ICBS Report for the years of funding by the Bill and Melinda Gates Foundation

By

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Background

In contrast to the high level of prevention of transfusion-transmissible infections (TTIs) in industrialized countries, most of the developing countries sadly do not enjoy the same degree of prevention. Blood transfusion therefore continues to be an important route of transmission of TTIs in the developing world. According to WHO more than 75 million units of blood are donated globally each year; and 40% (about 30 million units of blood) of this global blood supply is donated in countries with Low and Medium Human Development Index (HDI). Up to 13 million units of the global blood supply are not screened for all relevant TTIs, mainly in low or medium HDI countries. It is estimated that 43% of the blood collected in developing countries is not tested for TTIs (especially HIV, HCV, HBV; Syphilis, Chagas disease).

The International Consortium for Blood Safety (ICBS) was established in September 1998 because of grave concerns regarding the poor level of blood safety in most of the developing countries and to contribute to the alleviation and improvement of the poor and substandard level of blood safety in these countries. From the start ICBS was well aware that the organization of long-term national programs for a community-based blood-donor system on a purely voluntary, non-remunerated basis, with good donor selection criteria, would greatly contribute to the safety of blood donations. ICBS also recognized the importance of other elements such as quality assurance covering the entire spectrum of blood transfusion service, training of personnel and appropriate use of blood products. While many developed countries and international organizations, through bilateral agreements were and still are trying to assist developing countries to improve their blood transfusion services, little, if any, had been done to make available a sustainable supply of affordable, high quality, blood screening reagents. ICBS decided to complement the efforts of other organizations and focus its goals on this neglected area by working towards the elimination of the disparity between the industrialized and developing countries with regard to the sustainable availability of quality assured screening reagents. Approaches that received little attention from other providers have been emphasized by ICBS as reflected in its mission.

The causes of the problem of poor blood safety in the developing world are diverse and complex. Although many developing countries may claim to screen the donated blood, their screening may not necessarily cover all blood units throughout the country or be performed throughout the year. The lack of affordable and quality assured reagents for the screening of blood donations, a fact long recognized by ICBS, has largely contributed to the deplorable state of blood safety in countries with restricted economy. Due to the relatively high cost of blood

screening tests for viral markers in general, and, particularly for HBV and HCV, a lot of the blood collected in most of the developing world is not screened. In rural areas blood is often transfused without testing; and even in many urban blood banks the blood is far from safe. Besides, the sustainability of screening depends on the regular and uninterrupted availability of testing reagents, which is difficult to maintain in many developing countries, especially those depending on donations provided by some of the developed countries. The Ministries of Health of many countries in the developing world have no specific budget allocated for blood safety. The unsatisfactory quality of testing poses another grave problem. A number of local companies in developing countries have now begun manufacturing blood-screening reagents. The cost of these reagents is more affordable; however the important issue of the quality of these testing kits emerges.

Rationale

The rationale and basis of the ICBS project was the need for urgent and intensive intervention to slow down and eventually stop the continuous deterioration of the blood safety situation in many countries of the developing world and to prevent TTIs in these countries, predominantly HIV, HCV and HBV. TTIs in the developing world occur commonly among patients suffering from malaria induced anemia, pregnancy related complications requiring blood transfusion and patients suffering from other diseases requiring blood transfusion. A contributing factor to the demand for blood transfusion is its use, as the last resort, for the treatment of anemia which is still prevalent in some regions of the world and a lot of which is attributed to malaria in children especially in Africa.

Despite the fact that TTIs, compared to other routes of infection, are practically more preventable, blood transfusion continues to be an important route of transmission of TTIs in the developing world. As mentioned earlier, in contrast to the high level of prevention of TTIs in industrialized countries, most of the developing countries lag far behind. In principle TTIs should not occur (although we understand that transfusion cannot be absolutely safe). Both blood recipients and blood donors all over the world are entitled to proper care to ensure the prevention of TTIs, which are indeed preventable.

