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Commitment and Care Across the Globe

*Making a world of difference
in HIV/AIDS and TB*



Foreword

As a leading healthcare company, we believe Roche has a social responsibility to provide care where access is limited – sadly this is precisely where HIV/AIDS is taking its greatest toll. We take this responsibility very seriously and will therefore continue to expand our AmpliCare Initiative throughout the world's poorest countries.

AmpliCare is the Roche Group's proactive response to the enormous humanitarian challenge of HIV/AIDS and TB. We aim to take on this challenge by increasing access to diagnostic tests in countries where the need is most urgent. Since its inception in 2002, the programme has increased access to HIV viral load tests at substantially reduced prices in sub-Saharan Africa and countries where the disease burden is highest.

AmpliCare focuses on the complete continuum of care, from testing to monitoring and education, and works to optimise efforts on a regional basis. This concept has its origins in a tiered pricing model aimed at supporting government and public health programmes.

The realisation of the AmpliCare Initiative is a tale of innovation and partnerships. The fight against HIV/AIDS and TB is a global struggle and therefore requires a global solution. It requires a remarkable level of innovation and deep-rooted commitment. At Roche, we believe that delivering the highest standard of care to all patients must remain our priority. Roche has partnered with national governments, local healthcare facilities, communities and international agencies,



including the Clinton Health Access Initiative (CHAI) and Centres for Disease Control (CDC), to establish programmes that would go far beyond providing merely diagnostic tests. These partnerships are the critical link in ensuring that our efforts are appropriate for every community and every individual that we reach.

Despite the successes of recent years, there is much to be done in improving access to healthcare in the world's poorest countries. Through the AmpliCare Initiative, we at Roche pledge to continue our ongoing contribution to the global fight against HIV/AIDS and TB.

Yours faithfully,

Daniel O' Day
Chief Operating Officer, Roche Diagnostics

Timeline of Care

Through initiatives and technology

Roche has been integrally involved in combating HIV/AIDS since introducing its first HIV-1 test in 1985.

1985

Launch of first Roche test for diagnosis of HIV: the antibody ELISA HIV-1 Test (ELISA: Enzyme-Linked Immuno-Sorbent Assay). Within the first eight to twelve weeks after infection with HIV the body's immune system produces antibodies to fight the virus. This test provides simply a 'yes' or 'no' response of the body's reaction to an infection and does not detect or quantify the amount of actual virus in the body. Therefore this test cannot adequately detect HIV in immune-compromised patients, nor provide guidance on treatment success or failure.

1991

Roche acquires the rights to polymerase chain reaction (PCR) technology. One of the most widely used molecular biology techniques used from daily practicalities of medical diagnosis to the courts of law. PCR takes the analysis of tiny amounts of genetic material to a new level of precision and reliability putting genetic research within reach of all biologists – even those with no previous training in molecular biology.

1992

Introduction of the first molecular HIV test - AMPLICOR® HIV-1 DNA Test - for the direct detection of the HIV-1 virus in the pre-seroconversion window period, and for diagnosis of infants born to HIV-1-infected mothers.

1995

Start of Thailand HIV-NAT Initiative for research and monitoring. In line with the objective of providing care to people in need. This project was set up to translate findings of the West to the local situation in Thailand.

Launch of AMPLICOR® HIV-1 MONITOR Test, the first standardised 'quantitative' test for measuring the amount of virus. Launch outside of the United States providing essential monitoring of viral load levels to establish and monitor the effectiveness of therapeutic regimens, assess the potential of drug resistance, and identify treatment failure.

1996

First HIV medications are FDA approved using HIV viral load as a surrogate marker, decreasing time to approvals and increasing access to life-saving drugs.

1998

Roche inaugurated the Global Surveillance Programme at the International AIDS Conference in Geneva. Initially designed solely to monitor changes in the HIV-1 genome sequence, the Programme and its database has since expanded to include thousands of genomic sequences for multiple viruses, including HCV, HBV, and WNV, in the world's most relevant geographic regions. The Programme's efforts have played a monumental role in helping to maintain, and improve, the reliability of molecular assays.

1999

Launch of automated HIV-1 viral load monitoring with the COBAS® AMPLICOR analyser. Automation of testing reduces laboratory costs, allows higher throughput of tests and leads to faster availability of the results.

2002

Start of the CARE Africa treatment programme with the PharmAccess Foundation to extend access to HIV/AIDS care in the Ivory Coast, Senegal, Kenya and Uganda.

Botswana-Harvard AIDS Institute partnership: establishing state-of-the-art laboratories and care.

Birth of the AmpliCare Initiative.



2003

Introduction of the COBAS® TaqMan® analyser, the next generation in automation using real time PCR technology for enhanced sensitivity and extended dynamic range.

Start of the Cambodia Treatment Access Programme: increasing access to sustainable HIV care.

Launch of the PCR Academy in South Africa: providing training programmes and continuing education for healthcare professionals.

2004

William J. Clinton Presidential Foundation international partnership: Roche signs agreement with this foundation in order to broaden access to state-of-the-art HIV testing for people in developing countries.

2005/2007

COBAS® AmpliPrep/COBAS® TaqMan® HIV Test for automated sample preparation, amplification and quantitation of HIV-1 RNA approved for use. The test was the first to introduce fully automated real-time PCR testing of HIV-1 allowing for less hands-on time and faster time to results.



2008

Roche developed a turnkey solution – the COBAS® AmpliPrep/COBAS® TaqMan HIV-1 Qualitative Test – specifically for Sub-Saharan Africa. This is the first qualitative test with the ability to utilise plasma, whole blood and/or Dried Blood Spot (DBS) as a sample material making sample collection easy, even from the smallest of infants in the most rural of settings with limited technology.

Roche improves HIV-1 testing for HIV patients already taking antiretroviral therapies with the COBAS® AmpliPrep/COBAS® TaqMan® HIV Test v2.0, the first quantitative viral load test to amplify and detect two separate regions of current and emerging target genomic variants of HIV with increased sensitivity.

