clearance from both the Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) and the U.S. Food and Drug Administration (FDA).

Initial commercialization efforts will be focused in Dr. Agbo’s home country of Nigeria before expanding to other areas significantly affected by malaria. Nigeria accounts “for 25 percent of all malaria cases in the African region.”¹⁴⁰ Testing is also currently underway at Fyodor Biotechnologies for a “second generation broad-based Urine Malaria Test (UMT-Broad),” which will be useful for detecting other types of infections.¹⁴¹

Figure 1



Fyodor Biotechnologies stepped onto the global market specifically to meet the needs of people in malaria-endemic regions and to reduce the mortality rate associated with this treatable disease. The company relies heavily on its exclusive license to Johns Hopkins University’s patent, as research, development, and production of the UMT are currently its sole function.

Fyodor’s \$2, at-home test is the perfect counter to claims that intellectual property rights, specifically patents, result in expensive healthcare and a lack of access to necessary medical services. In fact, intellectual property rights have made quick, efficient, low-cost, and convenient testing for malaria a reality.

The UMT provides an ideal example of how patented innovation can conquer global challenges. It’s a reasonable, rapid, efficient, convenient, economic alternative to a system that cannot meet the needs of the rural poor. And it’s a reminder that innovation and intellectual property rights can, and often do, work together for the common good.

Chapter 4: Challenge: Improving HIV Diagnosis and Care

Point-of-Care Technology for HIV Diagnosis in Developing Countries

By Nigel Cory



Healthcare providers face daunting challenges in diagnosing HIV in remote, resource-poor areas in developing countries. First, the gold-standard process for testing people's blood requires expensive lab equipment and well-trained technicians, which means the equipment is often centralized in major cities. Additionally, after individuals have tested positive for the virus, they should be retested every six months during treatment, which creates further challenges. The lack of alternative diagnostic options has become a major roadblock to getting more people with HIV on the path to treatment and recovery. But an innovative new product may finally do this.

This product—Visitect CD4—will make HIV diagnosis quicker, cheaper, and more accessible. And intellectual property, which can play a key role in improving healthcare outcomes in developing countries, has been one key part of the long, complex, and difficult process involved in developing it.¹⁴²

Testing for the number of CD4 T-cells—which are a critical part of the body's immune system is a vital step for the management and care of people with HIV. It's required to prioritize people for treatment and encourage rapid linkage to care and treatment, especially antiretroviral treatment (ART).¹⁴³ Early detection is critical as HIV can destroy so many of the body's CD4 T-cells that it can't fight off infections and disease, such as malaria, bacterial infections, toxoplasmosis and pneumocystis pneumonia. Furthermore, testing is not a one off. The World Health Organization recommends patients be tested at least every six months thereafter to monitor their health during ART.

The problem is that the current way to make this diagnosis—flow cytometry—requires expensive laboratory-based equipment, well-trained laboratory technicians, power, clean water, regular maintenance, and cold chain storage for reagents, which results in centralized testing locations. Most laboratories and clinics in countries most affected by HIV and AIDS are unable to monitor T-cells, particularly in remote and rural settings.

The Visitect CD4 is a point-of-care test that uses a format similar to a pregnancy test in which a sample line of blood is checked against a test line to give a visual treat or no-treat result.¹⁴⁴ Visitect CD4 uses a small amount of blood from a finger-prick with results available after 40 minutes at a cost of approximately \$5, half the cost of a regular CD4 test. Furthermore, it shortens the diagnosis and treatment timeframe: a standard process would involve a visit to a clinic, a referral for CD4 testing, a visit to a laboratory for blood to be drawn, and an additional clinic visit to receive a CD4 test result and counselling.

This product could increase the number of people on ART and reduce the number of people whose health is negatively affected due to delays associated with centralized laboratory-based testing and in receiving follow-up treatment. Indicative of the potential positive impact, a U.S. Centers for Disease Control and Prevention (CDC) and Kenya Medical Research Institute study showed that carrying out a point-of-care CD4 count immediately after a person was diagnosed with HIV by home-based testing doubled the rate of linkage to HIV care.¹⁴⁵ It also showed that, even where HIV treatment performs best in Africa, around one in five people entered HIV care in 2014 or 2015 when their CD4 cell counts had already fallen below a critically low threshold (100 cells/mm³).¹⁴⁶

Intellectual property has played an important role in bringing Visitect CD4 to the market. Visitect was initially developed by the Burnet Institute in Melbourne, Australia, a not-for-profit research institution which focuses on accelerating the translation of research, including through licensing, into health solutions, especially for vulnerable communities. The Burnet Institute has already developed a number of rapid point-of-care diagnostic tests for use in developing countries, including for hepatitis E, hepatitis A, and Active Syphilis tests.¹⁴⁷ However, developing the technology involved risks, costs, and time investment.

It took the Burnet Institute six years to develop Visitect CD4. In 2012, the Burnet Institute entered into a licensing agreement with Omega Diagnostics to commercialize CD4 for use worldwide. A licensing agreement is a key way for research institutions, such as the Burnet Institute, to translate its work into real-world impact as it can leverage a private company's manufacturing and distribution networks and resources and expertise on product development. Omega Diagnostics Group is one of the United Kingdom's leading companies in the fast-growing area of immunoassay and has a global presence in over 100 countries worldwide.¹⁴⁸ Working to ensure the organization's intellectual property is widely protected, in 2013 the Burnet Institute applied for and received a U.S. patent, which builds on earlier patents granted in South Africa and from members of the African Intellectual Property Organization.¹⁴⁹

However, indicative of the risks involved in bringing new discoveries to market, subsequent testing showed discrepancies (due to temperature changes) between laboratory and field tests. Omega had to put the device through additional testing at hospitals in the United Kingdom (where it's based), which ultimately resulted in it having to redesign the product and to simplify the manufacturing process.¹⁵⁰ This extended the cost and timetable to reach commercialization. To further test the performance of the Visitect CD4, the Burnet Institute is leading a field study using the product among 175 HIV-infected pregnant women attending four antenatal care clinics in Kenya and South Africa.¹⁵¹ The risks and costs highlight the crucial role that intellectual property plays in incentivizing and protecting inventions and in facilitating product development, manufacturing, and distribution.

Furthermore, Visitect CD4 shows how intellectual property and public-private partnerships can work together to ensure the development and deployment of healthcare innovations for developing-country markets. In 2014, UNITAID (a global non-profit financed by an airline ticket tax in ten countries, along with other donations, including by the Bill and Melinda Gates Foundation) gave the Burnet Institute a grant that it, in part, passed onto Omega to allow it to build up an inventory of products and for it to establish a second manufacturing facility in India.¹⁵² In early 2017, Omega manufactured a pilot batch of 10,000 units, tested these at three British hospitals, and finalized the design for large-scale manufacturing at its plants in India and the United

Kingdom.¹⁵³ Locating the plant in India will also greatly improve access to life-saving anti-HIV drugs for potentially hundreds of thousands of HIV-positive citizens in India.

While Visitect CD4 has the potential to exert a significant impact on helping people with HIV in developing countries, it only addresses one specific issue, which may otherwise be undermined or negated by broader weaknesses in a country's healthcare system. A recent large study in South Africa showed that linkage to care after testing HIV positive is the biggest weakness in its treatment program in trying to achieve UNAID's 90–90–90 goal (to achieve 90 percent of people with HIV diagnosed, 90 percent of people diagnosed on treatment, and 90 percent of people on treatment with undetectable viral loads).¹⁵⁴ Visitect CD4 may make diagnosis quicker, easier, cheaper, and more accessible; however, its potential to improve an individual person's health will ultimately depend on the developing country's overall healthcare system. The potential benefits of Visitect CD4 will be largely determined by the developing country's ability to connect the person to treatment, and the health system's ability or inability to provide supplies, personnel, training, and funding.

Visitect CD4's history highlights the long, complex, uncertain, and potentially expensive path from invention, licensing, and delivery, to use. It's also an example of the intersection of how a public health issue is both a problem and a market, and how intellectual property can work as part of public-private partnerships that together seek to bring innovations to markets in countries around the world. However, the risks of failure during product development, manufacturing, and distribution demonstrates the essential role that intellectual property plays in incentivizing and protecting innovation. Weakening intellectual property protections will only slow down the potential for further progress. Without the ability to earn returns on investment, there isn't an incentive to invest in further research, or in the case of Omega, for it to negotiate future licensing agreements and to invest in further product development. Intellectual property is a key part, though just one of many, in what is a complex and difficult process of improving healthcare outcomes.

Daktari Diagnostics, Taking on Africa’s Healthcare Challenges One Diagnostic Device at a Time

By Alex Summerton and Nick Churchill



Africa’s predominantly rural characteristics and limited medical infrastructure are among the region’s greatest challenges to implementing effective healthcare programs and policies for its residents. The high costs for patients associated with diagnosis and treatment in terms of money, time, and travel, along with cultural barriers, often result in individuals failing to seek treatment or only making initial consultations before abandoning the matter. Coupled with poor infrastructure, inadequate facilities, substandard equipment, and insufficient personnel, it’s not difficult to see why Africa is still recognized as the setting for the world’s most difficult health crises by the World Health Organization.¹⁵⁵

One solution to these problems is to effectively move clinics to the patients through point-of-care technologies. Daktari Diagnostics, Inc., located in Cambridge, Massachusetts, is an innovator in this field focusing on microfluidic techniques. These techniques allow the company to develop products that do not require large-scale manipulation of high volumes of blood or other biological products. Thus, diagnostic technologies can be made smaller and used anywhere they are needed. Its slogan “Anywhere. Care.” underscores its commitment to developing a cheap, lightweight, portable diagnostic device to detect HIV, Hepatitis C Virus (HCV), and sickle cell disease.

Efforts toward eradicating disease are two-part, regardless of where the disease occurs: diagnosis and treatment. No matter how much time, effort, money, and technology are spent on improving the treatment phase, failures to accurately and affordably diagnose can undermine even the greatest plans. For a rural populace, diagnosis can be frustrated by a number of factors.¹⁵⁶ Many rural clinics do not have the facilities and equipment to conduct diagnostic tests. Reaching a medical clinic with laboratory services may require hours of travel by foot, and many patients fail to return for their results.

Africa is particularly susceptible to these problems. There exists a need for low-cost, portable, and durable systems that can be used to facilitate immediate and accurate diagnosis of diseases that commonly affect the

population.¹⁵⁷ Lightweight point-of-care diagnostic platforms aim to meet the World Health Organization's "ASSURED" criteria, a set of aspirational guidelines for creating diagnostic tools to meet the socioeconomic challenges of developing regions such as Africa.¹⁵⁸

However, developing point-of-care technology is costly, and attracting investors requires a reasonable expectation of return on their investments. The developing world is not often considered a lucrative market for the development of medical products. Developing technology that can meet the need of an effective point-of-care testing system and securing funding for the endeavor is a significant challenge.



Daktari (Swahili for "Doctor") Diagnostics, Inc. is working on the development of a point-of-care testing platform that meets the ASSURED standards. Daktari's portable point-of-care platform, Daktari Virology, uses microfluidic techniques to test for both HIV and HCV.¹⁵⁹ Microfluidic devices offer a number of advantages that directly address Africa's challenges, including small sample sizes, low production costs, fast sampling and processing, and low power consumption.¹⁶⁰ Using a single drop of blood, a microfluidic testing chip prepares the raw sample and performs the tests in one compact system.