The impact of TTIs is considerable. Transfusion of blood infected with blood borne pathogens leads to a substantial burden of infection among transfused patients. The efficiency of transmission of HIV from infected blood is more than 90%; and in the case of HBV and HCV it is more than 70% to 80%. Besides, due to depletion of work force and loss of skills, TTIs contribute to costs in the form of lost services, which in turn lead to lower national productivity and increased demands on the health and social sectors. When standards of blood safety are improved, lives are saved through the prevention of infections and complications that could otherwise result from transfusing unsafe blood. The consequence of improved standards of blood safety is a reduction of TTIs to the lowest achievable level by the use of available and appropriate technology. There is no doubt that a routine, quality assured screening of blood donors for TTIs has a remarkable impact on health by contributing to a marked reduction of TTIs.

Transfusing safe blood leads to considerable savings in the direct cost of treatment (when available) and other health expenditure. The use of safe blood would also reduce the indirect cost of lost output due to morbidity, disability and premature death. Although this preventive approach is of paramount importance, it should also be remembered that the option of treatment is not always available in many developing countries, or only available at relatively high cost to those who could afford it. Additionally the cost of treatment is not always considered or compared with the cost of preventive measures by decision makers in many developing

countries. The cost to society of each infection will depend on the cost of lost workdays, hospitalization etc. It is also worthy of mention that many policy makers in developing countries ignore the results of the scarce cost-effectiveness studies available in this field, because analysis of these studies compares an output indicator such as lives and disability-adjusted life years averted (which is not measured in monetary units), with costs that are measured in monetary units. These infections contribute to increased costs in the form of lost services due to depletion of the work force and loss of skills, which in turn lead to lower national productivity and increased demands on the health and social sectors. There is a bigger picture that one needs to look at besides cost-effectiveness. In addition to safety there are social and ethical issues; and related aspects need to also be taken into account such as considering equity and demonstrating a respect for human rights.

Mission, Goal & Objectives & Activities

The **mission** of ICBS is to improve blood safety in developing countries by achieving affordable and quality assured blood screening, establishing quality systems, providing requisite training and coordinating technology transfer. ICBS' activities complement national and international efforts in the area of blood safety, thus contributing to the elimination of the disparity between the industrialized and the developing world, agencies, or through bilateral agreements with developed countries and by collaborating / coordinating with the other providers.

The following are the major **goals and objectives** of ICBS:

1- Improve and upgrade the level of testing for blood safety in countries of the developing world.

Objective 1-1

Provision of the requisite quantity of needed test-kits to some public blood banks.

Objective 1-2

Identification, validation and provision of information on available high-quality, affordable tests kits

Objective 1-3

Achieving the commitments of governments to work towards sustainable testing for blood safety

2- Assist in establishing and upgrading quality assurance programs and setting up quality systems in blood transfusion centers and blood banks of developing countries.

Objective 2-1

Encourage establishment and upgrading of quality assurance programs and arrange for participation in External Quality Assessment Schemes

Objective 2-2

Establish Model Demonstration/Training Centers & Technology transfer

3- Collaboration with WHO and all other pertinent major organizations and institutions in order to complement efforts and maximize appropriate utilization.

Objective 3-1

Establish and maintain collaboration with major bodies supporting blood safety improvement in developing countries

Support provided by ICBS

Support provided by ICBS included the following:

- Assisting countries to achieve sustainable safety testing of all blood units collected by blood banks by:
    - Providing public blood banks in 15 countries (12 African countries, 2 countries in the Western Pacific Region and one Latin American country: *Benin, Burkina Faso,*

