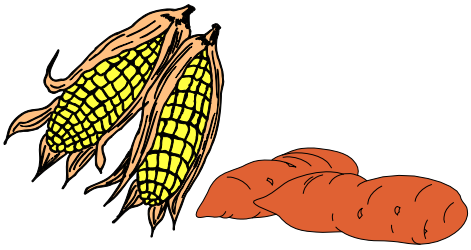
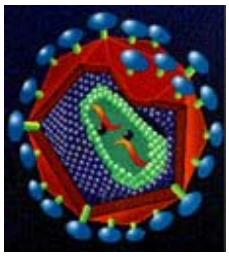
ProCell Corporation

TECHNOLOGY & PRODUCT INFORMATION





Dr Yvonne J Rosenberg Ph.D.

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ProCell Corporation

OVERVIEW:

ProCell's new delivery modalities will promote both stability (drug) and the appropriate cellular interactions (vaccines). This includes a novel vaccine adjuvant for boosting the immune responses induced by classical vaccines as well as individual vaccine components.

All products will be able to be taken by mucosal administration (drinking, eating, inhaling).

Employing plant production, cost of vaccines produced will be reduced to between 100th to 1,000th in cost. Vaccines include:

- Nerve Agent Antidote – Butyrylcholinesterase – (BCHe).
- Edible human immunodefiency virus (HIV) Vaccine (for developing countries).
- HIV p24-based viral load assay.
- HIV and any viral protein components, being plant derivatives, for production of vaccines and for diagnostics.
- Virus-based adjuvant future
- Orally administered treatment for haemophilia future

Utilizing the Company' novel technologies, *ProCell's* diagnostics assays, biologics, and vaccines will exert their benefit by providing significantly enhanced sensitivity, quality, ease of use, clinical efficacy, and safety.

Each of the core technologies listed above can be enabled and applied to specific aspects of HIV, hemophilia and nerve agent protection.

THE RESEARCH TEAM & COMPANY:

ProCell Corporation, a Delaware Corporation, was founded in 2000 to develop and commercialize discoveries made for the pre- and post-exposure treatment for nerve agent exposure and the treatment, diagnosis, and control of global infectious diseases of which HIV is the initial target.

The Chief Scientific Officer and President, of *ProCell*, Yvonne Rosenberg, Ph.D., CSO—has been involved in parasitology since 1969; malaria research since 1977; HIV and Simian immunodeficiency virus (SIV) research non-human primates since 1989.

Dr. Rosenberg is an internationally recognized immunologist with experience of autoimmune diseases, infectious diseases including HIV and SIV, especially as these diseases relate to the lymphoid system and host immunological responses. Over the last 10 years, Dr. Rosenberg has pioneered underlining concepts in viral pathogenesis, working on several vaccine trials involving non-human primates.

Dr. Rosenberg has been instrumental is securing the initial funds on which *ProCell* will operate, establishing anti-biowarfare agents as a key priority well before the recent devastations that occurred in New York and Washington DC. In addition to her research experience, Dr. Rosenberg has experience in establishing a successful biotechnology company. She was a Founder and past CSO for TherImmune Research Corp., a recent graduate of the Maryland Technology Development Center Incubator program. She received her Ph.D. at the Australian National University in Immunology; post-doctoral training at the National Institutes of Health; and worked closely with the U.S. Army for seven years while at the Henry M. Jackson Foundation for the Advancement of Military Research on HIV/AIDS research. Dr. Rosenberg presently holds an adjunct appointment in the Institute for Human Virology that is part of the Medical Biotechnology Center at the University of Maryland Biotechnology Institute.

BOARD OF DIRECTORS

Lowell Harmison,	Ph.D.	Chief Executive Officer, Chairman
Yvonne Rosenberg,	Ph.D.	Chief Scientific Officer, President
Jesse Schulman,	Ph.D.	Biotechnologist and Financier
Lewellys Barker,	MD.	Chief Medical Advisor

Walter Raleigh or representative of Funder

SCIENTIFIC ADVISORS & CONSULTANTS

Polly Matzinger,	Ph.D.	Solomon Tse,	Ph.D.
Mark Lewis,	Ph.D.	Oksana Lockridge,	Ph.D.
David Katzenstein,	M.D.	Yakov Ashani,	Ph.D.
Vanessa Hirsch,	DVM, D.Sc.	Bhupendra Doctor,	Ph.D.
Jay Levy	MD	Norman Letvin	MD, Ph.D.
Rainer Fischer	Ph.D.	Earl Rubright	(ret, US Central Command)
Pal Maliga	Ph.D.	MAJGEN Simon Willis	(Australian Defense Attache)