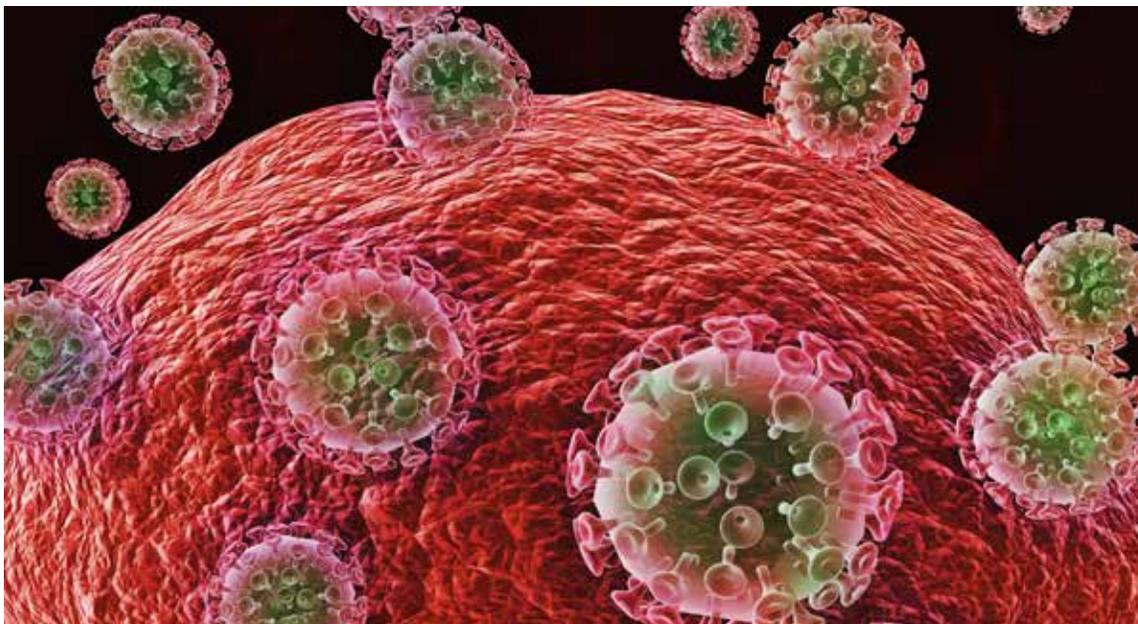
For HIV testing, the technology uses a novel microfluidic technique to capture a key cellular indicator for the management of antiretroviral therapy in a patient's blood.¹⁶¹ The device then uses non-optical detection to count them. The result is rapid testing that can give an accurate assessment of a patient's HIV viral load in approximately half an hour.

To secure rights for its microfluidics technology, Daktari has been diligently working to assemble a patent portfolio around its innovations. Its Website lists over 20 patents already granted internationally and even more applications pending.¹⁶² Leveraging these rights has helped Daktari overcome the challenges associated with conducting expensive R&D for the developing world by securing several rounds of funding.¹⁶³ Daktari is using this capital to develop its microfluidics assaying technology for other diseases. In January, Daktari met a funding milestone in a partnership with Merck by completing the design of a prototype HCV point-of-care system suitable for commercial production.¹⁶⁴ Recently, Daktari licensed its technology for integration into a connectivity platform that enables healthcare providers to assist global health officials by monitoring and reporting disease data in real time.¹⁶⁵

Point-of-care testing is a realistic approach to overcoming challenges in improving diagnostic and monitoring technologies in developing countries, where space, money, time and training are often limited. Utilizing its intellectual property rights, Daktari continues to develop the technologies that can address some of the world's most pressing health needs and connect its innovations with the communities that need them.

DNAe Enhances HIV Treatment By Monitoring the Effectiveness of Antiretroviral Therapy

By Alex Summerton



HIV/AIDS is a complex disease presenting a range of challenges for all stages of a patient's progression. Effective detection, diagnosis, management, and monitoring are all crucial, and problems anywhere in the treatment chain can make later stages more difficult or undo the careful work of earlier stages. Significant technological improvements in healthcare have increased the effectiveness of HIV/AIDS treatment in the developed world. However, many of these advances are inaccessible to developing-world countries for reasons of cost, size, complexity, or infrastructure requirements.

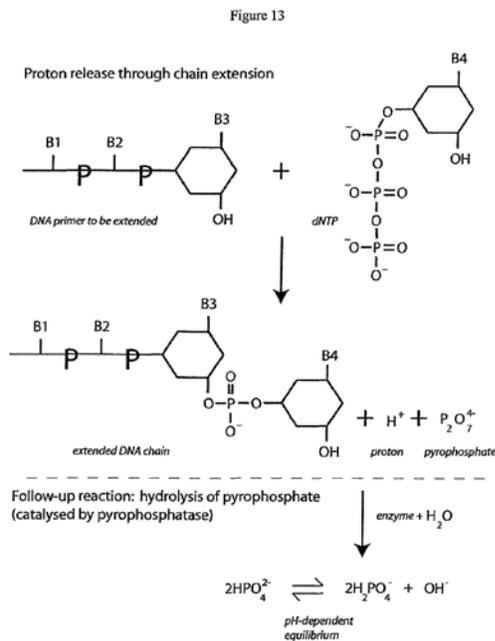
Developments in the use of Ion Sensitive Field Effect Transistors (ISFETs) by DNA Electronics (DNAe) has resulted in a new method for monitoring the effectiveness of antiretroviral therapy (ART). Where traditional ART effectiveness-monitoring techniques often require bulky, specialized equipment with a large laboratory footprint and long turnaround times, new ISFET-based testing is quicker and far more discrete as the entire testing platform has been reduced to a USB stick and requires only half an hour to perform a test.

ART comprises the administering of a combination of antiretroviral drugs inhibiting HIV's ability to infect and reproduce in healthy cells.¹⁶⁶ HIV, like any pathogen, can develop resistance to the drugs used to treat it. Monitoring is crucial to ensuring ART is effective, and when treatment isn't it becomes necessary to switch the drugs used. Several indicators can give a window into the efficacy of treatment, either by directly or indirectly monitoring the presence of HIV. The recommended method of monitoring for HIV treatment failure is testing the concentration of viral bodies in the blood stream, or the "viral load."¹⁶⁷ The World Health Organization recommends testing every six to twelve months to balance the cost of testing with the need to ensure the effectiveness of ART.¹⁶⁸

However, with accuracy comes costs. Testing equipment is roughly the size of a photocopier, requires support infrastructure, and takes up considerable laboratory space, limiting its deployment and making testing costly. Testing also requires preparatory work and trained support staff, further limiting where testing is carried out.

For developing countries with HIV/AIDS crises, these attributes often limit monitoring technology to large urban areas.¹⁶⁹ This imposes additional costs on persons living with HIV in rural areas who often must pay for a trip to test the efficacy of their ART and a return trip days later to receive the results.

Professor Christofer Toumazou of Imperial College London and DNAe have created a method for viral load testing using ISFETs to detect subtle changes in blood caused by the presence of HIV.¹⁷⁰ Using ISFET technology overcomes challenges of cost, time, and complexity. DNAe has also used ISFETs to overcome size and centralization issues by implementing its innovative testing technology on a USB stick. A USB-based ISFET testing platform boasts several advantages over traditional equipment that decrease the cost and burden imposed by testing. Dramatically smaller size means increased portability and reduced power demand, untethering testing from the lab and allowing it to travel to patients. ISFET testing technology also operates far more quickly than current testing methods. Current tests take days to perform.¹⁷¹ DNAe's USB test returns an accurate result in 20 minutes, allowing patients to receive results in a single visit.¹⁷² Furthermore, USB implementation reduces the complexity of testing and consequently the need for extensive training to perform tests.



Genealysis, DNAe's underlying ISFET technology, operates by detecting changes in pH caused by the reaction of HIV genes on a specialized microchip.¹⁷³ The change in pH is sufficient to change the electrical state of the chip and turn it on. Thus, Genealysis uses these pH changes to identify the presence or absence of HIV in the blood by measuring pH changes related to HIV RNA and monitoring if the ART is working.

Professor Toumazou formed DNAe to commercialize his innovations in DNA analysis with a mission "to bring dramatic, life-changing improvements to healthcare and beyond with fast, simple and scientifically sound products."¹⁷⁴ The patented ISFET technology serves as the backbone of DNAe's business operations, allowing it to secure the necessary funding for further research and development.¹⁷⁵ Genealysis is currently being adapted for a sepsis diagnosis platform with the same improvements in testing time, accuracy, and cost that ISFETs have shown

for HIV testing. DNAe's intellectual property rights have allowed it to secure over \$70 million in investment from the U.S. Department of Health and Human Services for research and development to expand its diagnostic technology to other innovative, life-saving applications, including rapid detection of biothreat agents, antimicrobial resistant infections, and influenza.¹⁷⁶ DNAe has also used its patents to increase the speed of innovation and adoption of this important technology by granting non-exclusive licenses to certain life-science companies.¹⁷⁷

HIV is a disease for which treatment lasts a lifetime. Technological improvements at all stages of a patient's progression, detection, diagnosis, treatment, and monitoring help lessen the burden HIV imposes. ISFET technology is a promising avenue to reduce the burden ART monitoring imposes on persons living with HIV in the developing world, and DNAe is poised to adapt its patented innovations for other life-saving applications.

Chapter 5: Challenge: Affordable Interventions to Meet Basic Needs in Challenging Environments

Nutriset Uses Patents and Trademarks to Fight Severe Malnutrition Across the Globe

By Nick Churchill



Malnutrition is one of the greatest global health challenges, particularly with regard to children and pregnant women in developing countries. Undernutrition contributes to nearly half of all deaths among children under the age of five and has lifelong consequences for physical and cognitive wellbeing.¹⁷⁸

Nutriset has confronted the global malnutrition problem head-on by developing a range of innovative nutritional products and using its intellectual property to help developing countries reach nutritional autonomy.¹⁷⁹

Malnutrition is a blanket term that includes both undernutrition and micronutrient deficiency. An estimated 11 percent of the world's population, or 815 million people, are undernourished.¹⁸⁰ Undernourished people are particularly vulnerable to disease and death, and both undernutrition and deficiencies in micronutrients can prevent proper growth and development.¹⁸¹ Undernutrition causes children to underperform in school and makes adults less able to work, perpetuating a cycle of poverty. It can also be deadly. Children suffering from severe acute malnutrition, characterized by very low weight and visible muscle wasting, require urgent treatment to survive.¹⁸²

Severely undernourished patients have traditionally been treated with powdered foods which are dissolved in water before consumption. These powdered products carry risks of dosage errors and bacterial contamination, and they are likely to cause diarrhea in undernourished patients. They also tend to have short shelf lives, particularly in tropical climates.

Nutriset was founded in 1986 by Michel Lescanne with the mission of “focusing on research in the field of humanitarian nutrition, developing innovative solutions and acting as an interface between the worlds of

humanitarian aid, nutritionists and food-industry technologies.”¹⁸³ Since then, Nutriset has developed several therapeutic milks, pastes, and tablets. In 1996, Nutriset partnered with Dr. Andre Briend to create Plumpy’Nut[®], the first ready-to-use therapeutic food (or, RUTF) for the treatment of severe acute malnutrition.

This new product was field tested in Malawi by Dr. Mark Manary, who discovered that RUTFs were much more effective than traditional treatments.¹⁸⁴ Dr. Manary was able to clear his hospital’s malnutrition ward and use RUTFs to treat his patients at their homes, while increasing the recovery rate from 25 to 95 percent.¹⁸⁵ Given the product’s success, Dr. Manary recognized the long-term impact RUTFs could have if they were manufactured in the countries that needed them. Together, the doctors simplified the recipe so it could be produced locally.