Burundi, Cape Verde, Congo, Ghana, Guinea, Laos, Liberia, Mali, Niger, Paraguay, Senegal, Togo, and Viet Nam) with blood screening reagents for a limited period;
    - Advising 24 countries which received ICBS assistance (*Benin, Burkina Faso, Burundi, Cape Verde, Congo, Ghana, Guinea, India, Indonesia, Kazakhstan, Kyrgyzstan, Laos, Liberia, Mali, Moldova, Niger, Pakistan, Paraguay, Senegal, Tajikistan, Togo, Turkmenistan Uzbekistan and Viet Nam*) on efficient reagents' purchase mechanisms; and
    - Informing the 24 countries which received ICBS assistance on the availability of affordable high quality reagents.
- Assisting in the evaluation of blood safety kits available in the market to identify reagents at low cost and of good quality. This was facilitated by means of :
    - Training scientists from a few countries (*India, Pakistan, Viet Nam and Moldova*) in proper systems for the evaluation and licensing of reagents;
    - Establishing ICBS Master Panels;
    - Initially providing, as appropriate, national control authority laboratories (*India*) with ICBS panels, and providing assistance to enable them to develop their own panels for continued use;
    - Training scientists in the preparation, characterization and establishment of national panels (*India and Viet Nam*);
    - Sponsoring a well-established center (*Paul-Ehrlich-Institut –PEI- in Langen, Germany*) for the evaluation of blood-screening test kits to identify affordable, high quality, screening reagents;
    - Providing this international center with ICBS Master Panels.
- Playing an important role in training in specific areas, especially assisting in training in blood safety laboratory testing techniques and conducting and sponsoring workshops to train trainers (from the 24 countries which received ICBS assistance) in the principles and practices of blood safety quality assurance.
- Establishing demonstration/training centers (Bandung- Indonesia, Bishkek- Kyrgyzstan and Islamabad- Pakistan)
- Helping, as appropriate, regions/countries to establish central confirmatory reference laboratories (India)

Prerequisites for ICBS to consider providing support:

The following were the prerequisites for ICBS to consider providing support:

1- Availability of necessary funds for ICBS to initiate activities
2- Assessment of the blood transfusion service in the country considered for support, based on information collected from various sources and/or an ICBS team fact-finding visit followed by identification of priorities
3- Government commitment
4- Presence of leadership
5- Non-duplication and maximization of resources by complementing existing support provided by other organizations, agencies or through bilateral agreements; and coordination with the other providers.

The scope of ICBS' activities in the countries that received ICBS assistance was directed towards contributing to the improvement of blood safety. This was accomplished by supporting national programs and projects aimed at achieving affordable and quality assured blood screening of all blood units collected by the blood banks. The support and its nature depended on the findings of situation assessment of blood transfusion services, recognizing problems and identifying priorities. Whenever possible and applicable, ICBS sought to maximize the resources by complementing existing support provided by other organizations.

The main activities carried out during the years of the project to meet the objectives are presented in this report under the following headings in line with the afore-mentioned goals and objectives:

1- Assistance to improve and upgrade the level of testing for blood safety:
   1-A- Provision to some public blood banks with the requisite quantity of needed test-kits
   1-B- Identification, validation and providing information on available high-quality, affordable tests kits
   1-C- Governments' commitments.
2- ICBS assistance in establishing and upgrading quality assurance programs and setting up quality systems in blood transfusion centers and blood banks of developing countries:
   2-A- External Quality Assessment Systems
   2-B- Model Demonstration/Training Centers & Technology transfer.
3- Collaboration with WHO and all other pertinent major organizations and institutions in order to complement efforts and maximize appropriate utilization.

1- Assistance to improve and upgrade the level of testing for blood safety

A- Provision of the requisite quantity of needed test-kits to some blood banks

ICBS provided public blood banks in 15 (12 African countries, 2 countries in the Western Pacific Region and one Latin American country). ICBS supported countries in accordance with the Memoranda of Understanding (MOUs) signed by the health authorities of these countries with the requisite quantity of blood screening reagents (HCV and HBV test kits - mainly HCV test kits) for a limited period with a gradual phasing out mostly within 3 years. In the MOUs the authorities in the respective Ministries of Health indicated their commitment to ensure the sustainability of screening of all the blood units collected by the blood banks.