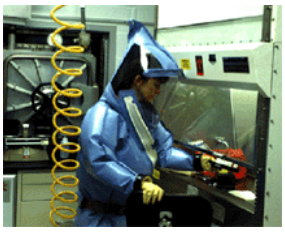
FACILITIES / EQUIPMENT DESCRIPTION:

1 ProCell Corporation Laboratories

ProCell's laboratories are located at 9610 Medical Center Drive, Suite 230, Rockville, MD and currently comprises 1,200 square feet of laboratory and office space. Key personnel each have G4 Macintosh computers and internet access. The laboratory conducts studies on immunology, tissue culture, molecular biology of infectious diseases, chemistry and molecular biology. This laboratory is equipped with a cold room, laminar flow hoods, low speed centrifuges, cell harvester, CO_2 incubators, -20^oC and -70^oC freezers, balances, an ELISA plate reader and washer and a Phase microscope.

The infectious disease laboratory operates under BL-2 conditions. Molecular / Chemistry capabilities include methods for small molecule, carbohydrate, protein and peptide testing. This laboratory contains, protein electrophoretic equipment for SDS-PAGE, IEF and Western blot analysis, UV-VIS

spectrophotometer, sample extraction and concentration equipment, bacterial incubator shakers, UV box / camera, microwave and thermal cyclers. A fermenter for the scaled up production of tobacco BY-2 cell cultures has been requested in the budget. These laboratories meet all environmental laws and regulations of federal, state and local governments. There is no radioactivity used in these studies.



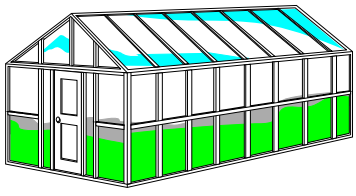
2 Southern Research Institute (SRI) Animal Facility

For much of ProCell's research requiring animals, monkeys, mice or guinea pigs will be housed at SRI under the direction of Dr. Mark Lewis, an advisor to ProCell and a long term collaborator of Dr. Rosenberg. TheSRI Facility is accredited by the Association for the Accreditation of Laboratory Animal Care (AAALAC) and hold an Assurance on file with the NIH, Office for Protection of Research Risks as required by the US Public Health Service Policy on Humane Care and Use of Laboratory Animals. It has a Board Certified (American College of Laboratory Animal Medicine) veterinarian and a well trained staff and with extensive experience working with rodents and macaques and with procedures for repeated animal bleeding and safe injections of enzymes.