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|---|--|-----------------------------|------------------------|
| (12) United States Patent | | (31) Patent No.: | US 6,346,284 B1 |
| Briend et al. | | (45) Date of Patent: | Feb. 12, 2002 |
| (54) FOOD OR NUTRITIONAL SUPPLEMENT, PREPARATION METHOD AND USES | | | |
| (75) Inventors: André Briend, Patric Michel Lescaume, Maloney, both of (FR) | | | |
| (73) Assignee: Nutriset (FR) | | | |
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| (74) Attorney, Agent, or Firm—Piper Marbury Rudick & Wolfe | | | |
| (57) ABSTRACT | | | |
| The invention concerns a complete food or nutritional supplement containing at most 10% of water by weight, preferably at most 5% of water, and more preferably at most 2% of water, with low osmolality, oxidation-stable, comprising a mixture of quality food products, said mixture being coated by at least a substance rich in lipids derived optionally from oleaginous seeds. | | | |
| 23 Claims, No Drawings | | | |

Plumpy’Nut[®] has a long, two-year shelf-life, is formulated to avoid diarrhea-type side effects, and can be eaten right out of the packet, eliminating the risks of dosage errors and contamination associated with mixing a powder with water.¹⁸⁶ Plumpy’Nut[®]’s long shelf-life, effectiveness, and ease-of-use have led to a rise in community-based treatment of acute malnutrition and have made it possible to treat children in areas that were not reached by traditional methods.

Nutriset has used its patent rights to further increase access to its technologies in developing countries through its PlumpyField[®] network.¹⁸⁷ Nutriset partners with local entrepreneurs in franchise-like relationships to create sustainable production systems in developing countries.¹⁸⁸ In addition to benefiting from Nutriset’s reputation and manufacturing experience, network partners are given access to Nutriset’s patents and trademarks.¹⁸⁹ The franchise-like system based on granting rights to use its intellectual property allows Nutriset to ensure that all products being locally produced by network members

embody the innovations that actually help those suffering from malnutrition. And by supporting the local manufacture of its innovative products, Nutriset enables its partners to provide jobs to local people, source raw materials from local farmers, and customize the products to address the specific nutritional needs of their communities, while decreasing dependency on foreign organizations.

The PlumpyField[®] network consists of 9 members based in Central America, Africa, Asia, Europe, and the United States. While the majority of the products are still manufactured in France and the United States, members in developing countries continue to increase their production capacity, bringing the network’s total capacity to 117,400 metric tons.¹⁹⁰ In 2016, the network’s products were used to treat nearly 8 million children.¹⁹¹ Thanks to Nutriset’s focus on incentivizing local capacity, that number will surely rise. According to the United Nation’s Food and Agriculture Organization, increasing local production is one of the best ways of ensuring long-term food security.¹⁹² Nutriset’s success in this endeavor would not be possible without its intellectual property rights.¹⁹³

The story of Plumpy’Nut[®] and PlumpyField[®] illustrates the power of intellectual property rights to improve and save lives. Not only do IP rights encourage the development of innovative products, they can be used to implement sustainable solutions to some of the world’s most pressing health challenges.

GRIT Leveraged Freedom Chair Brings Mobility to Developing World

By *Bhamati Viswanathan*



The World Health Organization estimates that over 65 million people in the developing world need an appropriate wheelchair.¹⁹⁴ Over 75 percent of people in the developing world live in rural areas, where standard wheelchairs do not work, as they are hard to mobilize over rugged terrain and rough local roads that may not be paved.¹⁹⁵ Further, most wheelchairs are difficult to maintain: they are comprised of many pieces that are easy to break and hard to repair, and they are expensive to replace.

The Leveraged Freedom Chair (LFC) is a wheelchair that solves this international humanitarian problem.¹⁹⁶ It enables people with disabilities in developing countries to gain mobility and independence, and it gives them the ability to navigate their environment in life-changing ways and at a viable cost. The LFC is built out of steel and bicycle parts that are commonly available in rural areas of developing countries. The parts and tools for maintenance and repair are inexpensive and commonly found. This makes it easier to repair the wheelchair at local bicycle shops or wherever spare parts may be found.



The construction of the LFC is engineered to meet the diverse challenges that arise in developing countries. The LFC uses a unique lever drivetrain which makes it both faster than conventional wheelchairs and sturdier when traveling over rough terrain.¹⁹⁷ It does not use gears and derailleurs, which can be expensive and easily broken; it instead uses levers connected to the drivetrain to control velocity and speed. By using readily available bicycle parts in the production of the LFC, costs are kept down and users can maintain and repair the chairs themselves.

The lever construction is one of the high points of inventiveness of the LFC. Instead of pushing on the wheels like a regular wheelchair, LFC riders push on two levers, which are designed to be biomechanically efficient.¹⁹⁸ LFC riders can shift gears by moving their hands up and down the levers. For smoother roads, riders push on a low part of the levers and shift into “high gear,” which enables them to travel 80 percent faster than a regular wheelchair on tarmac. For rougher terrain, riders push on a high part of the levers and shift into “low gear,” which enables them to ride over obstacles with 50 percent more torque than a regular wheelchair. The levers can be removed and stored on the wheelchair, which allows the LFC to be used like a regular wheelchair indoors.



The LFC was conceived and developed in 2007–2008 by four graduate students in the mechanical engineering program at MIT who then founded a company in 2012 called Global Research Innovation and Technology, or GRIT, to develop and commercialize their invention.¹⁹⁹ The LFC has been in development since 2008. First-generation prototypes of the LFC were constructed in Kenya and Vietnam with community partners who were also local wheelchair producers. In 2014, GRIT secured Patent No. 8,844,959 for the LFC, a “wheelchair with level drivetrain.”²⁰⁰

The company now manufactures the LFC in India with a local partner and sells it in bulk for \$250 per chair to non-governmental organizations (NGOs) and other development organizations.²⁰¹ The aid agencies and NGOs that purchase the chair generally distribute the LFC to users free of charge. In 2015, the GRIT management team estimated that it had shipped almost 1,200 LFCs to 17 countries, including Guatemala, Haiti, Kenya, Uganda, Tanzania, India, the Philippines, and Vietnam.²⁰²

The team at GRIT runs the company as a “social enterprise,” pursuing a social mission (like a nonprofit) but also retaining the ability to make money off their patented invention.²⁰³ As a for-profit social enterprise, GRIT can accept money from nonprofit foundations that are congruent with its mission, but it can also raise private equity like a regular startup.

GRIT has earned numerous awards and honors for the LFC, including winning a Patents for Humanity Award from the U.S. Patent and Trademark Office (USPTO) in 2015.²⁰⁴

After spending several years developing the LFC, GRIT decided to build upon its patented technology and develop wheelchairs similar to the LFC but more suited to use in first-world countries. The GRIT Freedom Chairs are somewhat sleeker in design, and have certain features that appeal to first-world riders, such as a lightweight frame, optional customization, and the ability to be folded and stored in the trunk of a car.²⁰⁵ The sale of these chairs is intended in part to defray the costs of distributing chairs at or below cost in developing-world countries.²⁰⁶ GRIT Freedom Chairs afford users access to previously inaccessible terrains, and offer versatility to a broad array of riders, including American veterans. They are directly marketed in the United States in order to keep costs down.

People with limited mobility in developing countries face many daunting obstacles, and the lack of appropriate wheelchairs can severely limit their mobility, opportunities, access, and independence. The GRIT Leveraged Freedom Chair is an elegantly simple, inexpensive, and ingenious device that confers freedom to wheelchair users in the developing world. Its underlying technology, secured by vital U.S. patents, is also the basis of the GRIT Freedom Chair, which likewise transforms the lives of users in the developed world. Both the LFC and the Freedom Chair rely on secure property rights that enable their parent company to develop and market life-changing products that users can afford to ride, repair, and maintain. The “all-terrain wheelchair” is truly an invention with worldwide relevance and reach.

Indian Startup Develops Nanomaterial Filter to Help Solve Global Drinking Water Crisis

By *Gleb Savich*



Access to clean water remains a critical issue on a global scale. According to the latest statistics from the World Health Organization, 844 million people lack a basic drinking water service and at least 2 billion people use contaminated water that can transmit cholera, dysentery, typhoid, polio, and other diseases.²⁰⁷ Contaminated drinking water causes more than 500,000 deaths each year. And in low- and middle-income countries, more than one-third of healthcare facilities lack even soap and water for handwashing.²⁰⁸

This drinking water crisis disproportionately affects the poor in the developing world. However, problems with access to safe drinking water may arise in any part of the world due to man-made or natural disasters—including in the United States. One recent example is the public health crisis that erupted in Flint, Michigan, where drinking water became contaminated with lead when the city switched to a different water source.²⁰⁹

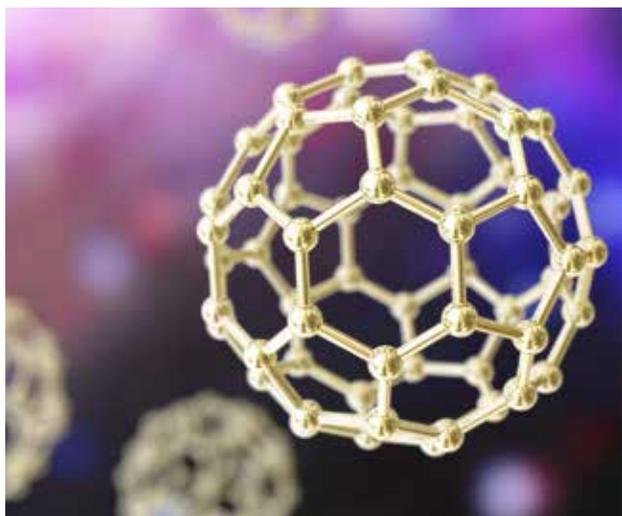
Natural disasters may disrupt the water supply in areas that normally have access to safe drinking water. As of October 2017, over a month after Hurricane Maria devastated the island of Puerto Rico, many of its residents still did not have access to clean water, precipitating an outbreak of leptospirosis, a rare bacterial disease.²¹⁰

Climate change, population growth, and urbanization pose further challenges to water supply systems. According to the World Health Organization, by 2025, half of the world’s population will be living in water-stressed

areas.²¹¹ These varied challenges to one of humanity's most fundamental problems require flexible and creative solutions.

Dr. Thalappil Pradeep is a professor in the Department of Chemistry at the Indian Institute of Technology (IIT) Madras.²¹² His decades of research focusing on nanomaterials has led to several discoveries that have already begun to help solve the global problem of access to clean drinking water.

The first breakthrough came in 2004 when Dr. Pradeep's team developed nanoparticles that can break down certain pesticides dissolved in water.²¹³ Many of these chemicals are not removable by standard water filters and have been shown to pose environmental and health risks. Although the use of some of these pesticides is banned, the compounds persist in the environment decades later. The problem is particularly relevant in India, one of the world's largest pesticide producers, where pesticide water contamination is a serious problem in certain areas.²¹⁴



The pesticide removal technology developed by Dr. Pradeep and his colleagues works by utilizing the ability of gold and silver nanoparticles to bind pesticides from flowing water through adsorption.²¹⁵ Dr. Pradeep and his coinventor obtained both Indian and U.S. patents on their technology and licensed it to Eureka Forbes, an Indian manufacturer of vacuum cleaners and water purifiers.²¹⁶

The technology is estimated to have reached 7.5 million people and is the first nanomaterials-based water filter to be commercialized.²¹⁷ To further develop nanomaterials-based water filtration technologies, Dr. Pradeep and his team founded a startup, InnoNano Research, in 2004.²¹⁸

Their next breakthrough came in 2012, when the team developed a novel nanomaterial capable of being adapted for the removal of multiple types of water contaminants. The new filter, dubbed AMRIT for Arsenic and Metal Removal by Indian Technology, can remove microbial contamination as well as arsenic, iron, and other heavy metals from drinking water.²¹⁹

The antimicrobial properties of silver ions were well known, but their large-scale implementation for water filtration had been hampered by technological obstacles, such as a lack of suitable substrates in which to embed the ions. The novel nanoparticle material developed by Dr. Pradeep and his team solves these issues.