From available data received from 10 African countries which reported having tested 140511 blood units per year for HCV antibody, 4065 blood units were discarded because they tested positive to HCV-antibody. The percentage is 2.89% (which is close to the WHO estimated prevalence for HCV worldwide i.e. 3%). Based on the reports and information from 36 African countries, it is reported that a total of 1 119 577 blood units were collected by the 36 countries. Fifteen of these countries (including the 12 countries supported by ICBS) test blood units for HCV, 17 do not test at all and 9 perform partial testing. The discarded blood in these countries ranged from 1 & 2 % to 32 % varying from one country to another. Out of 1 119 577 blood units collected in the 36 countries, 564 553 units were not tested for HCV antibodies. There were 16937 recipients, of whom the number of recipients not reacting positively to HCV prior to the transfusion would have been 16429 recipients. Based on the fact that 70% to 80% will develop infection with HCV as a result of receiving the infected blood units; in the 36 countries there would be at least 11500 to 13143 newly infected HCV persons per year, as result of receiving HCV though unscreened blood. This clearly demonstrates the importance of continuing the efforts to introduce HCV screening of all blood units collected by the blood banks in all countries.

B- Identification, validation and providing information on available high-quality, affordable test kits

ICBS established its HCV Master Panel and Negative Master Panel in September 2002. The HCV Master Panel is composed of 200 members distributed among all major known genotypes. The 200 anti-HCV positive members of the HCV panel were selected from 1021 units that were initially anti-HCV reactive after local testing in the countries of origin. The 1021 units were resourced by ICBS from various geographic zones with the assistance of collaborators in Brazil, Egypt, Indonesia, Ivory Coast, South Africa, Vietnam and the United States. The Negative Master Panel is composed of 200 members tested negative for anti-

HCV, HBsAg, and anti-HIV. Each unit was subsequently tested at the Division of Viral Hepatitis, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA for anti-HCV by HCV 3.0 (Ortho-Clinical Diagnostics, Raritan, New Jersey) and confirmed by RIBA 3.0 (Chiron Corp, Emeryville, California). All confirmed anti-HCV positive units were tested, in parallel at the CDC and Visible Genetics (VGI), NorCross, GA, USA, by PCR to quantitative HCV RNA (Amplicor HCV Monitor, Roche Molecular Systems, Roche Diagnostics Corporation, Indianapolis, Indiana). HCV genotype and subtype were determined by direct DNA sequencing using two different strategies. The 200 anti-HCV positive members were selected on the basis of the characterization results obtained by both institutions (CDC and VGI). Whenever possible, the samples were selected for use in the HCV Master Panel when positive by serology, PCR and show genotype concordance. The 200 member anti-HCV confirmed positive panel is composed of the following HCV genotypes: 1 (33.5%, n=67), 2 (11.5%, n=23), 3 (19.5%, n=39), 4 (18%, n=36), 5 (1.5%, n=3) and 6 (16%, n=32) collected from the afore-mentioned seven countries.

The last phase in establishing the ICBS HBsAg Master Panel and its corresponding Normal Panel were accomplished in mid-March 2005. Seven-hundred and twenty HBsAg positive units were collected from diverse regions around the world: Brazil (Sao Paolo and Manaus), Egypt, Ivory Coast, Jordan, Tunisia, Vietnam and USA (New York and Atlanta). These units were fully-characterized at CDC as well as at the partnering laboratory, the Department of Medical Sciences in the Toshiba General Hospital in Japan. The HBsAg Master Panel is composed of 200 members and includes representation of worldwide genotypes A, B, C, D, E, F and their corresponding variety of subtypes. Of these 200 members, 146 individual members are included for the purposes of testing clinical sensitivity. The remaining 54 members comprise HBsAg Dilution series for the purposes of testing analytical sensitivity. (This series is created from nine carefully-selected members, in a series of dilutions. These members represent all of the aforementioned major genotypes as well as a full-range of corresponding HBV subtypes (adw2, adw4, ayw1, ayw2, adr, ayw3, and ayw4). In addition, out of over 400 non-infectious plasma units received from the American Red Cross, Washington D.C. (U.S.A.), a corresponding Negative Panel composed of 200 members was also manufactured.