Public Private Partnership (PPP) agreement signed between UNITAID, Clinton Foundation and Roche. Part of the DNA PCR Infant Testing Initiative to supply diagnostic products to developing countries in sub-Saharan Africa as part of a paediatric scale-up programme. This PPP would give paediatric HIV a much needed boost and sees close to 300,000 infants enrolled into care and treatment in this period.

2009

Under the UNITAID/CHAI PPP, five new Turn Key Laboratories for Early Infant Diagnosis are set-up across sub-Saharan Africa in areas where the disease burden is highest and the need for infrastructure development is the greatest. Over 900,000 tests were made available to infants across sub-Saharan Africa.

2010

Launch of the LightCycler Mycobacterium detection test. This PCR based assay allows for a simple, rapid and accurate detection of *M. tuberculosis*, *M. avium* and *M. kansasii* from sputum. This assay was developed in South Africa, and is suitable for an African setting.

The AmpliCare Initiative: *A contribution by Roche*

According to the WHO and UNAIDS, it is estimated that close to 33 million people were living with HIV at the end of 2008. Of these, an alarming two thirds of HIV infections were in sub-Saharan Africa alone. In the same year, 2.7 million people became newly infected and 2 million died of AIDS, of which 280,000 were children.¹

People living with HIV are in need of care and treatment and often too poor to procure it along with the challenge that there is little healthcare infrastructure. Due to recent advances in therapeutic drugs and treatment programmes, and the commitment of national governments to prioritise treatment, many people living with HIV/AIDS today harbour a newfound level of hope. Through the AmpliCare Initiative, Roche expands access to laboratory tests for diagnosis and monitoring of those on therapy, a necessary component of HIV/AIDS treatment and management programmes.

In infants, early diagnosis is critical in determining HIV exposure. A single test can make the difference between life and death for an infant. As a result of the presence of maternal antibodies in the infant, a rapid test cannot be used for accurate diagnosis and a molecular test is required to make this diagnosis.

In adults, monitoring HIV viral load levels is crucial as this provides essential feedback on treatment success in caring for AIDS patients. The virus replicates at a very high rate and mutations occur. The end result can be the advent of a drug-resistant virus that will ultimately evade the drugs the patient is taking. Once a patient has started on anti-retroviral therapy, routine monitoring of HIV viral load is critical. With viral load results, physicians can determine increasing levels of HIV in the blood stream indicating a potential onset of drug resistance in a patient and, if necessary, a decision to modify a patient's treatment. Today, the Roche AmpliCare Initiative remains at the forefront of action and innovation in addressing the HIV/AIDS pandemic, making care possible for people affected by HIV.



What is the AmpliCare Initiative?

Founded in South Africa in 2002, the AmpliCare Initiative is a multifaceted programme that seeks to increase access to diagnostic and monitoring tools in HIV/AIDS to least developed countries.*

When anti-retrovirals (ARVs) became available and affordable to least developed countries, including sub-Saharan Africa, Roche realised that the cost of diagnostic tests used to diagnose HIV and monitor anti-retroviral therapy needed to be realigned with the drugs and decided to resolve this concern by creating a sustainable programme offering tests at substantially reduced prices. Through the AmpliCare Initiative, Roche is helping to develop effective local solutions for resource limited settings and providing more affordable diagnostic tests without compromising quality. An example of this 'effective localisation' is seen in the wide-spread uptake in the use of dried blood spots (DBS) as a suitable sample replacement for transport of blood from infants in the HIV early infant diagnosis (EID) programme.

Our healthcare priorities are based on the following principles:

- 1 Sustainable reduced pricing**
- 2 Business sustainability with measurable impact**
- 3 Research and development into 'high burden disease'**
- 4 Using skills transfer to empower rather than pure donations**
- 5 Capacity building initiatives**
- 6 Public-private partnerships**

The AmpliCare Initiative has evolved over the years and now seeks to address the inequalities in access, not just in HIV/AIDS, but with other diseases, such as TB as well.

* Least developed countries (LDCs) as defined by the UN – (i) low-income; (ii) human resource weakness and (iii) an economic vulnerability (www.un.org)



Tackling AIDS

One continent at a time

Africa



The AmpliCare programme encompasses a wide range of activities around the globe, reaching patients in the epicentre of the HIV/AIDS crisis.

Focus on education

For many years African countries have relied on the Roche AmpliCare Education booklet to help educate the public about HIV/AIDS. The booklet covers a wide range of topics, from explaining what HIV/AIDS is to safety procedures for handling blood. In March 2004, Roche released a French version of the booklet, making it available for patients and healthcare providers in Francophone countries.

In 2005, in partnership with the Centres for Disease Control (CDC), Roche supported and funded the development of a training DVD specifically for healthcare workers for use in the collection of dried blood spots (DBS) from infants exposed to HIV. This training tool is also available worldwide.

Patients and healthcare professionals interested in this educational material can contact their local Roche office. (www.roche.com/roche_worldwide)

South Africa: making an impact on early infant diagnosis

Since early 2000, in partnership with the Department of Health and the National Health Laboratory Services (NHLS), Roche has been providing access to their AMPLICOR HIV-1 DNA test used for the early infant diagnosis (EID) programme at a substantially reduced price. Today, in public hospitals throughout South Africa, the AmpliCare Initiative is helping to diagnose infants born of HIV-positive mothers. The AMPLICOR HIV-1 DNA test provides reliable information on whether the baby is infected with HIV or not.

The extensive HIV research conducted at these sites, as a result of the AmpliCare Initiative, has also had a direct impact on national policy. These studies have shown that testing infants at six weeks of age or earlier for HIV gives a clear and accurate diagnosis.² As a result, the government of South Africa officially recognises testing at six weeks as part of its national therapy guidelines for the South African AIDS treatment. This policy has also been recommended by the WHO.