Silver nanoparticles are embedded in this material to remove microbes, while the incorporation of other compounds allows for the removal of other contaminants. For example, the incorporation of iron achieves the removal of both iron and arsenic. Thus, this technology allows for manufacturing of multistage filtration systems suitable for particular needs.

Discussing this filtration system, Dr. Pradeep explains: "If this will be useful for water, it has to be very cheap, have a low carbon footprint, require no electricity, and should not contaminate water sources in the process."²²⁰ And his team's technology meets these challenges. According to Dr. Pradeep, manufacturing requires no heating or electricity and uses materials with a low carbon footprint.



Removal of arsenic from drinking water is of particular interest in India, where ground waters used for drinking and irrigation are often contaminated with dangerous levels of arsenic.²²¹ To begin addressing this problem, by the summer of 2016, AMRIT filters were installed in 750 locations in several Indian provinces, providing clean water to nearly half a million people.

In 2016, InnoNano Research succeeded in securing one of the largest investments for an Indian tech startup when it obtained \$18 million from Nanoholdings LLC, a U.S. venture capital firm specializing in investing into material science-based energy and water startups.²²² This investment is particularly significant in light of the difficulties that Indian startups often face when it comes to scaling up their technologies.

Dr. Pradeep explains: “We have no efficient mechanisms for partnering, scaling and incubating—those are the lacunae in our system.”²²³ While universities provide startups with access to labs and research grants, more funding is needed to achieve the scale necessary for further product development.

Leveraging intellectual property enables startups to raise funds necessary to bring their innovations to those who need them most. With the help of Nanoholdings LLC, Dr. Pradeep hopes to expand the company’s operations into Africa, Southeast Asia, and Latin America, and to continue developing the technology to filter out other dangerous contaminants found in drinking water.

Innovation Helps Solve Basic Sanitation Problems

By Michael O’Keefe



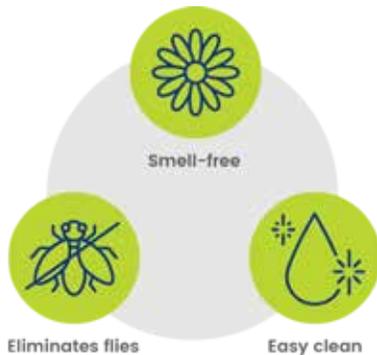
Poor sanitation poses an ongoing threat to the health and well-being of people in the developing world. Severe health problems, death, and disease can be directly linked to unsafe hygiene practices that continue to plague many countries. A United Nations fact sheet notes that 2.3 billion people lack access to improved sanitation.²²⁴ Open-air defecation in particular is a widespread concern, as it leads to the spread of communicable diseases. According to the World Health Organization, “Poor sanitation is linked to transmission of diseases such as cholera, diarrhea, dysentery, hepatitis A, typhoid and polio.”²²⁵

One way in which these diseases spread is through the lack of proper toilet or latrine facilities. The WHO claims that 2.4 billion people do not have access to such facilities, with 946 million instead practicing open-air defecation.



In 2012, with support from the Bill and Melinda Gates Foundation’s Water, Sanitation, and Hygiene Strategy and International Development Enterprises (iDE), American Standard Brands developed a potential solution to the hygiene problems stemming from the lack of proper toilet facilities.²²⁶ The SaTo pan—deriving its name from “Safe Toilet”—is an attempt to limit the transmission of disease by ensuring that the toilets being used are closed off from the open air, thus preventing insects or other vectors from communicating those diseases. The basic design is a plastic mold that fits into a concrete base over a pit, which means it can be used even when basic plumbing or sewer infrastructure is absent.

Access to proper sanitation and clean water is vital for the health and safety of growing populations in both urban and rural areas.²²⁷ When human feces are not disposed of effectively, it can cause a number of health problems. Chronic illnesses spread by feces such as enteropathy, encephalitis, and diarrhea can weaken adults as well as children and prevent them from retaining nutrients, potentially causing health problems for their offspring as well. Even when human waste is disposed of in a pit, rather than left out in the open, disease vectors such as flies can potentially still access it, turning latrines into persistent sources of disease for whole communities.



Invented by Jim McHale, Daigo Ishiyama, and Greg Gatarz, the SaTo pan operates much like a trap door, using a counterweight to stay closed except for allowing the passage of waste.²²⁸ The plastic design is cheap and acts as an effective seal over the toilet. In addition to the sanitary benefits, the SaTo pan also acts as a basic safety measure. Because of the nature of some open-pit latrines, young children face the risk of falling inside. When installing SaTo pans in Uganda, one organization reported this as a notable benefit to the communities due to the particular design of latrines in the areas they worked in.²²⁹

The research team at American Standard settled on the SaTo pan concept after observing the open-pit style latrines commonly used in Bangladesh. Before the pans were installed, such latrines remained open to the air at all times, which meant that not only was the smell free to travel, but flies and other insects could enter and exit the pit, carrying a host of diseases with them. The toilet covered by the pan can be ‘flushed’ after use with a pot of water, but otherwise blocks any unwanted traffic such as insects.

Crucially, the design of the pan allows for potential variations according to local customs and demands, such as using the facilities by squatting or sitting or adapting to the shape of the pit for the latrine. The core concept around which the pan is based is the counterweighted “flapper” itself. The counterweight is specifically set so

that the flap remains closed until the additional force of water—not just the waste itself—is poured into the pan. The pour-flush mechanic also creates a liquid seal, with a minimal amount of water remaining on top of the flap after use to help ensure prevention of transmission of insects or gases. This approach, utilizing a basic mechanism while leaving room for responsive adjustments in design, allows the SaTo pan to be adapted globally while maintaining a simple but effective means of providing basic health benefits.

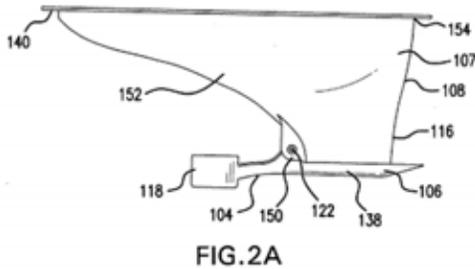


FIG. 2A

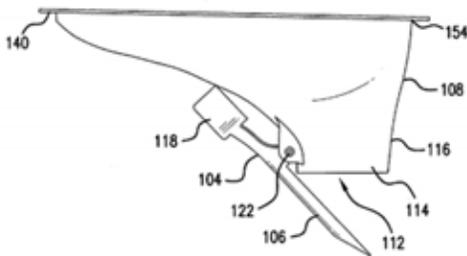


FIG. 2B

In 2015, American Standard received the Patents for Humanity award from the USPTO for its design of the (then-pending patent application) SaTo pan toilet.²³⁰ The counterweighted trapdoor is significantly more effective than standard squat-hole covers and avoids the risk of blockage that comes with more complex, alternative designs. Utilizing the patented design also allows American Standard to fully gauge the needs of the market, providing the basis for ongoing production and development.

Although American Standard is more generally known as a plumbing manufacturer, the SaTo pan has become a key part of its business structure. American Standard was purchased by the LIXIL Corporation in 2013, and brought within the LIXIL Water Technology (LWT) business unit in 2015. In 2016, LIXIL announced that it was establishing a special unit within LWT devoted to supporting continued development of the SaTo.²³¹ Currently, three new alternative models of

the SaTo pan are in development to meet the varying need of different regions. Although the initial design functions well in areas such as Bangladesh, bringing it to Sub-Saharan Africa presents new challenges, primarily that there's significantly less access to water. As the counterweight system relies on water for its operation, this poses a hurdle to its effectiveness in such regions.

American Standard has been able to use the SaTo pan design as the basis for a broad-ranging business strategy. From 2013 to 2014, American Standard implemented a donation program, Flush for Good, with each sale of one of its Champion toilets funding the donation of a SaTo pan.²³² 500,000 have been donated to Bangladesh alone. Other donation programs include sending SaTo pans to Nepal after the recent earthquakes and partnerships with NGOs such as UNICEF and Save the Children. By the middle of 2016, SaTo pans had been installed in 14 countries, including Uganda, Haiti, Malawi, Nigeria, and the Philippines.

Protecting Patients with VanishPoint Retractable Syringes

By David Lund



Needlesticks are not just the fear of four-year-olds receiving their vaccinations; they are also the source of blood-borne infections afflicting millions of healthcare practitioners. When a conventional needle is left exposed after use on a patient, it can accidentally stick another person, such as a healthcare worker. The accidental needlestick can infect that person if the patient had any blood-borne diseases. Recent estimates place the number of needlestick injuries in the United States at more than 300,000 per year, with infection by HIV or Hepatitis as possible consequences.²³³

The spring-retractable syringe, VanishPoint, was created to prevent needlestick injuries and ameliorate other unsafe injection practices.²³⁴

Worldwide, the problem from needle injuries is even greater.²³⁵ The risks from needlestick injuries can increase with other unsafe injection practices, such as needle reuse and improper medical waste collection. These practices are more likely to occur in developing countries. The consequences of these unsafe injection practices include 21 million hepatitis B infections per year and 41 percent of new cases of hepatitis C.²³⁶



The conventional syringe leaves the needle exposed after the injection is complete. Until a healthcare worker places the syringe in a specially designed plastic garbage container, it remains exposed and capable of harming anyone nearby. Unfortunately, over 1.8 billion conventional syringes are sold each year in the United States.²³⁷ These outdated syringes account for more than half of needlestick injuries.²³⁸

Thomas J. Shaw, founder of Retractable Technologies, created a technological solution to the problem after seeing a television report of a doctor who contracted HIV from an accidental needlestick. He designed a single use, spring-loaded syringe that immediately pulls the needle back inside the just-used syringe. Thus, the needle is automatically covered and incapable of harming anyone.

The basics of how the syringe works are simple enough to explain.²³⁹ The needle is engaged for use when the package is opened. A nurse or other practitioner fills the syringe normally. However, when the plunger is fully depressed to inject the patient, a spring pulls the needle back into the body of the syringe. Before the nurse has moved the syringe away from the patient, the needle is already covered and incapable of causing injury.

Despite the simple concept, designing a functional and usable product took ingenuity and persistence. Shaw purchased pigs feet from a local butcher to test his designs in his workshop.²⁴⁰ In the classic mode of biomedical innovators including Jonas Salk (inventor of the polio vaccine), he first tested his device on himself.²⁴¹



From these initial tests, Shaw founded Retractable Technologies, and the value of his innovation was immediately recognized. He received awards from the National Institute for Drug Abuse at the National Institutes of Health to further develop his work and eventually commercialize it.²⁴² Congressional representatives touted the important advances of this small business.²⁴³ The final product, the VanishPoint syringe, embodies his innovation.

The challenges faced by Shaw and Retractable Technologies in entering the medical device market have been extensively chronicled.²⁴⁴ The way hospitals purchase supplies such as syringes advantages large incumbent sellers and manufacturers over small startups such as Retractable Technologies.²⁴⁵ The story of Shaw's disruption of the automatic safety syringe market was even turned into a feature-length movie.²⁴⁶

Retractable Technologies confronted this challenge by relying on its patent portfolio. The patents covering the syringe included patents on the retractable needle design as well as tamperproof features that protect against intentional as well as accidental misuse.²⁴⁷ Large, established manufacturers could have easily copied Retractable Technologies' designs from the published patents. However, these patents assured that Retractable Technologies could protect its innovation against invasion.²⁴⁸

The value of the retractable syringe design has been important to advancing health care goals worldwide. The World Health Organization has recognized the value of the technology in Australia, China, Indonesia, and Gambia among other nations.²⁴⁹ According to the Global Alliance for Vaccines and Immunizations, African countries continued using auto-disable syringes after the completion of international aid programs because of the public health benefits.²⁵⁰ These benefits include not only the prevention of needlestick injuries, but preventing needle reuse, which had undermined other vaccine initiatives.