The concept of setting up the "ICBS Test–Kit Evaluation Center" became a reality because the majority of countries in the developing world do not have regulatory institutions / laboratories capable of evaluating test-kits for blood screening. ICBS and the Paul-Ehrlich-Institut (PEI) in Langen, Germany, agreed to collaborate and established the center within PEI's structure. ICBS used and continues to use, through the Test-kit Evaluation Center, its HCV Master Panel and Negative Master Panel to evaluate HCV test-kits bought directly from the market in countries with limited resources from all over the world, with most of them having been produced in developing countries or countries with transition economies. So far, forty-two assays for the detection of antibodies to hepatitis C virus (HCV) and sixty nine HBsAg test kits were evaluated for their sensitivity and specificity performance as well as other characteristics.

C- Governments' commitments

C-1 In India: Since the first visit of ICBS experts to India, one of the important decisions made by the Government of India with regard to blood safety was to mandate universal testing of all transfused blood for HCV. Funds were made available by the government and testing of blood units collected by public blood banks for anti-HCV has been implemented since 2001.

C-2 In Pakistan: Steps were taken to fulfill one of the government's commitments in the Memorandum of Understanding (MOU) signed with ICBS. The Government of Pakistan passed legislation on both compulsory screening for all TTIs as well as the maintenance of essential standards by the blood banks in all the provinces. Since 2003 the Government committed funds for purchasing Hepatitis C test-kits. The legislation on compulsory screening for all TTIs and creating a budget line to purchase Hepatitis C test-kits (in addition to test-kits for other transfusion transmitted infections) is the right path leading to sustainability.

C-3 In Indonesia: Both the Government and the Indonesian Red Cross are working towards improving blood transfusion services. On a regulatory level the Ministry of Health is updating the Government Regulation and Policy on Blood Transfusion. The National Agency of Drug and Food Control of the Republic of Indonesia also submitted a regulatory document of Good Manufacturing Practices for human blood and blood products to the authorities for approval. For its part the Indonesian Red Cross continues, despite many constraints, to make an effort to strengthen blood transfusion centers at central, provincial and district levels. Emphasis is put on improving the quality of services and training. Blood units are screened for syphilis, HBV, HCV and HIV. However quality of testing still needs improvement.

2- ICBS assistance in establishing and upgrading quality assurance programs and setting up quality systems in blood transfusion centers and blood banks of developing countries

ICBS contributed to the improvement of the quality of testing and to the development and upgrading of quality assurance programs in countries which received ICBS assistance. The tools used were: conducting External Quality Assessment Schemes, training in establishing quality systems and establishing model demonstration centers for training of trainers and technology transfer.

A- External Quality Assessment Schemes

A-1 The Institute for Infectious Diseases at the Free University of Berlin, Germany and the Institute for Diagnostics and Biotechnology, Berlin, Germany agreed to include ICBS in its External Quality Assessment Schemes (EQAS), at no cost to ICBS, thus permitting major focal laboratories in developing countries usually in charge of national quality assurance for blood safety programs (46 laboratories from 40 countries), to participate free of charge in their virology international external quality assessment schemes conducted on behalf of the German Institute for Documentation and Standardization (INSTAND), ICBS and WHO. The following are the countries participating in the program:- Sixteen countries (19 laboratories) from the African Region (AFR): Algeria (1 laboratory), Botswana (1 laboratory), Burkina Faso (1 laboratory), Congo (1 laboratory), Eritrea (1 laboratory), Ethiopia (1 laboratory), Ghana (2 laboratories), Kenya (3 laboratories), Lesotho (1 laboratory), Madagascar (1 laboratory), Mali (1 laboratory), Senegal (1 laboratory), Tanzania (1 laboratory), Chad (1 laboratory), Togo (1 laboratory) and Zambia (1 laboratory).
Three countries (3 laboratories) from the Americas: Brazil (1 laboratory), Nicaragua (1 laboratory) and Trinidad (1 laboratory).
Ten countries (12 laboratories) from the Eastern Mediterranean Region (EMR):- Iran (2 laboratories), Morocco (1 laboratory),Oman (2 laboratories), Pakistan (1 laboratory), Qatar (1 laboratory), Syria (1 laboratory), Tunisia (1 laboratory), Turkey (1 laboratory), United Arab Emirates (1 laboratory), Yemen (1 laboratory) and Zambia (1 laboratory).
Two countries (2 laboratories) from the European Region (EUR):- Cyprus (1 laboratory) am Malta (1 laboratory).