Providing training

As part of Roche's continued investment in South Africa, the PCR Academy was established at the National Institute for Communicable Diseases (NICD) in Johannesburg, South Africa in 2003. The PCR Academy provides training for people from across sub-Saharan Africa and creates training programmes for medical scientists and technologists. It provides assistance for laboratories and addresses the rising need for continuing education of healthcare professionals working with sexually transmitted diseases, including HIV/AIDS. The PCR Academy is an accredited facility and is fully equipped with state-of-the-art instrumentation. The extensive training covers all platforms, instruments and tests used in the AmpliCare programme, as well as PCR technology in general and good laboratory practices with world-class standards. To date, the PCR Academy has held over 500 training workshops, both on site and using PCR Academy experts in field locations.

Botswana: pioneering treatment programmes

Botswana has one of the highest HIV infection rates in the world, but is a prime example of an African country demonstrating tremendous efforts to fight HIV/AIDS. Since January 2002, the Botswana Government implemented a national programme to distribute anti-retroviral therapy and HIV viral load monitoring to over 300,000 people with HIV/AIDS. Initiated as a joint partnership between the Harvard AIDS Institute and the Government of Botswana, the centre of excellence was built in Gaborone, which initiated the monitoring arm of the ARV programme. This massive programme is an example of the success a committed partnership can achieve.

Working in partnership

As the global leader in its field, Roche was invited to offer a solution to the vast testing infrastructure demands of such a project and demonstrated its capacity to offer a fully integrated and scalable testing portfolio, further supported by a complete data management system. Subsequently, other partners have joined the fight against HIV/AIDS in Botswana such as the Centres for Disease Control (CDC) and the Bill and Melinda Gates Foundation. Together with the Botswana Government, these partnerships have increased and ensured access to world-class HIV diagnostic tests in what are now among the most advanced research and testing facilities in Africa. In addition, laboratories have been built in Botswana with fully automated instruments for clinical monitoring and real time viral load testing.

Enabling HIV ground-breaking studies

These laboratory facilities have fostered a host of new research on HIV and AIDS, including groundbreaking studies on mother-to-child transmission and on new technologies for isolated patient populations. Through the Botswana programme, Roche is supplying one of the most advanced technologies in HIV testing to one of the world's least developed nations. Botswana



The PCR Academy at the National Institute for Communicable Diseases (NICD) in Johannesburg, South Africa.

has become a reference and model for other African countries.

More recently, Roche has partnered with the Namibian Government to support their ARV programme and is currently assisting in their National ARV scale-up plans.

Asia

Thailand: 100,000 HIV/AIDS patients under managed care

Since 1995, Roche has been working with HIV-NAT – an international collaboration between The Netherlands, Australia and the HIV Research Centre of the Thai Red Cross Society – to establish an HIV clinical research organisation to conduct studies in Thailand and other countries in Asia. In addition to providing anti-retrovirals and diagnostic testing for the programme, Roche also provides ongoing scientific input and problem-solving expertise to help ensure the long-term success of this initiative. An estimated 1,200 people living with HIV/AIDS in Thailand are now benefiting from this initiative. Since 2008, the National Security Health Office (NHSO) has begun to implement an HIV patient management programme to provide anti-retroviral drugs and monitoring assays, including HIV drug resistance testing for HIV patients. Currently, an estimated 100,000 HIV/AIDS patients are under the care of this programme. NHSO plans to increase this number year by year.

Cambodia: over 1,000 HIV/AIDS patients received free healthcare

The prevalence of HIV amongst adults in Cambodia is estimated to be the highest in Asia. In response, Roche teamed up with two key partners – namely the Cambodian Ministry of Health and the National Centre in HIV Epidemiology and Clinical Research at the University of New South Wales, Australia – to launch the Cambodia Treatment Access Project in 2003. The project has successfully provided access to HIV healthcare, including anti-retroviral therapy, as well as training of healthcare professionals. The company's support includes funding, medicines and HIV viral load testing which has in turn led to this worthwhile initiative enrolling over 1,000 people living with HIV/AIDS. A clinic has been built, patient counselling provided, screening, laboratory monitoring and clinical care are offered, as well as preventative treatment for opportunistic infections and HIV/AIDS therapy in Cambodia's capital, Phnom Penh. The Clinton Foundation is currently working with the Cambodian Ministry of Health to provide support for HIV patient management. This includes the supply of medicines and HIV viral load tests.

In Asia, Roche has established strong international partnerships.



Latin America and the Caribbean

In Latin America and the Caribbean, Roche supports major mother-to-child transmission studies.

Brazil: reducing transmission

Clinical studies show that in Brazil currently 90% of children infected with HIV-1 under 13 years of age are infected by vertical transmission (from mother to fetus) and that among these, 15-45% of children born to untreated positive mothers. Among the validated methods for direct diagnosis of HIV-1 infection in the newborn, the most applicable is a qualitative way to detect pro-viral DNA.

In order to tackle Brazil's limited resources to provide tests to analyse viral DNA within the National STD/AIDS Programme, the Brazilian Health Ministry developed a programme utilising the Roche AMPLICOR HIV-1 DNA Test. This programme has been implemented in laboratories throughout the country that provide around 40,000 tests to people living with HIV/AIDS per year. Pregnant women with no determined serology for HIV-1 and children of HIV positive mothers will also participate in the study.

Prior to the programme, other methods such as ELISA, Western Blot and Indirect Immunofluorescence were used to detect HIV, which are ineffective in children below 18 months of age.

In addition, the COBAS® AmpliPrep/COBAS® TaqMan® HIV Qualitative Test has addressed growing concerns regarding HIV infection in infants as a result of mother-to-child infection in this South American region.

This project has been implemented in close collaboration with Roche Diagnostics South Africa, Roche



Molecular Systems, USA and the Clinton Foundation. Countries included in this project within the Caribbean Region are Guyana, Jamaica, Barbados and Bahamas.