PATH, a non-profit organization devoted to health innovation, highlighted the introduction of VanishPoint syringes in Peru as an important step in advancing public health goals.²⁵¹ In addition to preventing injuries in the clinic, PATH noted that the syringes increased safety in waste disposal, where some waste handlers had described needlestick injuries as "common."

Prevention of needlestick injuries and infections has been a decades-long challenge for public health. From humble beginnings and the story of one infected doctor, Thomas Shaw's invention shows how one innovator can revolutionize health care. Patents have given him protection in the United States, but his innovation knows no borders.

Nike's Innovations Provide Comfort and Independence to People with Disabilities

By Nick Churchill



Many amputees, stroke victims, and people with movement disabilities rely on specialized clothing to support their daily lives. Participation in society, whether in the developing or developed world, requires being appropriately dressed. Not only can difficulty in dressing inhibit social and professional interactions, but it can also make it difficult to travel to a healthcare facility to receive treatment for a disability.

This problem is particularly acute with respect to shoes. Not everyone has the dexterity required to insert their foot into the small opening of a standard sneaker, let alone to tie traditional laces. Unlike a loose-fitting sweater or elastic waistband, which can be sufficient to make shirts and pants functional, a shoe must be well-fitted to support a person who has difficulty walking.

Nike addressed the problem of well-fitting shoes for disabled individuals by developing FlyEase technology, which incorporates a zipper that extends around the heel of the shoe. This allows the wearer to create a large opening in the back or side of the shoe, slide in his or her foot, and close and tighten the shoe, all with one hand. Following on its success, Nike is currently working on a design for completely hands-free athletic shoes that can accommodate people of all abilities.

The original impetus for a shoe design with improved accessibility was CEO Mark Parker's desire to help a Nike employee who had recently suffered a stroke.²⁵² Renewed attention was given to the project in 2012 when high school student Matthew Walzer wrote an open letter to Nike explaining the importance of accessible, supportive footwear.²⁵³ Walzer has cerebral palsy, and his doctors predicted that he would never walk on his own. But with the help of crutches and Nike basketball shoes, which provide sufficient ankle support, he can. Nevertheless, Walzer's independence was limited because he only had flexibility in one hand, which made it impossible for him to tie his own shoes.

The letter from Walzer explaining the challenges he faced made its way to Tobie Hatfield, the Senior Director of Athlete Innovation at Nike, who reached out to Walzer and began working on prototypes that could address

his needs.²⁵⁴ After testing several iterations, Hatfield developed the patented FlyEase system, which has given Walzer the independence he sought.²⁵⁵ Nike sells several styles of basketball and running shoes that incorporate the FlyEase technology.²⁵⁶

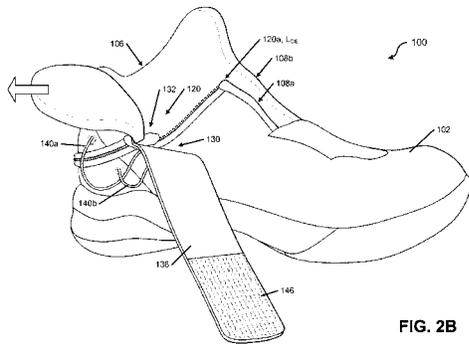


FIG. 2B

Nike went a step further to support innovation in shoes to help those with physical challenges by hosting the Nike Ease Challenge, an open innovation competition that sought a more hands-free design for performance footwear.²⁵⁷ The winner of the \$50,000 cash award was Brett Drake, a civil engineer from Cheyenne, Wyoming.²⁵⁸ Drake's design, which was inspired by snowboard boots, incorporates a hinged rear panel that pops open, allowing the wearer to slide in his or her foot before locking the panel back into place.²⁵⁹ The panel is secured by magnets strong enough to secure the shoe on the wearer's feet, but light enough not to significantly add to the weight of the shoe. Drake will continue to work with Nike as it refines and tests his concept.

Open innovation contests like the Nike Ease Challenge are enabled by strong, well-defined IP rights. Collaborating with other firms or individuals provides opportunities for new, innovative ideas, but it also involves inherent risks and uncertainties. A carefully planned IP strategy can mitigate these risks and thereby facilitate cooperation. Collaborators can delineate existing IP rights and establish guidelines for how to share the value of the anticipated innovations up front. It's often irrational for a company to invest such resources into a development project without IP protections, which can provide reasonable expectation of return on investment.²⁶⁰

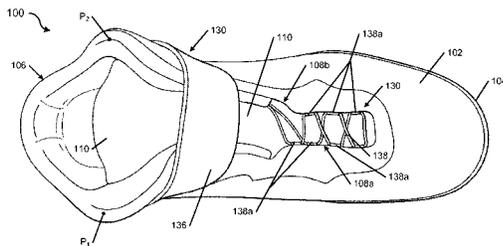


FIG. 1C

The Nike Ease Challenge Official Rules provide some insight into how Nike overcame the risks associated with an open innovation contest.²⁶¹ Participants granted Nike a limited license to all rights in their designs for the purposes of reviewing and testing them. Participants also granted Nike the right to use their likenesses for purposes related to the competition or a resulting product. The conditions allow the innovation contest to take place in an orderly manner, while preserving the ability of both parties to manage commercialization of any viable final product.

Nike rose to the challenge issued by Matthew Walzer, and it continues its efforts to develop an athletic shoe that is supportive and truly hands-free. Shoes featuring Nike's FlyEase technology are available in men's, women's, and kids' sizes and styles. Through an open innovation plan made possible by an intelligent IP strategy, Nike took another step toward a laudable goal: it crowdsourced an ingenious design that could help people of all ability levels achieve a new degree of independence and comfort.

Chapter 6: Challenge: Getting Healthcare to People in Places Where It's Hard for People to Come to Healthcare Providers

Global Good's "Arktek": A Life-Saving Super-Thermos Vaccine Cooler

By Bhamati Viswanathan



More than 1.5 million children die every year from diseases that existing vaccines could prevent. Why aren't these children vaccinated? One big reason is that vaccines need to be kept cool until they reach patients, but that's a really hard task in parts of the world where power is unreliable.

A new, patented "super thermos," the Arktek Passive Vaccine Storage Device, aims to solve this global challenge.²⁶² The Arktek was developed by Global Good, a collaboration between the Gates Foundation and the innovation lab of Intellectual Ventures.

The Arktek mends gaps in the "cold chain," the refrigerated vaccine supply chain. Breaks in the cold chain occur because power is unreliable or minimal in many places. Also, many people live in places that cannot be reached by refrigerated transport. These gaps make it impossible to keep the vaccines fresh, and thus render them unusable in less than a week's time.

In 2008, the Gates Foundation challenged Intellectual Ventures to help fix the cold chain problem. The resulting collaborative effort, spearheaded by Global Good, invented the Arktek Passive Vaccine Storage Device, nicknamed the "super-thermos" and the "keg of life" by Bill Gates.²⁶³

The Arktek keeps vaccines at a temperature between zero and eight degrees Celsius for 30 to 60 days, depending on outside temperatures and humidity. Testing shows that it retains its cooling capacity even when outdoor temperatures rise to 43 degrees Celsius (110 degrees Fahrenheit).²⁶⁴ It does not rely on outside sources of electricity or other power. This is a major step forward in vaccine cooling systems, especially in much of the developing world, in which stand-alone cold storage devices struggle to keep vaccines at proper temperatures for a maximum of five days.

The “super-thermos” bears some resemblance to an ordinary coffee thermos. In 2013, the leader of the vaccine cooler development team described it as “a super-insulated, double-walled [bottle] that holds the vaccine and ice in the middle in an inner bottle. A vacuum space separates it from the outer bottle, like a large coffee thermos.”²⁶⁵ The device combines a double-walled bottle filled with vacuum insulation with multi-layer insulation technology of the type used to protect spacecraft from extreme temperatures. It holds approximately 16 pounds of ice.

Incredibly, a vaccine kept in the Arktek for weeks will be as cold as the moment it was placed inside. No powered refrigeration or additional ice is needed.

Keeping vaccines cold isn't the only problem that the Arktek solves. Gaps in the cold chain tend to occur in places where travel is rugged and environments are challenging. Also, sophisticated medical facilities are rarely waiting at the end of a gap in the cold chain. Any solution has to be extremely tough and user-friendly.

The Arktek meets these challenges by providing near-indestructible structural integrity and high-usability in the field. To make the device sturdy, user-friendly, and easy to maintain and use, the development team at Global Good sacrificed a bit of longevity in favor of efficiency.²⁶⁶ The sixth and current prototype is therefore created for maximum efficiency, and can hold routine vaccinations for approximately 200 children or a village with a population of 6,000.

Other features help both local users and remote health officials to monitor the integrity of the vaccines.²⁶⁷ Sensors measure key information at 15 minute intervals, including the Arktek's interior temperature, its exterior temperature, and how long it has been opened. It alerts users when temperatures begin to rise too much, and it even has a LED light that comes on when a user opens the lid.

The data collected by the Arktek's sensors is extremely accessible to all concerned. On-site users can download data logs using a simple USB stick.²⁶⁸ Meanwhile, an antenna sends data via SMS to a local telephone number every day at midnight. It provides remote personnel a summary of the day's temperatures, location, and statistics recording when the device has been opened and for how long a period. Finally, a GPS sensor allows health officials to track the location of the devices at any given time.

During pilot testing, Global Good found the sensors to be particularly useful. For instance, if a health official was not using the device properly, Global Good was notified, and could contact the official directly and assist with training them appropriately. Cold Chain project director Kurt Armbruster observed that this kind of monitoring could eventually be relegated to local ministries of health to enable them to ensure that “they have a reliable cold chain all the way to the end point.”²⁶⁹

Armbruster sees the Arktek as best-suited to modest villages of 5,000 to 15,000 people, in which it will be cost-effective to have a device that can be refreshed once a month by health officials. He says it may be somewhat less-suited to larger villages of 25,000 to 50,000 people, in which a large solar-powered or ice-lined refrigerator is feasible. And it may not be necessary in locales that have a reliable and consistent source of power. The cost per unit for this device currently ranges from \$1,200 to \$2,400, which makes it relatively affordable to health officials in the developing world.²⁷⁰

Currently, the Arktek is in the early adoption stage of development. The WHO has “prequalified” the Arkteks under its Performance, Quality, and Safety (PQS) program, which is an important seal of approval for government procurement.²⁷¹ Global Good has collaborated with the Clinton Health Access Initiative, PATH, UNICEF, and other United Nations organizations to conduct field trials of the Arktek in Ghana, Senegal, Ethiopia, and Nigeria.²⁷²

While the Arktek is still being refined for further roll-outs, it has already seen some action where it could do the most good. For example, it has stored vaccines for tuberculosis, polio, influenza, whooping cough, tetanus, hepatitis B, and diphtheria. In 2014, Global Good donated 30 Arkteks to help the WHO deliver vaccines during the Ebola outbreak; and in the following year, it donated Arkteks to Nepal to assist with vaccinations after the 2015 earthquake.²⁷³