Six countries (7 laboratories) from the (South East Asian Region - SEAR):- India (2 laboratories), Korea (1 laboratory), Myanmar (1 laboratory), Philippines (1 laboratory), Sri Lanka (1 laboratory) and Thailand (1 laboratory) and
Three countries (three laboratories) from the Western Pacific Region (WPR):- China (1 laboratory), Malaysia (1 laboratory) and Vietnam (1 laboratory).

A-2 For all of Indonesia's blood banks ICBS has provided external quality assessment panels to evaluate the sensitivity and specificity of testing for TTIs. Of 147 participating Indonesian Red Cross blood transfusion centers, the results obtained were correct from 128 blood transfusion centers (87%) for HBsAg testing, 70 blood transfusion centers (48%) for anti-HCV testing and 130 blood transfusion centers (88%) for anti-HIV testing. In response to the unsatisfactory results of the external quality assessment scheme (EQAS), corrective action was undertaken wherever needed. The corrective action included retraining of personnel, improving equipment maintenance, using ELISA assays rather than rapid test kits, abandoning of pooling in serological testing and advising on centralization of blood screening. As expected, the corrective measures undertaken to improve the quality of services lead to an almost one hundred percent increase in the blood service cost in the country.

A-3 Fundação Pró-Sangue/Hemocentro de São Paulo is conducting PAHO/ICBS/ Pró-Sangue/Hemocentro EQAS for the Latin American countries and countries of the Caribbean Region.

B- Model Demonstration/Training Centers & Technology transfer

ICBS continued to support the model demonstration/training centers in Indonesia, Pakistan and Central Asia.

B-1 In **Indonesia**, ICBS provided help to set up a centralized blood safety quality management system and establish a provincial demonstration model at the Bandung Blood Transfusion Center. The Bandung Center will provide quality service and will be able to both teach and provide training for other similar blood centers in Indonesia. Several training workshops have already been conducted in this center.

B-2 In **Pakistan** ICBS supported towards the establishment of the National Reference Center for Blood Transfusion Services at National Institute of Health (NIH), which has been officially designated by the Ministry of Health. ICBS obtained a contribution from WHO-EMRO to train Pakistani scientists at the ICBS Collaborating Centers in Berlin and Langen in Germany and in Groningen in the Netherlands. They were trained in virology (genomic amplification techniques, genotyping, constructing and utilizing serological panels, conventional techniques) and Quality Assurance/GLP, with particular reference to virology testing. Additionally WHO-EMRO support to this project was provided under the Work plan entitled 'Blood Safety 2004-05' to cover a variety of activities.

B-3 In **Central Asia** ICBS established a Demonstration/Training Center located in Bishkek, Kyrgyzstan for the five countries of Central Asia (*Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan*). Several activities took place in this model-training center. The activities addressed the following aspects: putting in place essential elements of quality systems and good laboratory practice in virology screening as an illustration of the principles of quality assurance/GLP as well as total quality management and their application. ICBS, in collaboration with WHO-EURO, conducted a series of training workshops in Bishkek on Quality Management; Quality Assurance of HIV and Hepatitis Testing and Biosafety in the Laboratory. The workshops were attended by participants from the five countries of Central

Asia. In addition, ICBS in collaboration with CDC/CAR, conducted a series of training workshops (6 in total) on blood safety in *Kyrgyzstan, Uzbekistan, Tajikistan, Turkmenistan and Kazakhstan*.