3 WRAIR Animal Facility

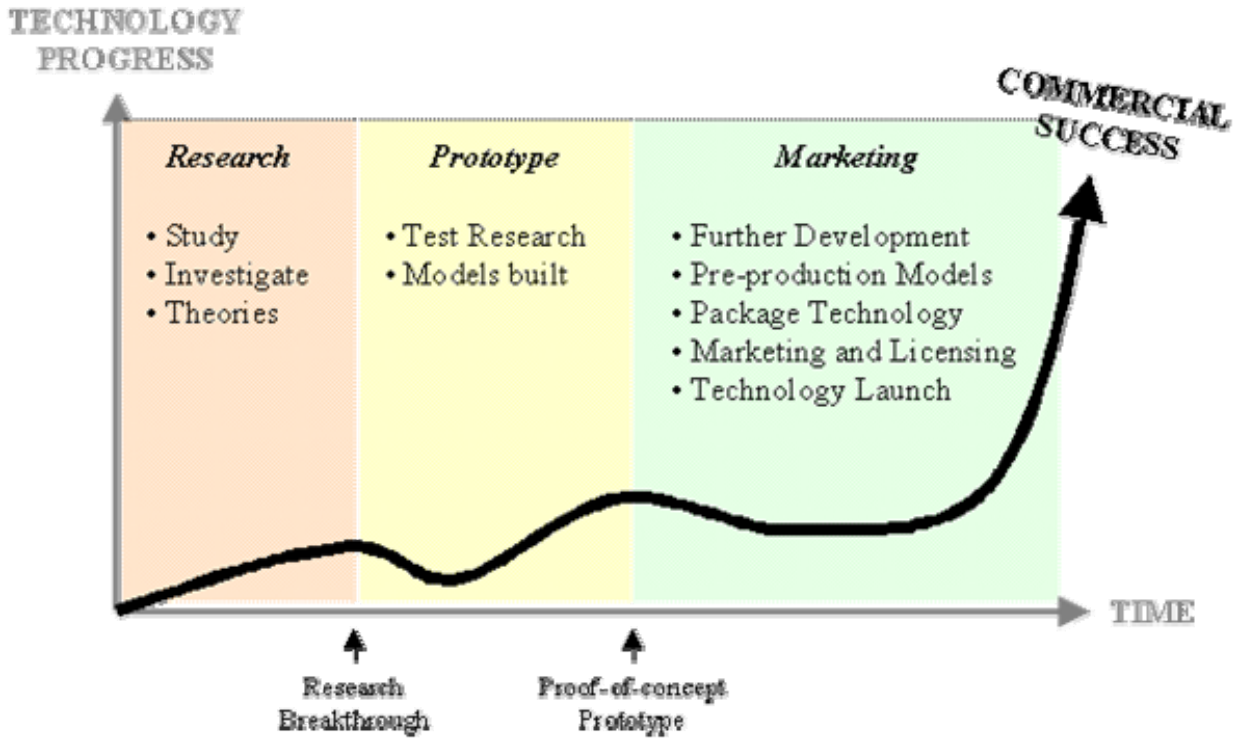
All mice and monkey holding, injection and bleeding will be performed at WRAIR Animal Facility under the direction of Col. Patricia Nossov. These studies will be performed under an approved IACUC using mice and rhesus macaques (monkeys). The WRAIR Facility is accredited by the Association for the Accreditation of Laboratory Animal Care (AAALAC) and hold an Assurance on file with the NIH, Office for Protection of Research Risks as required by the US Public Health Service Policy on Humane Care and Use of Laboratory Animals. It has a Board Certified (American College of Laboratory Animal Medicine) veterinarian and a well trained staff and with extensive experience working with rodents and macaques and with procedures for repeated animal bleeding and safe injections of enzymes.

4 Green house Facility



In the event that the tobacco transgenic tobacco plants successfully produces rBChE with high circulatory retention times, greenhouse space is available in a new Facility in Elizabeth City, North Carolina, owned by TerraVerde, Inc.

Research to Product Stages



PRODUCTS:

ProCell has a focused product portfolio covering several compelling applications of its platform technologies. Product development occurs in two divisions according to their stage of development and their intended applications.

Research & Development Division

This division will focus on the development of novel therapeutic and prophylactic treatments that will usually involve pre-clinical testing in non-human primate models for assessing the most efficacious route of immunization / injection, dose of drug / vaccine, and quality of adjuvants in preparation for human use**.** Two products will be developed **an inhaler to deliver butyrylcholinesterase,** a biological scavenger of toxic substances such as nerve agents, insecticides, succinyl choline, and cocaine and **an edible HIV vaccine**.

Butyrylcholinesterase - BChE

The role of acetylcholinesterase is to hydrolyze the neuro-transmitter acetylcholine at neuromuscular junctions and other cholinergic synapses, thereby limiting repetitive neuronal stimulation that may result in convulsions, respiratory failure, and death (such as that seen using roach and ant killer). Compounds capable of inhibiting acetylcholinesterase activity, such as those containing carboxylic or phosphoric esters bonds, result in the accumulation of acetylcholine and potentially serve as potent neurotoxins, posing a threat to both military and civilian arenas. Such a compound is Butyrylcholinesterase (EC 3.1.1.8 acylcholine, acylhydrolase, pseudocholinesterase, non-specific cholinesterase): a serine esterase (MW =345,000) comprised of four identical subunits held together by non-covalent bonds and contains 36 carbohydrate chains (23.9% by weight).