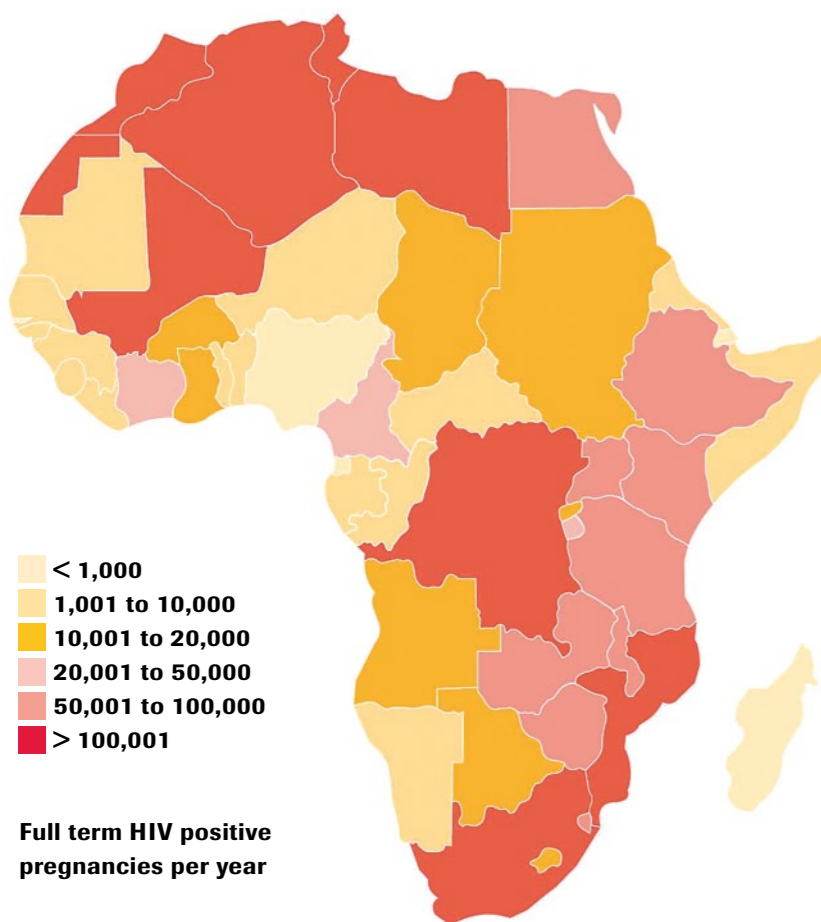
Peru: supporting treatment compliance

The Peruvian National Institute of Health (INS) leads and owns the HIV National Programme offering treatment, monitoring and training courses for patients and technologists as well as medical assistance for HIV/AIDS patients in Peru.

Roche provides the INS with instruments for 27,000 samples per year, therefore supporting antiretroviral therapy efficacy and adherence. Roche also makes a contribution in terms of technical support for training programmes, good laboratory practices, quality control and PCR technology.

Early Infant Diagnosis

Giving HIV exposed infants their best chance



Reducing Mother-to-child-transmission of HIV

In sub-Saharan Africa, mother-to-child-transmission (MTCT) of HIV is considered the primary cause of HIV infection in children. This transmission can occur at one of three time points: in utero (across the placental barrier), peri-partum (during labour) or post partum (through breastfeeding). In 2007, the WHO estimated that 2.5 million children under the age of 15 years are infected with HIV worldwide, of which 420,000 were new infections. In the same year, more than 280,000 children under 15 years died of AIDS. Without prevention measures, children born to HIV positive mothers will become infected. Without treatment, one third of children living with HIV die before the age of one year and almost 50% by the second year. The good news is that with current intervention strategies, transmission rates can be reduced depending on the intervention available.

The percentage of HIV-positive pregnant women who received antiretrovirals to prevent HIV transmission to their children increased from 35% in 2007 to 45% in 2008. Within sub-Saharan Africa, countries in Eastern and Southern Africa reported substantial progress, reaching a coverage of 58% in 2008. The coverage of infant antiretroviral prophylaxis also increased, reaching 32% in 2008, up from 20% in 2007.³

Although the transmission of HIV from mother to their infant is reduced through effective prevention of mother-to-child-transmission (pMTCT) programmes, some infants can become infected with HIV post-partum, through breast feeding. Early diagnosis of HIV allows babies to receive appropriate care. This includes medical intervention in case they are HIV infected and often before they have significant illnesses. This allows the infant to remain healthy despite their HIV status.

However, the issue of MTCT cannot be viewed apart from other preventive strategies, especially in resource limited settings. Voluntary counseling and testing, infant nutrition and infant diagnosis go hand-in-hand with the pMTCT programmes, and should be viewed as complex interventions. All the components need to be addressed,

even if only with robust policies to ensure sustainable and impactful programmes.

Early diagnosis – reducing the period of uncertainty

All children born to HIV-positive mothers passively receive antibodies across the placenta. While the use of rapid tests may prove useful in determining whether there was any exposure to HIV in-utero or peri-partum, these antibody based tests cannot diagnose true infection. This complicates early diagnosis of these infants where standard RAPID* or ELISA based immunoassays are used alone. Maternal antibodies can persist for up to 18 months, and the uncertainty surrounding the HIV status of the child has a negative effect on the potential clinical management of the child.

Enabling early and appropriate care

Early diagnosis of HIV in infants is made possible using molecular based tests and allows for rapid implementation of anti-retroviral therapy (ART) in infected children. Roche's HIV Qualitative assay reduces this time of uncertainty significantly by providing reliable and accurate information on whether the baby is truly infected with HIV or not. This period can be a very trying time for a new mother as her well-being is closely tied to the well-being of her infant. Correctly diagnosing the infant's status, whether negative or positive, can impact the care the infant must receive within these vital few weeks. Furthermore, the diagnostic information will allow the healthcare worker to advise the mother to adopt the best practices for her child once they have departed the clinic.

Early testing of HIV-exposed infants must be given priority within the global and national scale-up of pMTCT programmes. Much can be learned from the successful interventions implemented by a number of countries in sub-Saharan Africa with substantially higher coverage of early infant diagnosis: as much as 80%. It is also important for these countries to improve the follow-up of known HIV-exposed infants and continue to invest in innovative approaches such as using mobile technology.