3- <u>Collaboration with WHO and all other pertinent major organizations and institutions in order to complement efforts and maximize appropriate utilization of resources.</u>

During a relatively short period, ICBS became recognized by the majority of international organizations and institutions dealing with blood safety. Today, eighteen international organizations and institutions dealing with blood safety have liaison members to ICBS. Whenever possible, these organizations, associations, institutions and others were involved in collaborative activities in the developing countries. ICBS closely collaborated with organizations and institutions that significantly contributed to the ICBS activities in kind and/or cash.

In order to maximize resources and to enable institutions with the requisite capability and willingness to contribute to ICBS' efforts and to the improvement of blood safety in the developing world, ICBS decided to establish co-operative arrangements (***Collaborating Centers***) with some key institutions in both the developed and developing world. These Collaborating Centers were intended to support ICBS' activities and to provide a roster of technical experts and laboratories to assist ICBS in meeting its goals. The following (in order of date of designation) are the current 11 ICBS collaborating centers: 1) Sanquin Blood Bank Region Noord Oost, The Netherlands. 2) Laboratory Of Virology, Lindsley F Kimball Research Institute at The New York Blood Center (NYBC), New York, USA., 3) The Institute For Infectious Diseases At The Free University of Berlin, Germany, 4) The German Institute for Standardization and Documentation in Laboratory Medicine, Duesseldorf, Germany, 5) The Institute For Diagnostics and Biotechnology, Berlin, Germany, 6) The Paul-Ehrlich-Institut (PEI), Langen, Germany, 7) The National Blood Transfusion Center, Abidjan, Ivory Coast, 8) Hepatitis Division, Centers For Disease Control (CDC), Atlanta, GA, U.S.A., 9) Shanghai Blood Center, Shanghai, China, 10) Fundação Pró-Sangue Hemocentro de São Paulo, Brazil, and 11) National Reference Laboratory in Tashkent, Uzbekistan.

Each of the Collaborating Centers supported ICBS and provided, and some of them continue to provide, assistance in some or all of the following areas:

- Training in:
  - –Structure and organization of blood supply systems
  - –Donor selection
  - –Laboratory blood-screening techniques
  - – Quality assurance
  - –How to implement quality systems and total quality management
  - –Biosafety
  - –Preparation, characterization and establishment of national/regional panels and standards
  - –Proper systems for the evaluation and licensing of reagents
  - –Clinical use of blood.
- Providing support towards the establishment of fully characterized ICBS Master Panels
- Contributing to:
  - –Development of training material and guidelines
  - –Improvement of quality assurance and installing quality systems in the blood testing facilities of blood banks
  - –Monitoring process of performance through external quality assessment.

–ICBS assessment process to evaluate the performance characteristics of currently available commercial screening test kits for blood safety by fostering the ICBS Test Kits Evaluation Center.

- Providing batch-to-batch test kits evaluation services to manufacturers especially from the developing world.
- Helping to establish national reference laboratories in some developing countries.
- Providing information about the prevalence of TTIs, especially in the developing world.
- Providing consultation services, information, advice and reference service.
- Collaborating and providing support, as appropriate, to ICBS country projects.
- Assisting in technology transfer.

Based on the advice of the Health Program of the Bill and Melinda Gates Foundation, ICBS decided at its Annual Meeting in July 2003 to postpone the establishment of the ICBS HIV Master Panel until the necessary additional funds were raised.

The plans and implementation of activities were made in accordance with the major goals while, whenever required, effecting necessary adjustments in the implementation process to adapt to local circumstances and conditions. As an example, following the visit of the ICBS team to India, the decision of the Indian Government to mandate universal testing of blood collected for transfusion purposes for antibodies to HCV led ICBS to consider extending assistance to countries in other geographic areas in Asia, Africa and Latin America, while continuing to assist India in upgrading quality assurance programs and establishing reference confirmatory laboratories.