Exogenous administration of Butyrylcholinesterase in several heterologous (mismatched) animal models has been successfully used as a safe and efficacious prophylactic treatment to prevent organophosphate poisoning, drug overdose and alleviate post exposure incapacitation eg apnea. However, the clearance of the "foreign" glycoprotein has usually been rapid; presumably a combination of both (1) the presentation of novel epitopes on the enzyme molecules with subsequent induction of anti-enzyme antibodies and (2) heterogeneity in the carbohydrate structure (subunit assembly, location and number of the non-sialylated galactose residues) of the "non-self" enzyme preparations leading to more rapid uptake by receptors in the liver.

High threat environments clearly vary. In some situations, rapid administration of high doses of enzyme immediately prior to an unexpected nerve agent attack will be necessary to prevent lethality or toxic manifestations while in others, multiple prophylactic treatments aimed at long-term maintenance of protective levels of circulating enzyme may be more appropriate. In the latter case, measures to maximize prolonged enzyme stability are crucial. The military importance of this is highlighted by the fact that during Desert Storm, soldiers could be sent out into the field for only three days due to the limited length of

time the current drug treatment is considered protective**.** In the pursuit of highly efficacious and safe pre- and post-exposure treatment military and civilian personnel for a nerve agent antidote, *ProCell* scientists have to date:

1. Performed the only pre-clinical study involving the injection of homologous "self" rhesus macaques butyrylcholinesterase into monkeys of the same species. Such injections lead to long retention times of butyrylcholinesterase (>10 days) in plasma without inducing anti-butyrylcholinesterase antibodies or adverse effects.
2. Although stable, rhesus macaques butyrylcholinesterase given as a small dose, even in the apparent absence of cross-reactive anti-butyrylcholinesterase antibodies, was still rapidly cleared and marked variability in the rate of enzyme clearance in individual monkeys was observed.
3. *ProCell* will receive funding to optimize parameters such as timing, dose, and form of the administered enzyme to sustain the necessary prophylactic levels in the circulation.
4. In association with our pharmaceutical consultant Solomon Tse, an expert in inhalation delivery systems, *ProCell* is researching a "puffer" method for pulmonary delivery of the enzyme, including both "PEGylated" and unmodified forms of the enzyme.
5. Designed a new expression / *in vitro* glycosylation methodology for the production of recombinant butyrylcholinesterase—this is important because of the increased risks associated with blood-derived products—a patent for this procedure has been submitted.

Value Proposition

- **Fewer side effects—**Traditional treatment for poisoning by organophosphates and anti-cholinesterase compounds consist of a combination of drugs such as carbamates (For example, pyridostigmine), antimuscarinics, reactivators of inhibited acetylcholinesterase and anti-convulsants in pre- and post-exposure modalities. However, while this approach results in preventing fatal effects of organophosphates toxicity, it is far from optimal since the best pretreatment / therapy regimen is pyridostigmine pretreatment and atropine / oxime reactivator, and anti-convulsant drug therapy does not prevent severe post-exposure convulsions, respiratory distress, tremors, and periods of unconsciousness, and behavioral impairment.

- **Pulmonary delivery—**More simple treatment by pulmonary delivery is possible. This may replace the use of autoinjectors (intramuscular injections) that have to pierce protective clothing required to be worm by people in exposed areas.

- **Highly experienced team**—In collaboration with scientists at Walter Reid Army Institute of Research (WRAIR) and The University of Nebraska and in conjunction with appropriate corporate partners, *ProCell* is in a favorably positioned to establish itself as the core provider of Butyrylcholinesterase for treatment of humans exposed to agents for which the enzyme has been shown to neutralize**.**

- **Pre-exposure treatments-** Will replace the need for masks and protective clothing that soldiers are now required to wear in high threat environments.

Edible HIV Vaccine:

The major objective is to demonstrate the utility of a novel non-invasive oral (edible) delivery system for administering an HIV vaccine into the human body. This delivery system will be initially tested by assessing the ability of SHIV (a recombinant virus between HIV and SIV used for vaccine studies) Gag and gp120 envelope proteins produced in plants (lettuce, spinach, corn, tomatoes) to induce robust cellular and humoral immune responses sufficient to prevent either infection (prophylactic vaccine) or disease progression (therapeutic vaccine) in monkeys and humans. If successful, this will greatly reduce the production costs of candidate HIV proteins by up to 1,000-fold and makes a mucosal edible vaccine for developing countries a real possibility in countries where the majority of people have a similar vegetable diet. In the past the cost of producing envelope proteins has greatly limited our ability to explore gp120 variants and the generation of and anti-viral effects of neutralization antibody.