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|--|--|-----------|---------------|-------------|--------------------|-------------|----------------|-------------|------------------------|-------------|----------------|-------------|--------------------|
| <p>(12) United States Patent Hyde et al.</p> <hr/> <p>(54) TEMPERATURE-STABILIZED STORAGE CONTAINERS WITH DIRECTED ACCESS</p> <p>(75) Inventors: Roderick A. Hyde, Redmond, WA (US); Edward K. Y. Jung, Bellevue, WA (US); Nathan P. Myhrvold, Medina, WA (US); Clarence I. Tegreene, Bellevue, WA (US); William H. Gates, III, Redmond, WA (US); Charles Whitmer, North Bend, WA (US); Lowell L. Wood, Jr., Bellevue, WA (US)</p> <p>(73) Assignee: Takhtae LLC, Bellevue, WA (US)</p> | <p>(10) Patent No.: US 8,215,518 B2</p> <p>(45) Date of Patent: Jul. 10, 2012</p> <hr/> <p>(58) Field of Classification Search 220/592.26, 220/592.27, 705, 708, 710, DIG. 9; 215/388, 215/247, 249</p> <p>See application file for complete search history.</p> <p>(56) References Cited</p> <p style="text-align: center;">U.S. PATENT DOCUMENTS</p> <table border="0" style="width: 100%;"> <tr> <td style="width: 50%;">520,584 A</td> <td style="width: 50%;">5/1894 Turner</td> </tr> <tr> <td>2,717,937 A</td> <td>9/1955 Lehr et al.</td> </tr> <tr> <td>3,034,845 A</td> <td>5/1962 Haumann</td> </tr> <tr> <td>3,069,045 A</td> <td>12/1962 Haumann et al.</td> </tr> <tr> <td>3,921,844 A</td> <td>11/1975 Watles</td> </tr> <tr> <td>4,003,426 A</td> <td>1/1977 Best et al.</td> </tr> </table> | 520,584 A | 5/1894 Turner | 2,717,937 A | 9/1955 Lehr et al. | 3,034,845 A | 5/1962 Haumann | 3,069,045 A | 12/1962 Haumann et al. | 3,921,844 A | 11/1975 Watles | 4,003,426 A | 1/1977 Best et al. |
| 520,584 A | 5/1894 Turner | | | | | | | | | | | | |
| 2,717,937 A | 9/1955 Lehr et al. | | | | | | | | | | | | |
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| 3,069,045 A | 12/1962 Haumann et al. | | | | | | | | | | | | |
| 3,921,844 A | 11/1975 Watles | | | | | | | | | | | | |
| 4,003,426 A | 1/1977 Best et al. | | | | | | | | | | | | |

Global Good is relying on property rights and commercial distribution to develop and deploy the Arktek. Aspects of the technology have been patented.²⁷⁴ Meanwhile, Global Good is currently partnering with AUCMA, a leading refrigeration manufacturer, to help commercialize Arktek and produce it at scale at an affordable price.²⁷⁵

In 2016, Global Good received a “Patents for Humanity” award for the Arktek from the U.S. Patent and Trademark Office.²⁷⁶

The Arktek is a vivid illustration of how patented innovation can tackle global challenges. It’s a clever, pragmatic, and practical invention with global reach and import. It reminds us that secure property rights can help generate, develop, and disseminate life-saving solutions to seeming intractable problems.

Eye Exams On-the-Go with PEEK

By *Maryna Koberidze*



Hundreds of millions of people worldwide have vision problems that could be fixed or relieved if only they were diagnosed early enough. Unfortunately, current eye screening equipment is expensive, bulky, and requires specialists to operate. As a result, the vast majority of patients in the developing world have limited or no access to eye screening services and often suffer unnecessarily from eye problems.

Innovative new applications for smartphones promise to take eye exams out of the doctor’s office and bring them to the people who need them most. Several promising solutions have emerged.²⁷⁷ Not only are they mobile, but they are also affordable and non-specialists can operate them.

These solutions could benefit vast numbers of people. According to data from the World Health Organization, 253 million people worldwide are visually impaired.²⁷⁸ Of this group, 36 million are blind and 217 million have low vision.²⁷⁹ About 90 percent of visually impaired people live in low-income countries, where there is an acute shortage of practicing ophthalmologists. Yet, 80 percent of all visual disorders could be treated or even prevented if diagnosed at the outset.²⁸⁰

When it comes to eye disorders, early diagnostics is the key. In fact, four out of five cases of visual impairment can be prevented or cured if timely detected.²⁸¹ But in developing countries, there is a huge disparity between population size and the number of eye care providers. In Kenya, for example, there are only 86 ophthalmologists to cover a population of over 40 million people.²⁸² Many of those who need eye care live in rural, distant areas and are often unable to get to clinics or hospitals to seek help until after it's too late.²⁸³ As a result, millions of people in low-income countries are losing their vision.

One promising example of these new mobile diagnostic applications for eye care is the Portable Eye Examination Kit, or PEEK. PEEK is essentially an eye clinic that fits in a pocket.²⁸⁴ It combines both a traditional ophthalmoscope and a retinal camera in a smartphone, enabling affordable, fast, and easy eye examinations in the remotest of communities.²⁸⁵ PEEK consists of an app and a clip-on camera adapter that slides over a smartphone. Designed to be operated by community workers with minimum to no training, PEEK brings a low-cost and simple-to-use eye screening technology to the most underserved places in the world.

PEEK was born from Dr. Andrew Bastawrous' frustrating experience trying to bring eye care to rural Kenyans.²⁸⁶ Bastawrous, a British eye surgeon, experienced a logistical nightmare attempting to transport the bulky, costly, and fragile eye equipment to remote areas of Kenya in 2007.²⁸⁷ Back then, Bastawrous was a PhD student at the London School of Hygiene and Tropical Medicine, working on a study of eye diseases that involved setting up 100 clinics in rural Kenya. One of the biggest problems facing Bastawrous was that the villages he visited often had no electricity or road access, making it very difficult to transport and use medical equipment.²⁸⁸

However, Bastawrous observed that these remote villages did have cellular phone coverage.²⁸⁹ From that observation came the idea of a smartphone-based ophthalmic tool. To make this idea a reality, Bastawrous teamed up with software developer Stewart Jordan, biomedical engineer Mario Giardini, and ophthalmologist Iain Livingstone to found PEEK Vision.²⁹⁰ Since 2011, the PEEK team has relied on its expertise in international eye health, biomedical engineering, and ophthalmic research to develop smartphone-based visual assessment tools.



How does PEEK work? An app and a clip-on adapter use the smartphone's built-in camera and flash to perform various eye exams within seconds.²⁹¹ From basic testing for visual acuity, color and contrast sensitivity, and cataracts to scanning the retina, PEEK examination tools can help identify patients who need cataract surgery and detect early signs of diabetes, malaria, and other diseases. The PEEK clip-on adapter itself can be made with a 3D printer and works with common smartphone models such as iPhone, Samsung, HTC, and Sony.²⁹²

PEEK also enables efficient remote screening and treatment. A healthcare worker using PEEK can scan over 1,000 people per week. With minimal training, even non-healthcare workers can operate PEEK. Workers in the field can send information to eye care specialists, as PEEK makes high-quality images for further diagnosis and treatment readily available. PEEK also records patient contact information and GPS data, which it then emails to the treating physician.

The developers of PEEK have used IP rights to coordinate the development and deployment of this technology. They applied for a U.S. patent and have already obtained a U.S. trademark registration.²⁹³ PEEK tools are still in the process of being approved by the U.K. Medicines and Healthcare Products Regulatory Agency and the U.S. Food and Drug Administration.²⁹⁴

PEEK is working with NGOs and private donors to deploy the technology. It received funding from the Queen Elizabeth Diamond Jubilee Trust in 2013 toward testing the technology in different communities around the world.²⁹⁵ In 2014, the company started a crowdfunding campaign on Indiegogo to seek additional funds.²⁹⁶ Donors had an option to either purchase a PEEK kit for themselves or to donate it to a clinic in need.

PEEK is a great example of how innovation can address global healthcare challenges. It is a low-cost and easy-to-use invention that builds on widely available, popular technology. It has tremendous potential to improve millions of lives.

Zipline Enables Real-time Delivery of Essential Medical Supplies in Rwanda

By Stephen Ezell



Rwanda’s government, which has declared a vision of making the country a technology and innovation hub for Africa, has partnered with the startup Zipline to facilitate the real-time delivery of urgent medical supplies, such as blood or vaccines, to patients in remote locations via drones.²⁹⁷ In doing so, Rwanda became the first African country to author regulations integrating drones into its airspace and to begin regular operations to deliver medical supplies via unmanned aerial vehicles.

Zipline’s fixed-wing drones, called “Zips,” began operations in October 2016 out of the Zipline Muhanga Distribution Center, providing initial service to Rwanda’s Kabgayi District Hospital.²⁹⁸ The Zips, which have a 75-kilometer service radius and can carry 1.5 kilograms of payload per sortie and can operate in all-weather conditions, facilitate the real-time delivery of essential medical supplies, seamlessly flying over treacherous terrain in as little as 30 minutes, which it traditionally took as much as four hours to cover in a vehicle (when roads weren’t washed out by the frequent torrential rains).²⁹⁹

Zipline now serves 21 Rwandan hospitals nationwide and, as of May 2017, Zipline has completed over 350 delivery flights, with deliveries now averaging more than 20 per week.³⁰⁰ In total, Zipline's drones provide instant access to life-saving blood products for over 8 million Rwandans, nearly two-thirds of the country's total population of 12 million.³⁰¹

The drone-delivery platform has saved lives and improved quality of life for hundreds of Rwandans. As Espoir Kajibwami, a surgeon who previously served as Kabgayi's medical director, noted, "Before, it was a serious problem to have blood when we needed it," explaining that, in emergency cases, the hospital would often send the patient to the national referral hospital in Kigali rather than wait for blood to arrive.³⁰² Kajibwami cited a case in which a woman began hemorrhaging after surgery to remove an ectopic pregnancy and the ability to immediately contact Zipline for an emergency blood delivery (with the correct blood type for the patient) may have been the difference between the patient's life and death. Beyond such dramatic instances, the service enables remote, regional clinics to see more patients in the field (saving patients long commutes to larger medical centers) and also frees up time for staff to perform their duties.

While Zipline started with a focus on blood deliveries (including blood units of all types, platelets, fresh frozen plasma, and cryoprecipitate), as Jonathan Rosen writes in "Zipline's Ambitious Medical Drone Delivery in Africa," in the *MIT Technology Review*, Zipline's future plans in Rwanda include scaling up to a much wider range of medical products, including: emergency rabies vaccines; drugs treating HIV, tuberculosis, and malaria; contraceptives; and diagnostic testing kits.³⁰³ As Rosen continues, what Zipline really makes possible is a far more agile, more adaptable supply chain—for blood and durable products such as pharmaceutical medicines alike—in which fewer items must be kept at last-mile facilities, thus minimizing waste and ensuring availability. Moreover, the ability to deliver these supplies rapidly and in real time also enables facilities to access products with shorter shelf lives or unique storage requirements and even promotes the use of medicines (such as blood-clotting agents) that were previously underutilized because they were too difficult to store at remote health facilities.

Throughout the developing world more than two billion individuals lack adequate access to essential medical products, from blood and vaccines to medicines and medical products, due in part to challenging terrain and gaps in infrastructure. Technology-based innovations such as near-real-time drone delivery can play an important role in getting a wide variety of medical goods to patients living in remote agents on a timely and cost-competitive basis (especially over time, as sorties increase and costs per delivery falls). Zipline plans to launch soon in other African nations, such as Tanzania.³⁰⁴ Elsewhere, the UN Children's Emergency Fund (UNICEF) has explored the feasibility of using drones to transport the HIV test samples of newborn babies in Malawi.³⁰⁵ While the opportunities are seemingly limitless, the case of Zipline highlights the importance of forward-thinking policy leadership on the part of the Rwandan government to create the conditions in which drone operations can flourish, in part in response to pressing medical needs. It's another example of innovation improving access to medicines and improving lives for citizens in the developing world.