* RAPID: A rapid test is an easy-to perform, point-of-care investigation for detecting antibody to HIV, the result of which is provided at the same setting of the consultation.



Innovative approaches for challenging situations

Dried blood spot (DBS) technology for resource limited settings

In many resource constrained countries, the lack of infrastructure such as roads, hospitals and laboratories, as well as qualified personnel poses major obstacles for patients' access to effective diagnostic testing.

The challenge starts with key elements, such as uninterrupted supplies of clean water or food. In rural areas, access to general medical care is difficult or even impossible for many people in need, and a day long trip needed to see a physician is not unusual. This is even more valid for special care required to treat more medically demanding conditions such as opportunistic

infections in HIV positive patients. While experience shows that the latest technology for diagnosis can be used in resource constrained settings, the long distances the patients would have to travel to get to these centres remain a very high or even insurmountable hurdle.

For many years, Roche has invested in innovative approaches to overcome these hurdles, for example assisting in validating the use of dried blood spots (DBS) technology for PCR testing. The main aim in the development of this technology was that it would allow the samples to be easily collected at remote clinics. Samples could be sent by standard mail and stored more easily than whole blood samples. The ultimate goal of expanding access dramatically to remote areas was realised through DBS.

Today, PCR testing can be reliably performed on site with adequate laboratory capacity using DBS specimens. Despite the in-roads achieved, the roll-out of diagnostic protocols is often challenged by a lack of technical competencies, under-developed laboratory capacity and weak systems for transporting specimens and results. Despite these challenges, many countries in sub-Saharan Africa have made significant progress in expanding access to infant HIV testing services. In 2008, close to 67% of countries reported that they provide HIV testing services, on site, through the use of DBS. This represents an increase of 46% from countries that reported in 2007. However, globally, the uptake of infant HIV testing still remains low.

Understanding loss to follow-up

In 2008, in some countries in sub-Saharan Africa the percentage of children accessing Early Infant Diagnosis (EID) within the first two months of life – was as low as 15%. Even with the availability of PCR technology, the uptake of infants into ARV programmes remains low owing to a high attrition rate post partum. This low uptake is mainly attributable to loss of follow-up. Loss of follow-up further accounts for the limited uptake of essential interventions, such as

co-trimoxazole prophylaxis. This creates a weakness and lack of integration of post-natal follow-up systems in maternal, newborn and child health settings.

Loss of follow-up is a complex issue; the result of logistical bottlenecks, for example, getting samples from the site, getting results back to the clinic; socio-economic constraints that prevent the mother returning to the clinic to collect the results and technological limitations which are well documented in public health literature.^{4,5,6} A singular event, such as returning of results to the clinic, can vary from 6 weeks to 3 months, during which time, many of the exposed infants may have died or the mother is de-motivated for a variety of reasons to return to the clinic, specifically for the result.

Short message (SMS) reporting solutions

The use of mobile technology has recently been hailed as the innovation to watch in healthcare. The penetration of mobile phones in sub-Saharan Africa, has surpassed expectation, given the low levels of income in some of these communities. Many organisations have tried to harness this tool, for use in HIV/AIDS education and awareness campaigns.

More recently, mobile technology has been integrated in some health systems, whereby patients receive reminders to take their medication and also to request clinic visits.

Roche has been exploring the use of this technology to address one link in sample referral systems; getting results back to the clinic. In early 2009, in conjunction with a few key stakeholders – Clinton Foundation, National Health Laboratory Service (NHLS) and Industry IT solution providers – initiated a working group to explore this option for Roche's EID solution. Since the introduction of an increased throughput automation for high-volume EID programmes, Roche has developed an interface to a cost-effective SMS printer which would allow results to be directly transmitted from the laboratory to the clinic, sometimes a few hundred kilometers away, via a short message (SMS)



within a few seconds. This simple change in the referral system means that now the infants' HIV results can be transmitted to clinics without the need for transport networks.