As a rapid proof of concept, the p55 Gag and gp120 envelope proteins will be transiently expressed in a plant expression system either in the tobacco YT-2 cells and leaves. Once it has been shown these plant derived molecules are immunogenic, the HIV genes will be expressed in plants that are edible e.g. corn, lettuce, spinach. HIV-I Gag protein assembles into immature HIV-1 capsids (100-120 nm particles) containing from ~1,500 to 3,000 Gag (p55) polyproteins by budding from the host cell plasma membrane. The HIV surface gp120 and transmembrane gp41 determinants play major roles in viral tropism, fusion, entry and immune escape. They are also the major targets for anti-viral neutralizing antibodies

The company believes that the *delivery* of vaccines proteins by eating will provide a broad platform for developing and commercializing biotherapy and biopharmaceutical products at substantial cost advantages. The technology is adaptable to many targeted antigenic molecules in conjunction with co-stimulatory molecules (COS) required for an optimal immune response, *ProCell* scientists have extensive experience in performing SIV/HIV vaccine trials using the non-human primate model. Based on immunogenicity studies in rodents, vaccine trials in monkeys involving biological carriers will be performed according to previous protocols.

Value Proposition

- **Lower Cost**—plant derived proteins can be produced in green houses at up to 1,000 times less than classical mammalian expression systems.
- **Flexibility ---** Many different edible plants can be used to deliver vaccine depending on the diet of the vaccinees.
- **Simplicity of delivery ---** this is a non-invasive and simple means of administering vaccine.
- **Off-the-shelf**—product can be produced in plants which are then dried so the shelf life is very long.
- **Adaptability ---** Viral proteins for vaccines can be produced in plants at a low cost, purified and delivered by conventional means (i.m.).
- **Safety -** plants are not infected by potential human pathogens. For example, HIV, prions, HBV, West Nile Virus

Diagnostic Development Division:

This division will focus on the development of individual reagents and/or complete diagnostic kits for HIV and other infectious diseases. The effort in this division involves refining and optimizing methodology rather than performing additional research and animal testing. In addition, certain products will be readily available for the market. Two products will be the initial focus of *ProCell*: the development of an inexpensive **HIV p24 ELISA assay** for the detecting of HIV viral loads and the production of **HIV viral protein components.** In selected cases, the proteins will be actually components of the ELISA assay under development.

Ultra-sensitive HIV Detection Assay

Currently several techniques are used to detect HIV-1 infection***:***

- Assays detecting host antibodies to HIV-1, usually anti-p24 antibody.
- Immunoassays for p24 antigen.
- Nucleic acid-based diagnostics, mainly PCR-based assays.

The development of a new hypersensitive inexpensive p24 ELISA assay is being done in collaboration with *BioTraces Inc*. in Herndon, Virginia. The rationale for developing an immunoassay with sensitivity similar to the currently used RNA-based viral load, is that the p24 assay is both an inexpensive and simple to use detection assay that could replace the expensive RNA-based method for measuring HIV viral loads in the clinic. The ability of personnel with minimal training and lack of "high tech" laboratory facilities to perform these assays is critical for third world HIV vaccine trials.

BIOTRACES Inc. has developed a proprietary Multi Photon Detection^{TM} (MPD^{TM}) technology which permits quantitation of HIV-1 p24 to the equivalent of about ten virions. MPD enhanced immunoassays have achieved this unparalleled sensitivity and reliability of identification through the reduction of artefacts and non-specific biological background (NSBB). Currently this assay is being developed into a commercially and clinically viable format and validated for quantification of viral load. MPD permits full automation, including miniaturization and semi-automation to test hundreds of samples in parallel. The commercialisation of an optimised Clade B assay for the western world market and an in–house testing service for outside organizations will be considered in Phase III.