The Handheld Cardio-Pad: Tackling Cardiovascular Disease in Africa Through Innovation

By Stephen Ezell



Healthcare challenges in the developed and developing worlds are converging, forcing life-sciences innovators to deal with similar challenges, even if from unique perspectives. Consider heart disease. Today, it is the leading cause of death in sub-Saharan Africa for citizens over the age of 30.³⁰⁶ Meanwhile, on the continent as a whole, 46 percent of Africans over 25 suffer from hypertension—more than anywhere else in the world—though the challenge isn't limited to Africa.³⁰⁷ Indeed, citizens of low- and middle-income countries bear 80 percent of the world's death burden from cardiovascular disease.³⁰⁸ And, in fact, by 2020, non-communicable diseases such as cardiovascular disease and diabetes will account for 70 percent of fatalities in developing countries.³⁰⁹ Fortunately, developing-country innovators are stepping up to address the challenge.

Meet Arthur Zang, a 29 year-old Cameroonian engineer who invented the handheld Cardio-Pad, the world's first medical tablet facilitating heart examinations and remote diagnosis.³¹⁰ The Cardio-Pad is a touch-screen tablet device for conducting cardiac tests such as electrocardiograms in remote locations and then sending the results to cardiologists in city centers often hundreds of miles away. The system works in pairs: Nurses in remote villages (or patients' homes) apply wireless electrodes that record patients' heart signals, which are transmitted over-the-air to nurses' Cardio-Pads. The data is then sent to a cardiologist's Cardio-Pad, so the doctor can remotely assess and diagnose a patient's condition.

As is the case in many developing nations, fewer than 50 cardiologists support Cameroon's population of over 23 million citizens.³¹¹ Without solutions that close the distance between cardiologists located in cities such as Douala (Cameroon's largest) and Yaoundé (the capital), many citizens, and especially those living in remote locations or those in the most urgent need of care, will simply lack access to proper cardiovascular care. Facilitating remote diagnosis and evaluation of heart conditions further substantially improves conditions for patients, alleviating the need for expensive, time-consuming, and often difficult journeys (especially for elderly patients) to city centers, and eliminates the need to wait in offices while doctors make their diagnoses. At the same time, the solution improves the efficiency of Cameroon's health care system, allowing cardiologists to

service more patients and helping to digitalize health records, so that information on patients' conditions are more readily accessible to individuals and healthcare providers alike.

Mr. Zang founded a startup company, Himore Medical, to market the Cardio-Pad, providing an excellent example of “reverse innovation,” which refers to products that were initially developed to serve the needs of developing markets, but which, often by dint of being more cost-competitive, find wider appeal in large global markets.³¹² With a typical cardiac examination in central Africa costing about \$40, while most citizens live on less than \$5 per day, the need for cost-efficient solutions is paramount. That's why Himore initially sought to price the Cardio-Pad at €2,200 (\$2,700), a fraction of the cost of commercially available, less-portable devices.³¹³ (Himore estimates the manufacturing of a complete kit used to perform a 12-leads heart examination costs about \$2,000.)³¹⁴ In addition to being economical, Zang designed the Cardio-Pad attuned to specific needs encountered in developing countries: The device is humidity-resistant and easy for healthcare providers to read and manipulate.³¹⁵ Reflecting on the simplicity and user-friendliness of the Cardio-Pad for patients and medical professionals alike, Zang explains that “the basis of innovation often [comes from] a desire to solve other peoples' problems.”³¹⁶

Innovation lies at the heart of Zang's Cardio-Pad, but the entrepreneur-innovator was quick to secure intellectual property rights for his invention. He filed a patent for the Cardio-Pad (specifically the novel hardware/software combination constituting it) with the African Intellectual Property Organization (AIPO) in 2011.³¹⁷ As Zang astutely observes, “patents enable you to protect yourself against rivals who simply want to copy your work.”³¹⁸ Zang further notes that the intellectual property system in Africa “helps us give credibility to African products” and has been instrumental as a validator as his company seeks investors to support its expansion.³¹⁹ And that actually points to one of the most significant benefits of intellectual property rights for innovators: It affords them the ability to capture a reasonable share of profits from one generation of innovation to finance investments in the next. Indeed, Himore has leveraged the core hardware/software technology behind the Cardio-Pad to develop additional products, such as ultrasound devices for scanning and radiology. Zang has also sought trademark protection for both the Cardio-Pad and his company, Himore Medical.³²⁰

Zang hopes that Himore's success with innovative, low-cost medical device solutions may give rise to a medical diagnostics cluster in Cameroon.³²¹ He also attributes his success to the thoughtful innovation policies of Cameroon's government, which provided him a modest €30,000 grant as a promising young engineer-entrepreneur (Zang initially conceived the Cardio-Pad at age 24) as part of a series of seed grants designed to bolster Cameroon's startup and innovation economy. Mr. Zang has justifiably received numerous awards, including the 2016 Africa Prize for Engineering Innovation awarded by the UK's Royal Academy of Engineering.³²²

The Cardio-Pad provides an excellent example of how the convergence of advanced information and communication technologies, including semiconductor-enabled devices, wireless, software, algorithms, and big data, are enabling the creation of transformative healthcare technologies that improve the lives of citizens in developed and developing countries alike. It also shows the power of intellectual property to protect innovators and facilitate a virtuous cycle of innovation that enables them to continue developing innovative products and solutions that benefit citizens far downstream from the initial innovation.

Proximie: Augmented Reality Technology Helps Bring Surgical Expertise to Conflict Zones and the Developing World

By Gleb Savich



The majority of the world's people do not have access to safe and affordable surgical care.³²³ More than 2 billion people cannot receive surgical care simply because there are no surgical facilities where they live. Up to 3 billion more people do not have access to surgical care that is safe, timely, and affordable. The availability of surgical care is extremely uneven around the world. While 95 percent of the population of South Asia and several regions of Africa lack access to surgical care, less than 5 percent of the population of the high-income areas of North America and Western Europe lack such access.

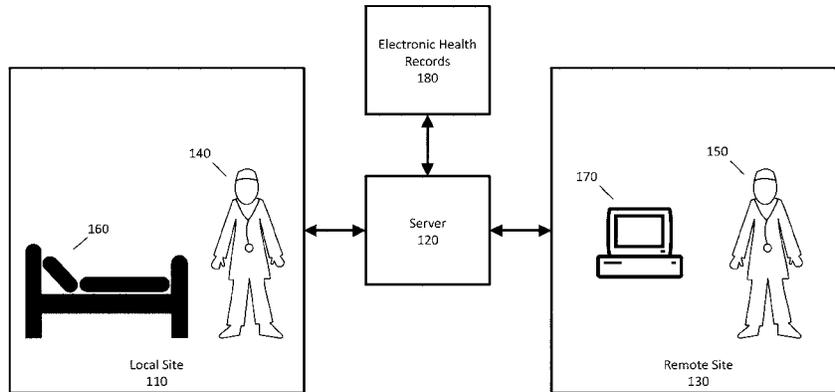
The problem of access to surgical care may be particularly acute in conflict zones, where the need is often the greatest. Getting much-needed surgical expertise to war-ravaged countries is already a nearly impossible task. To make matters worse, in such countries as Syria, Yemen, and Sudan, targeting healthcare workers and facilities for destruction has become a warfare strategy.³²⁴

Talal Ali Ahmad is a Boston-based Lebanese entrepreneur who built his career in mobile phone development.³²⁵ While on a mission to El Salvador as a volunteer for the Global Smile Foundation, he observed firsthand the obstacles faced by doctors providing healthcare in remote regions. Leveraging his background in mobile phone technology, Ahmad began developing tools that allow surgeons to remotely assist their colleagues with surgical procedures.³²⁶

To further develop and implement the technology, Ahmad teamed up with Nadine Hachach-Haram, a London-based Lebanese surgeon.³²⁷ Together, they founded Proximie, bringing together a team of clinicians, engineers, and designers.³²⁸ In 2016, Ahmad obtained a patent on his invention and secured the backing of a Lebanese venture capital firm, Cedar Mundi Holdings.³²⁹

The augmented reality technology that Ahmad and his team developed, also called Proximie, is simple. It uses any pair of computers, tablets, or smartphones with cameras. One unit is located at the site of surgery, and

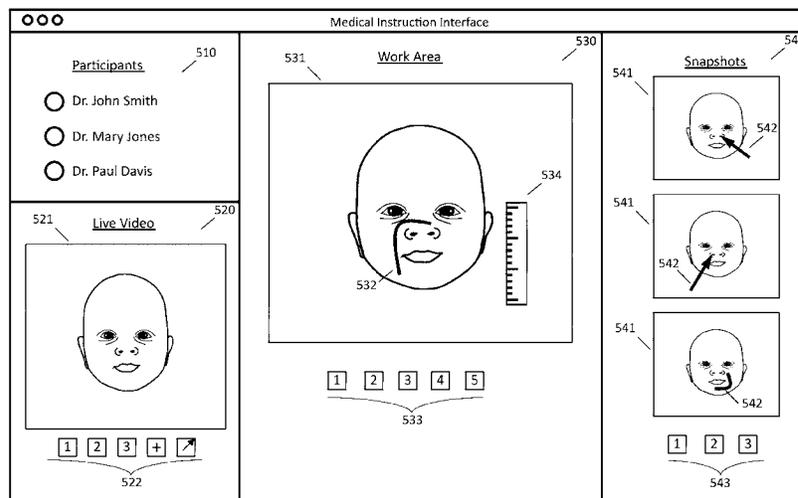
the other is at a remote location. A surgeon at the remote location can observe the surgical field as 2D or 3D images or a real-time video feed. Using a touchscreen, the remote surgeon can make markings that are overlaid on the images of the surgical field and transmitted to the surgical site. For example, the remote surgeon can mark where to make an incision. The remote surgeon and the local team can communicate with each other by audio or text.



A more sophisticated version of Proximie utilizes a dataglove that senses the position and movements of the wearer’s hand. The hand movements of the remote surgeon wearing such a glove are overlaid on the images of the surgical field and transmitted to the site of surgery, guiding the local team on how to perform a procedure.

Proximie utilizes existing technology and can be implemented on any suitable device or platform.³³⁰ Its simple interface allows doctors to use the platform with just a few days of training. This simplicity and accessibility is critical. Dr. Hachach-Haram explains: “What attracts us to this is that the challenges facing public healthcare are hugely complex, yet the solutions offered by technology are beautifully simple. This idea of bringing forms of surgery to places where they haven’t been available before with nothing more than an Internet connection and mobile devices seems very powerful to us.”³³¹

Proximie conducted its initial trials in 2015 in collaboration with the Global Smile Foundation. Surgeons in the U.S. guided teams in Peru and El Salvador in repairing cleft palates of local children. The following year, surgeons in Gaza, Syria, and Iraq performed wound surgeries assisted by their colleagues in Lebanon using Proximie.



Dr. Abu-Sitta, a plastic surgeon, used Proximie to lead surgeries in the Gaza strip from his home base in Beirut, hundreds of miles away.³³² In one such surgery, he showed the local surgeons in Gaza how to repair a blast injury. In another, he showed them how to operate on a congenital hand anomaly. Previously, Dr. Abu-Sitta tried helping overseas surgeons by sending them audio recordings, photos, and X-rays. But Proximie is far more interactive. Dr. Abu-Sitta notes: “We wanted to push the idea that with only the minimum hardware, and minimum infrastructure you can still pull it off. With just two tablets, iPad to iPad, we’re able to perform this surgery.”