Turn key laboratory solutions

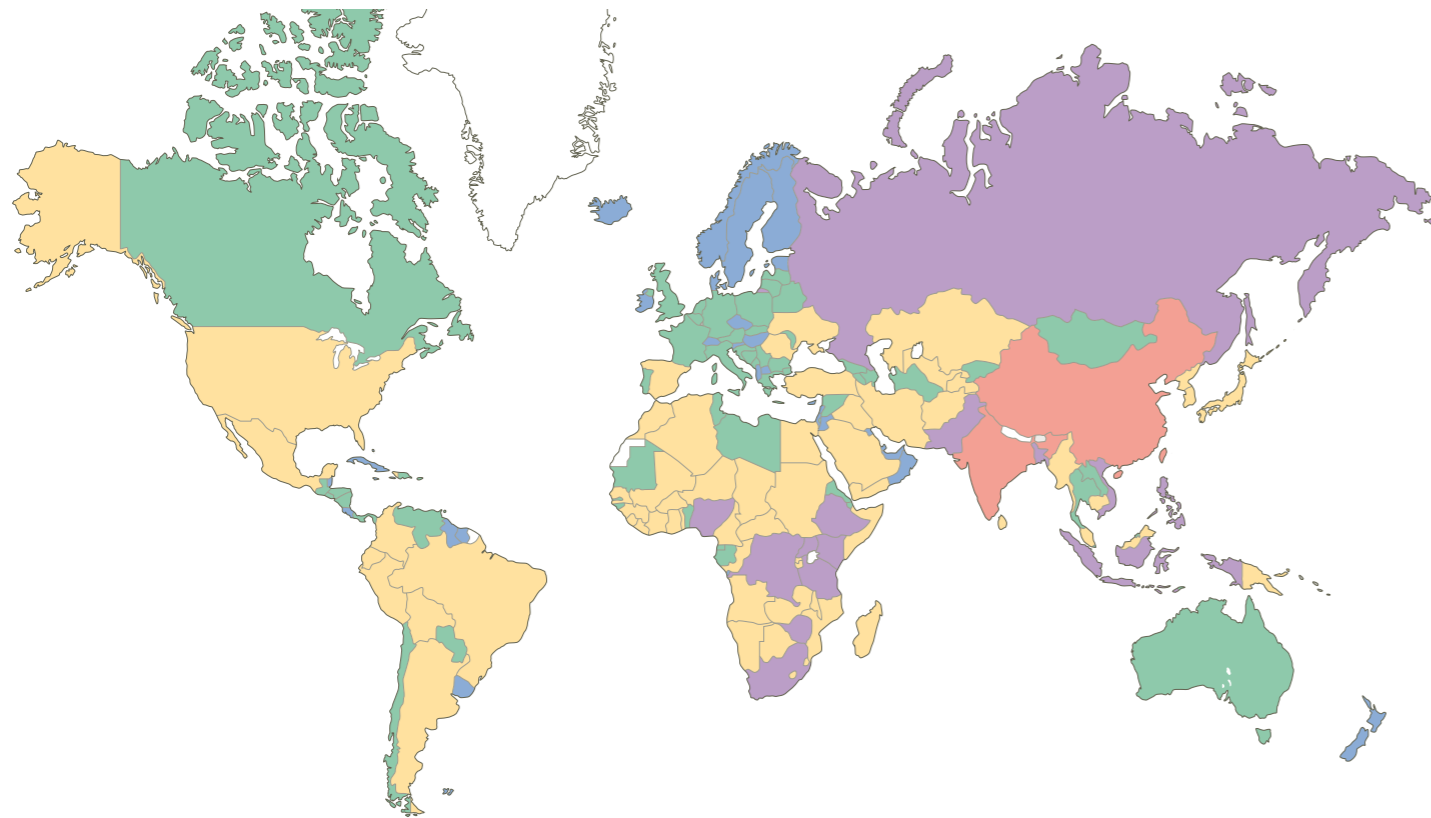
In 2008, Roche entered into a Public Private Partnership (PPP) with French Funder UNITAID and the Clinton Foundation. The main aim was to provide diagnostic products for infant HIV testing. One of the products that was uniquely designed to service this PPP, was a 'Turn Key Laboratory', where all components required for the establishment of a diagnostic laboratory for EID would be provided by Roche. This paradigm shift in expanding laboratory services translates into a considerably reduced lead time to roll out of EID services. As part of the turn key offering, capacity building was reinforced through off-site and on-site certified workshops for all laboratory staff. As a result, PCR testing is now routine in more than 100 laboratories in sub-Saharan Africa.



Dried blood spots on a collection card. The DBS technology is an innovative approach to expand access to remote areas.

The Challenge of Tuberculosis

HIV and TB: a lethal combination



Estimated number of new TB cases, by country, 2007 (all forms)

- 0–999
- 1,000–9,999
- 10,000–99,000
- 100,000–999,999
- ≥ 1,000,000
- No estimate

Tuberculosis (TB), an infectious disease caused by bacteria, is curable yet kills 5,000 people a day worldwide and the WHO estimates that a quarter of TB deaths are HIV associated, most of them being in Africa.⁷ On the African continent alone, HIV is the single most important factor determining the increased incidence of TB in the past 10 years.

In many people infected with TB bacilli, the immune system fends off the infection resulting in the infection lying dormant for years. However, when the immune system of a respective person is already weak, this 'silent' infection can progress. This makes TB a leading killer amongst people living with the HIV infection who have an already weakened immune system, accounting for about 13% of AIDS deaths worldwide.

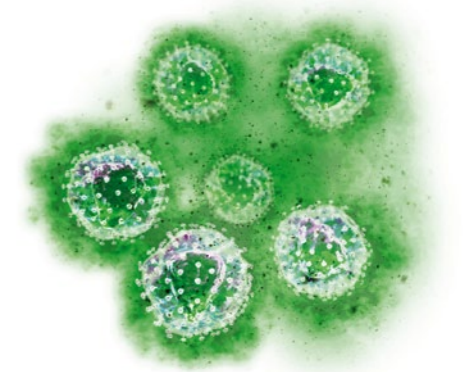
HIV and TB each speed the other's progress

HIV and TB form a lethal combination, each speeding the other's progress. A respective person who is HIV-positive and infected with TB bacilli is more likely to become sick with TB than someone infected with TB bacilli who is HIV-negative. TB is a leading cause of death among people who are HIV-positive. In Africa, HIV is the single most important factor contributing to the increase in the incidence of TB since 1990.

The WHO and its international partners have formed the TB/HIV Working Group, which develops global policy on the control of HIV-related TB, and advises on how those fighting against TB and HIV can work together to tackle this lethal combination. The interim policy on collaborative TB/HIV activities describes steps to create mechanisms of collaboration between TB and HIV/AIDS programmes, to reduce the burden of TB among people and in turn reducing the burden of HIV among TB patients.



***Mycobacterium tuberculosis* bacteria (top) and human immunodeficiency viruses under high magnification.**



The LightCycler® Mycobacterium detection kit

Roche remains committed to finding a workable diagnostics solution that improves on the current tools being utilised in resource limited settings to screen and/or detect tuberculosis. Several investigations were undertaken to develop a cost-effective, easy access, quick turnaround time, reliable PCR-based molecular solution for Africa and the developing world. A successful example of this undertaking is the LightCycler Mycobacterium detection test which was developed primarily for the health requirements of South Africa. This convenient and easy to perform test offers a number of advantages over the current methods. It enables differentiation between different species of the tuberculosis bacteria from human sputum samples, and provides laboratories with reliable, accurate and objective results within hours, significantly improving patient management. Use of the test result could lead to significant improvements in turnaround times for the patient.



Beyond AmpliCare

The Roche Group's commitment to HIV



Future directions

Expanding into new countries

Roche plans to extend AmpliCare to countries in need of this programme throughout the world, focusing on the United Nation's designated least developed countries. Outside of sub-Saharan Africa, considerations are made based on the individual needs of a specific country. Through these efforts, the AmpliCare initiative intends to create sustainable programmes to bring access to diagnostics in line with HIV therapies worldwide.