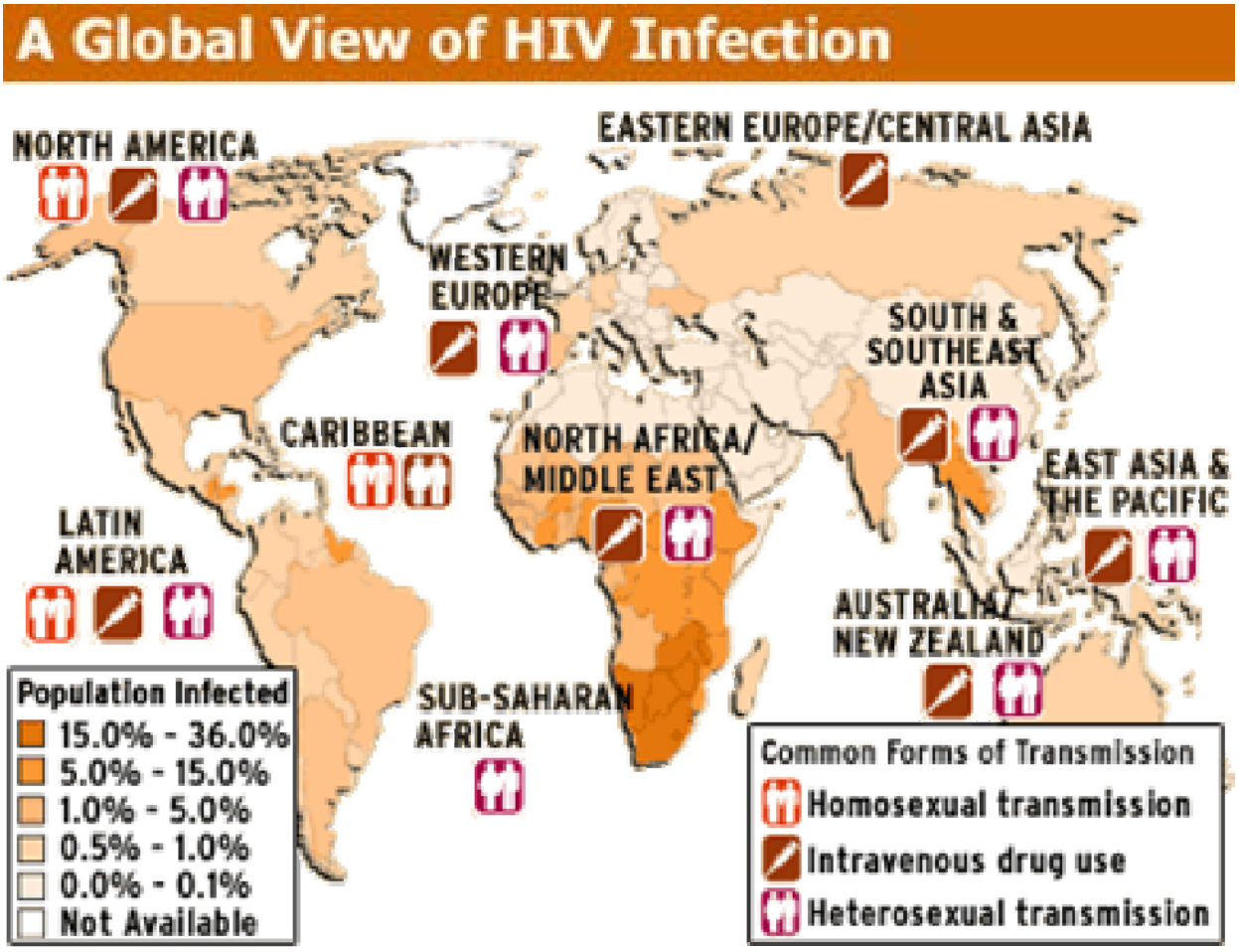
The prototype application of the immunoassay (IA-MPD) methodology to HIV-1 quantification is the detection of HIV in the breast milk of African women. *ProCell* is involved with the development of the appropriate HIV subtype C assay and the validation of the assay using breast milk from Zimbabwean and Zambian women. HIV-1 can be vertically transmitted from mother to child during the pre-, peri-, and/or post-partum periods. Breast-feeding further increases the risk of postnatal transmission. About 5.4% of children who had documented evidence of being uninfected in the postnatal period became infected following breast milk transmission of HIV ("late postnatal transmission"). While HIV-1 positive mothers in the USA do not breast feed their children, interventions to reduce the number of infants becoming infected are critical for women in developing countries where breast feeding is important to infant survival, but can also result in 30-50% infection. The risk of breastfeeding transmission was estimated to be 3% per year among infants who were documented to be HIV uninfected in the first 3 months of life. The risk of HIV transmission probably