One of the surgeons that conducted the surgery in Gaza described his experience: “It is like the consultant is with you in the same room, giving you an opinion so that the surgery can be perfect.”³³³

In addition to helping surgeons in remote areas and conflict zones to benefit from the expertise and real-time guidance of experts located elsewhere in the world, Proximie can be a valuable training tool.³³⁴ Proximie has partnered with the Royal Free Hospital and University College London in the United Kingdom and Yale Medical School in the United States to provide support for medical students. “Surgeries are being streamed from the Royal Free Hospital theaters and the students can log on and interact directly with the operating surgeon. Students can also capture and store photos and videos on Proximie’s cloud-based server for future learning,” explains Dr. Hachach-Haram.

Driven by their belief that everyone should benefit from the same high quality of healthcare and training opportunities, no matter where they live, the Proximie team continues to develop their technology to increase access to surgical care and training around the world.

Chapter 7: Challenge: Fostering Health Innovation in Emerging Economies

Intellectual Property Helping to Drive Healthcare Innovations in India

By Nigel Cory



Intellectual property can facilitate healthcare innovation—regardless of a country’s level of development. GE’s and Philips’ experience in India is a clear example of how global companies—whose business models rely on intellectual property—can leverage technology transfer, intellectual property, and global research and production networks to develop innovative solutions to local health problems. The experience of these companies and their India-inspired products shows the potential should India strengthen its intellectual property protections and stop viewing intellectual property as problematic, as it sometimes seems to do with regard to pharmaceuticals and life-sciences technology.

India is a large and growing market for healthcare, but local conditions, including limited government investment in healthcare (less than 1 percent of GDP), income, remoteness, and education, mean that local adaption is often needed. GE’s mantra—“Made in India, for India”—reflects this. This mantra guides the more than 5,000 employees that work at GE’s research centers in Mumbai, Chennai, Hyderabad, and Bengaluru, which together make India the company’s largest center for research operations outside of the United States.³³⁵

GE’s success in designing products for local conditions shows that its approach is working, while also showing how intellectual property plays a key supporting role, often unseen in the background. For instance, GE’s Lullaby baby warmer is a great example of such “reverse innovation.”³³⁶ India has among the highest rate of preterm baby deaths in the world. Each year, more than 15 million Indian babies are born prematurely.³³⁷ These babies need incubators to keep them alive, but many state-run hospitals in India cannot afford expensive traditional models.

So, in 2009, GE modified its Giraffe Warmer—a high-end incubator that sells for \$25,000—to develop a baby warmer in its Bangalore research center that costs only \$3,000.³³⁸ The Lullaby Baby adapted to local

conditions. It works without a voltage stabilizer, so that it can adapt to volatile electricity conditions. It uses 50 percent less electricity. It includes pictorial warnings and color coding so that rural healthcare workers who have difficulty reading can operate the machine. The product was so successful in India that GE now exports it to over 80 countries.

Likewise, consider GE's development of a localized electrocardiogram (ECG) device for India—the MACi. Again, GE adapted an existing model to suit local conditions. The MACi is fast-charging, has a long-life battery, is robust and portable, and, at \$500, sells far below the price of GE's other models (which cost \$2,000 to \$10,000).³³⁹ A key part of this innovation process was GE's ability to leverage its global research network and its use of intellectual property to transfer specific technology from other parts of its network for the development of new, local products—and new intellectual property. In 2008, GE filed for a patent for MACi in India.

Similarly, Philips' Innovation Campus in Bengaluru shows that local innovation doesn't have to be just about products, but can also be about new and innovative services. Philips uses new technologies, such as mobile, cloud, and big data analytics to improve local patient outcomes, including through the use of algorithms and artificial intelligence—both of which are typically protected by trade secrets and forms of intellectual property, as would the accompanying software and physical products that form part of the service.³⁴⁰ For example, Philips developed software that—based on deep-learning algorithms and large patient data sets—can scan chest X-rays and tell radiologists if and where there is tuberculosis.

Philips' India unit also developed the Mobile Obstetrical Monitoring (MOM) device, a mobile application that monitors expectant mothers and detects risks they are prone to during the early stages of pregnancy.³⁴¹ Again, it's adapted to local conditions—light, robust, and easy to use, it has built-in batteries that provide up to 10 hours of use and when no main energy supply is available, a wind-up handle that can power it. Showing the utility of telemedicine in rural India, the MOM device uploads data to a central server, allowing obstetricians and gynecologists to remotely monitor patients from hospitals or home. The product and service has since been expanded to Indonesia, where during a one-year pilot, it improved the detection of high-risk pregnancies by 300 percent.³⁴²

GE and Philips' efforts in India are not side projects, but central to global operations. For GE, India is central to its “Healthyimagination” project, which is a \$6 billion-dollar effort to provide high-quality affordable healthcare products in developing countries. GE hope to earn \$1 billion in revenues in India by 2020.³⁴³ These firms play important roles in helping to provide better healthcare as well as in developing local innovations, and intellectual property helps to accomplish this. The 2015–2016 annual report on patent filings in India shows the critical role played by foreign firms, who filed over 70 percent of the nearly 47,000 patents.³⁴⁴ Philips and General Electric are consistently among the top patent filers in India—in 2015–16, Philips filed the second most patents of foreign firms (949), while GE was fifth (446).³⁴⁵

India still has a long way to go toward getting the intellectual property framework in place to become a global leader in life-sciences and biomedical innovation.³⁴⁶ India's intellectual property framework suffers from inadequate and inconsistent IP processes and enforcement, and a sometimes-hostile attitude toward intellectual property at home and abroad (at multilateral institutions), especially those involved in pharmaceuticals. Indian Prime Minister Modi has sent some positive signals that he wants to change this through the “Make in India” initiative and the new National Intellectual Property Rights Policy, but these signals have yet to be translated into action. India needs to recognize the critical role that intellectual property plays in driving innovation if it wants its economy to move up the value chain, and just as importantly, if it wants to ensure its citizens have access to the latest life-saving technologies.

How Strengthened IP Rights Unlocked the Potential of Biomedical Innovation in Brazil

By Stephen Ezell



Cordia verbenacea is a perennial bush plant that grows widely along the southeastern coast of Brazil. For decades, local fishermen in Brazil had used the plant, mashed into oil, directly on sprains and cuts as an anti-inflammatory and anti-scarring medicine to aid healing.³⁴⁷ Managers at Ache Laboratorios Farmaceuticos, established in 1966 and the biggest local manufacturer and marketer of branded generics in Brazil, came to know of the medicinal potential for the plant by the early 1980s. In the 1980s and early 1990s, researchers at the company considered trying to isolate the active ingredient in *cordia verbenacea* into a medicinal compound, but, recognizing that Brazil's lack of pharmaceutical patent rights meant they would be unable to protect their intellectual property and investments if they were successful, decided to delay doing so. However, in 1996, (in part as an effort to come into compliance with the Trade-Related Aspects of Intellectual Property (TRIPS) Agreement), the Brazilian Congress amended Brazil's patent laws with Law No 9,279 which introduced pharmaceutical product patent rights, so that, subject to procedural processes and some restrictions, only patent-holders or their licensees would be permitted to market under-patent medicines.

As Georgetown University Professor Mike Ryan writes in *Patent Incentives, Technology Markets, and Public–Private Bio-Medical Innovation Networks in Brazil*, the implication of the patent law reform for Ache managers was that they could finally invest in innovative medicinal product development, such as the *cordia* anti-inflammatory project, because the stronger IP rights enshrined in Brazil's new patent law gave them confidence that their risky and expensive investments to develop the active ingredient in *cordia verbenacea* would be protected. In other words, the strengthening of IP rights gave Brazil's innovators opportunity and incentive to tap into the rich ecological diversity of the country to produce novel medicines for the benefit of Brazilians and citizens throughout the world.

As Ryan observes, Ache managers in the early 1990s knew that in order to develop a product from the plant, Ache would need to isolate the active ingredient and take it through laboratory toxicology studies, animal testing, and human clinical trials to demonstrate safety and efficacy in order to introduce the innovation to the marketplace. But, Brazilian patent law at the time forbade pharmaceutical product patents and, thus, Ache would only be permitted to file for a process patent regarding the method of manufacture of the medicine. Thus, should the product prove popular, Ache's competitors would be free to reverse engineer and sell the medicine themselves despite the fact that they had not made the investment into the product discovery, refinement, and

safety and efficacy testing. Accordingly, Ache did some exploratory research into the active ingredient in the early 1990s but did not pursue the project further.

With the 1996 change to Brazil's patent laws, Ache managers decided to restart the *cordia verbenacea* project in 1998. But lacking sufficient internal capacity to conduct the research, Ache established a research partnership with a local university professor to renew a study of the plant and its chemistry. Even that agreement with the local university was difficult to negotiate, in the words of an Ache senior manager, because there was "no patent culture" in Brazil. When isolation of the active chemical was achieved, again lacking internal capacity, Ache hired an outside research organization to design and carry out the toxicology, safety, and efficacy studies in order to gain market-release approval from Brazilian pharmaceutical regulators. Ache managers estimated that some 100 university agronomists, biochemists, pharmacologists, and medical doctors at a number of universities participated from 1998 to 2004 in the product-development process. Agreements regarding IP rights, confidentiality, and compensation were negotiated with all these outside specialists. While parties reported that these agreements proved difficult to negotiate because of university inexperience with IP rights, as Ryan notes, it was in fact the advent of pharmaceutical patent rights that gave rise to the impetus to develop these broader biomedical innovation networks among companies, universities, researchers, and research institutes in Brazil. Accordingly, the evolution of local biomedical innovation networks should also be viewed as an important contribution made by strengthened IP rights in developing countries.

Ache's investments in research and network development paid off, and cream-form Acheflan, an anti-inflammatory drug, was introduced as a prescription medicine in the summer of 2005, becoming the first medicine to be developed and introduced into the marketplace by a Brazilian company. Ache's attorneys submitted patent applications to the Brazilian National Institute of Industrial Property that indicated the inventiveness of the product and explained how the company's anti-inflammatory would contribute a valuable new therapy to the betterment of the Brazilian health system. Ache's attorneys also submitted patent applications for Acheflan, both the cream form and the aerosol form, to the Patent Cooperation Treaty administrative unit of the World Intellectual Property Organization in Geneva in order to seek patent protections in the United States, Europe, and other countries.

By 2006, Acheflan garnered a 30 percent share of the Brazilian anti-inflammatory market and by the end of 2007 its market share exceeded 40 percent, despite the fact it competed directly with products from Aventis, Novartis, and Pfizer. The company subsequently initiated development of a cream-form Acheflan for the American and European marketplaces, development of an aerosol-form Acheflan for Brazilian and international markets, and development of an oral-form Acheflan for Brazilian and international markets.

The Brazilian experience demonstrates that even in countries where IP has not traditionally been viewed as a priority, innovations can be created to fulfill global needs. Yet the reality remains that Ache's managers waited some 15 years, until after the 1996 patent reforms, to develop and patent a biodiversity-based anti-inflammatory technology; 15 years in which an innovative medical product could have been brought more quickly to the Brazilian and global public had stronger IP rights existed to protect the investments and efforts of biomedical innovators.

Ultimately, stronger IP rights provide necessary incentives for local biomedical innovators to tap into the robust ecological diversity of their countries, and the brains of their own citizens, as a powerful basis for novel biomedical innovation.

Content in this case study was drawn with the permission of Professor Michael Ryan, Georgetown University, based on the paper: Michael P. Ryan, "Patent Incentives, Technology Markets, and Public-Private Bio-Medical Innovation Networks in Brazil," *World Development*, vol. 38(8), (August 2010): 1082-1093.

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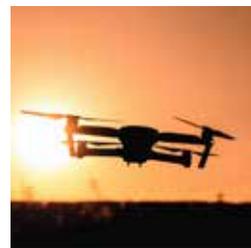
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