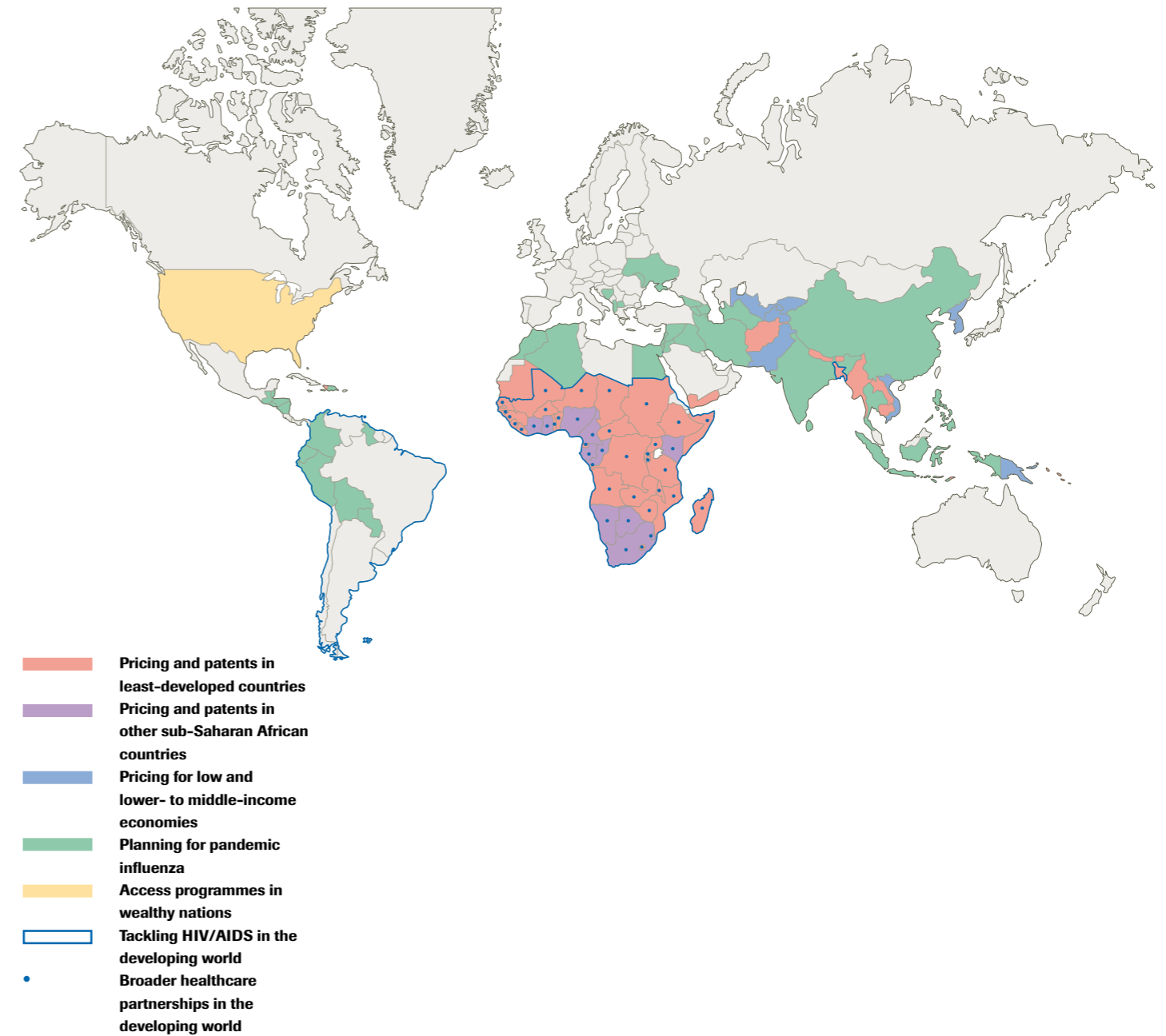
Surveillance to monitor change

As part of our efforts, Roche inaugurated the Global Surveillance Programme in 1998 at the International AIDS Conference in Geneva. Initially designed solely to monitor changes in the HIV-1 genome sequence, the programme and its database has since expanded to include thousands of genomic sequences for multiple viruses, including HCV, HBV, and WNV. The result is continuous analysis and improvement, leading ultimately to better diagnostics, better prognostics, and better disease management. The programme's efforts and many achievements have played a monumental role in helping to maintain and improve the reliability of molecular assays. Innumerable researchers, physicians and patients around the world have benefited as a result.

Providing access to vital HIV treatment

For people living with HIV/AIDS, therapy is a life-long commitment. Delivering HIV medicines for effective HIV/AIDS treatment is not the same as delivering food aid. At Roche, we recognise the extent and the complex nature of this challenge and understand that continued collaboration with various partners throughout the world is indispensable. Large-scale change cannot happen without a significant, coordinated effort. Roche began by looking internally: joining forces between its diagnostic and pharmaceutical divisions on projects in Africa, Cambodia and Thailand. Roche also has formed strong partnerships with independent non-profit organisations, academic centres, governments

Roche's programmes helping access to medicines for people living with HIV





and non-governmental organisations to help deliver comprehensive and sustainable HIV/AIDS healthcare where it is most needed.

Enabling 45-fold increase in patients receiving HIV treatment

One such collaboration is the Accelerating Access Initiative (AAI), the first broad-based public/private partnership to explore ways to provide sustainable access to HIV care in resource-poor countries. Roche became a founding member of AAI in May 2000. This has resulted in an over 45-fold increase in the number of people being treated with medicines supplied by AAI companies in Africa since its establishment.

Commitment not to file patents in LDCs

The commitment of Roche to constantly innovate its approach to addressing the challenges of HIV/AIDS treatment, particularly helping those people living in the poorest and hardest hit countries is reflected in its patent and pricing policies as well as technology transfer. No patents for any of Roche medicines – across all disease areas – are being filed in the world's Least Developed Countries (LDCs), as defined by the UN. Roche does not file patents on new HIV/AIDS medicines in Least Developed Countries or sub-Saharan Africa and Roche will not take action in these countries against the sale or manufacture of generic versions of anti-retroviral medicines. Generic versions of such HIV medicines can therefore be produced in LDCs and sub-Saharan Africa without the need for a voluntary or compulsory license.