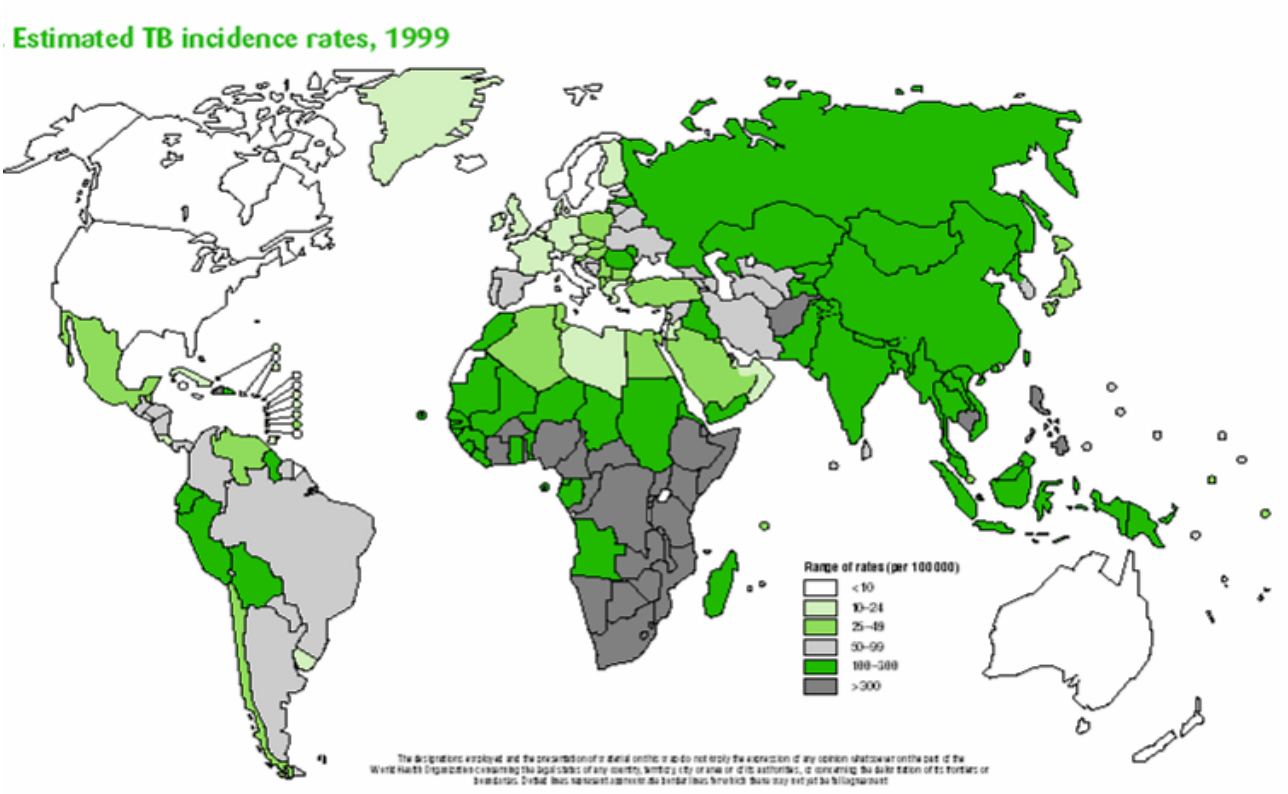
exceeds the mortality benefit of breast feeding beyond 3-7 months. The best estimates indicate that a lack of breastfeeding puts infants in developing countries at a two-fold increase in mortality; protective effects being greatest in the first 6 months of life.

PRODUCT SUMMARY:

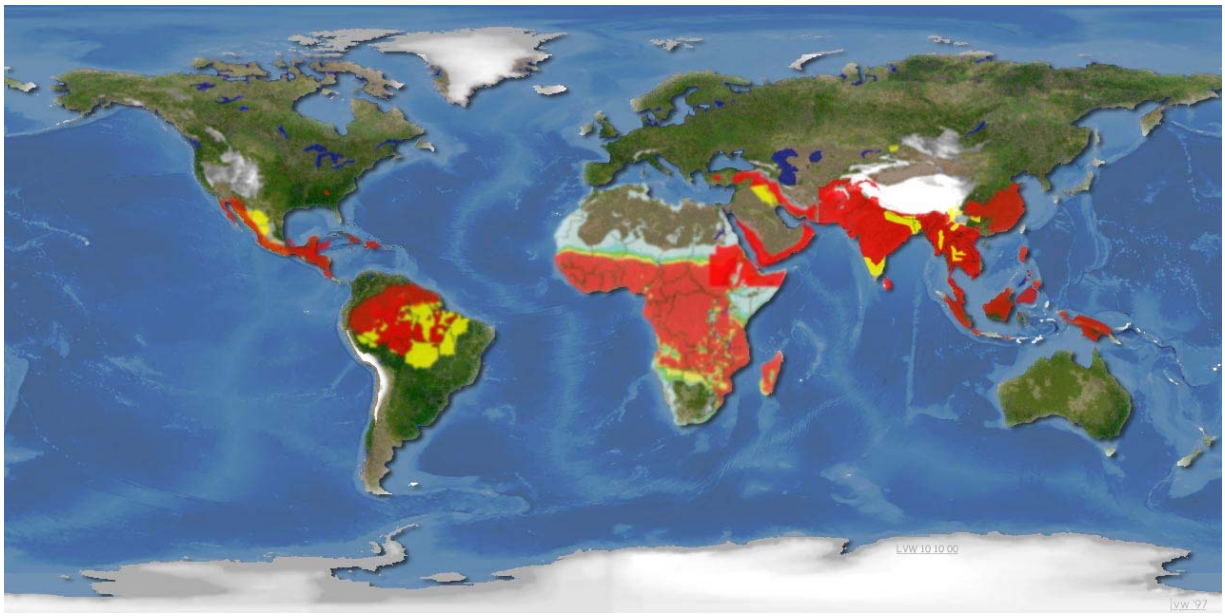
The benefits for the customer in utilising the Company's product and services are:

PRODUCT FEATURES		
FEATURE	BENEFIT	PROJECTED CAPABILITIES
Nerve Agent Antidote - BChE	Nerve agent scavenger	Fewer side effects
Edible HIV Vaccine	Inexpensive – delivered through the mouth	Halt progression of HIV to AIDS
HIV p24-based viral load assay	Inexpensive	Diction of HIV viral loads and production of HIV Lysates
HIV and any viral protein	Costs significantly reduced	Low cost components for many drugs.




Estimated TB incidence rates, 1999
Range of rates (per 100 000)
<10
10–24
25–49
50–99
100–300
>300

MALARIA



ProCell Corporation

PROFIT BENEFITS for INDUSTRY USERS of TECHNOLOGY

Product development: "Nerve Agent Antidote – Butyrylcholinesterase – BchE":

- **A potent and proven broadly based nerve agent scavenger.**
- **Prophylactic (before exposure) treatment for nerve agent exposure.**
- **Therapeutic (post exposure) treatment for nerve agent and drug exposure.**
- **ProCell is to develop an efficient pulmonary "puffer" deliver system.**
- **Fewer side effects.**

Product Development: "Edible HIV Vaccine":

Have a cookie!

- **A vaccine against Human Immunodeficiency Virus (HIV).**
- **Halts the progression of HIV to AIDS.**
- **Plant derived proteins produced in green houses at a mere fraction of the cost of classical mammalian expression system typically employed to manufacture drugs.**
- **Many different edible plants can be used to deliver vaccines.**
- **Product can be produced in plants which are then dried so the shelf life is very long.**
- **Delivery of vaccines is by way of uncooked "cookies".**

Application: "HIV p24-based viral load assay":

- **Complete diagnostic kits to accurately detect and monitor the levels of HIV in blood.**
- **Inexpensive alternative for monitoring HIV viral load.**
- **Subtype C HIV detection in breast milk of African women solved (not undertaken currently).**
- **Subtype B for western countries.**
- **Subtypes A & C for India, Russia and China.**

Product Development: "HIV and any viral or anti-viral protein components"

- **Individual plant-derived vaccine components can be sold separately.**

Product Development: "Virus-based adjuvant" - future

- **Novel vaccine adjuvant for boosting the immune responses induced by classical vaccines as well as individual vaccine components.**

Product Development: "Orally administered treatment for haemophilia" - future

- **Orally fed Factor VIII or Factor IX clotting agents for the treatment of Haemophilia A and B by feeding or inhalation.**