Sharing knowledge and expertise

As part of our commitment to increase access to HIV treatment and to address the need for second-line therapy options, in 2006 Roche commenced an 'AIDS Technology Transfer Initiative.' The aim of the initiative was to share the knowledge we have developed to manufacture our HIV protease inhibitor, saquinavir, and provide hands-on guidance to local manufacturers from least developed countries and those within sub-Saharan Africa.

The initiative has been well received and a total of 13 agreements have been signed with local manufacturers and institutions from eligible countries. Since the launch of the initiative, Roche has received expressions of interest from 41 manufacturers and institutions in 17 eligible countries. We have also conducted assessment visits with 39 companies to determine timing and delivery of technical expertise.

No-profit pricing

Further, Roche makes its HIV protease inhibitors Invi-rase and Viracept available at no profit prices for direct supplies from Roche Basel to LDCs and sub-Saharan Africa. (see www.roche-hiv.com)

Sustainable solutions

Roche has come a long way in the fight against HIV/AIDS and TB, but there remains much to be done. As a company, we have made great strides through our dedication and partnerships. However, Roche recognises that we cannot achieve this goal on our own. In understanding successful interventions, we believe that the common thread linking these successes is strong political will and leadership at the highest levels.

The commitment of Roche to constantly innovate its approach in addressing the challenges of HIV/AIDS and TB is reflected in the AmpliCare principles. Roche believes that part of its responsibility as one of the world's leading healthcare companies is to use its expertise to improve access to healthcare. The company is committed to finding healthcare solutions that are sustainable and have a long-term impact, particularly on the lives of people in least developed countries, especially sub-Saharan Africa.



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The AmpliCare Portfolio

Advancing healthcare priorities through technology



The AmpliCare Initiative relies upon a variety of instruments and tests, which are based on the Nobel prize-winning PCR technology. This technology allows for accurate testing. Since acquiring the rights to PCR technology in 1991, Roche has developed and led the molecular diagnostics testing market, and has made PCR the world's leading nucleic acid testing technology.

Diagnostic testing requires a varying range of services and technical support. The AmpliCare Initiative works with each laboratory or health centre to determine which of these products will be both possible and most useful in their setting and offers a tailor-made solution. The products included in the initiative consist of a set of reagent kits and the instruments that support them.



Instruments

Below are instruments currently available for sample preparation and amplification / detection / analysis.

COBAS® AmpliPrep Instrument

The COBAS® AmpliPrep Instrument automates the sample preparation steps for PCR with robotic precision, dramatically reducing hands-on time and increasing laboratory productivity.

The COBAS® AmpliPrep Instrument can be used together with both detection instruments.

COBAS® TaqMan® Analyser

This is Roche's clinical 'real-time PCR instrument', designed for clinical diagnostics laboratories that are seeking a solution to the complexity of molecular diagnostics testing, and require a single, simple system for all of their real-time PCR needs.

The COBAS® TaqMan® 48 Analyser is a semi-automated, closed-tube system that makes molecular testing practical for everyday lab use. The compact footprint requires little space and provides fast results, advanced assay performance, enhanced workflow and reduces contamination risks.



The LightCycler® System

The LightCycler® System is the fastest real-time thermal cycler available. This system combines real-time PCR with product detection using fluorogenic hybridisation probes to achieve rapid PCR results.



Tests

There are many reagent kits for HIV diagnosis and HIV-1 RNA viral load monitoring. Available HIV-1 RNA viral load tests range from the manual AMPLICOR HIV-1 Monitor test up to the new, fully automated COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Tests.

AMPLICOR HIV DNA Test

The AMPLICOR HIV-1 DNA Test is the 'gold standard' for the amplification, detection and results reporting associated with HIV-1 qualitative tests for early detection of infection in infants. This assay will continue to be available in the foreseeable future for all international public health interventions in resource limited settings, and until Roche is available to provide a suitable alternative for low demand countries.

COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Qual Test

The COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Qual Test is a qualitative nucleic acid amplification test for the detection of Human Immunodeficiency Virus Type 1 (HIV-1) RNA and proviral DNA in plasma, anticoagulated fresh whole blood and dried blood spots. This test is run on the COBAS® AmpliPrep Instrument for automated sample processing and the COBAS® TaqMan® Analyser or COBAS® TaqMan® 48 Analyser for automated amplification and detection.

COBAS® TaqMan® HIV-1 v2.0 Monitor Test

The COBAS® TaqMan® HIV-1 Test, runs real-time PCR instrumentation. The use of real-time PCR technology

assists accurate detection of HIV-1 viral load Group M subtypes A-H with an improved dynamic range over the original COBAS® Amplicor viral load test. COBAS® TaqMan® HIV-1 v2.0 assays offer highly sensitive and specific HIV-1 viral load tests. The high specificity reduces expensive repeat testing and prevents false positive results that can compromise long-term therapeutic management. The use of a dual target means that the sensitivity is improved, especially in the presence of recombinant versions of the virus. This simplifies ordering of HIV-1 viral load tests for physicians, and also prevents unnecessary repeat testing. With the prevalence of non-B subtypes increasing worldwide, the ability of Roche's viral load tests to accurately detect and quantify diverse subtypes, has become critical in HIV/AIDS patient care.

Continued advances in HIV-1 drug therapy require the measurement and detection of low levels of the virus. AmpliCare provides the most sophisticated automated tests to remote laboratories to offer accurate, sensitive and uncompromised monitoring of patients' HIV-1 RNA viral load. This enables field doctors to assess their patients' responses to anti-retroviral therapies.

Roche's groundbreaking dual-target approach for HIV-1 RNA viral load testing compensates for the possibility of resistant HIV-1 strains circulating in the patients blood as a result of antiviral therapy. This innovative approach ensures security and reliability of test results and more confidence in assessing viral loads.