Some of major accomplishments

If we would like to only mention to 6 major accomplishments for this project within the terms of the Bill and Melinda Gates Foundation's grant agreement (for more accomplishments and details please see above under description of activities), these 6 major accomplishments are as follows:

1. Establishment of the Master Panels to serve for the evaluation of commercially available test kits, especially those used and/or produced by the developing countries.
2. Establishment of the Evaluation Center & Evaluation of test-kits with the purpose of identifying affordable high quality blood screening reagents.
3. Introduction of the policy of testing blood units for HCV antibody thus contributing to the safety of blood units collected in the blood banks in the developing countries supported by ICBS.
4. Establishment of demonstration/training centers
5. Activities to establish quality systems in the working place (blood banks).
6. Designation of ICBS Collaborating Centers- which ensures that certain important activities conducted by these centers on behalf of ICBS would continue at no cost to ICBS even when ICBS lacks funds.

Impact

- We believe that the evaluation of test kits used to screen for TTIs markers utilizing the fully characterized ICBS Master Panels and providing information on the availability of affordable high quality blood screening reagents will significantly contribute to the sustainability of testing blood units in the developing world and subsequent decrease in TTIs.
- The World Bank project in Viet Nam, which was preceded by a preparatory phase of ICBS support, will hopefully result in a long lasting improvement in blood safety.

- The legislation of the Government of Pakistan on compulsory screening for all transfusion-transmitted infections and creating a budget line to purchase Hepatitis C test-kits (in addition to test-kits for other transfusion transmitted infections) is the right path to sustainability.
- The collaboration and close cooperation between PAHO and ICBS in supporting training activities and the introduction of screening for HCV of blood collected by the blood banks, has resulted in the marked increase of screening for HCV, of blood units collected today by the blood banks in Latin American and Caribbean countries. Eleven (of 19) Latin American countries and eight (of 22) Caribbean countries are testing all blood units collected by public blood banks for HCV.
- In Indonesia as a result of ICBS helping to establish both a blood safety quality management system at the central level and a provincial demonstration model at the Bandung Blood Transfusion Center, significant improvements have been achieved including:
    a- Standard operating procedures for blood donor selection, blood collection, blood screening for transfusion transmitted infection, blood storage and blood component preparation are now being applied; and cross matching has been developed.
    b- Upon the recommendations of ICBS, the blood banks also abandoned "specimens-pooling" for testing blood units.
    c- Hygiene and waste disposal were improved.
    d- External Quality Assessment to evaluate performance of testing screening laboratories of the blood banks was introduced.
- Although it is difficult to predict how things will proceed in the future in many African countries, the increasing number of countries committed to continue testing and the introduction of a budget line in a few of them, provides room for optimism that there will be sustainability, at least in some countries.
- The demonstration/training centers in Central Asia and Indonesia where training workshops have already been conducted and will continue to be conducted in the future have played and will continue to play an important role in establishing quality systems in blood transfusion services.

Lessons Learned

In 1999 an ICBS pilot project proposal to help fund the achievement of universal blood safety in developing countries was submitted to the Bill and Melinda Gates Foundation. ICBS chose to initially limit its request to a relatively modest budget. It was however intended to solicit further financial support and / or submit a complementary expanded project at a later stage, after articulating the use of the requested limited funds, evaluating ICBS's progress and the results of initial ongoing specific activities and determining the scope of future activities and areas to be covered. In the light of the experience gained during the course of implementing ICBS's activities and the significant achievements during the short period of this pilot project, it became evident that in order to achieve its goals to improve blood safety, ICBS had to expand the project to other needy countries and regions in the developing world. ICBS then started to look for funds/grants for its new proposal.

Challenges

Among challenged and limiting factors that could limit success in certain countries are: political instability, lack of government commitment in some countries, insufficient funds and the absence of dedicated and committed leadership in charge of blood transfusion programs. In order to overcome the afore-mentioned limiting factors, ICBS tried to address these challenges and limiting factors by means of: (**a**) the provision of information available on the evaluation of

blood screening test-kits (evaluated by the ICBS Blood Screening Test-kit Evaluation Center at the Paul-Ehrlich-Institut in Langen, Germany) on the sensitivity , specificity and cost as well as other characteristics of tests; (**b**) generation of Memoranda of Understanding with ICBS requiring governments' commitment to ensure the sustainability of screening; (**c**) prioritization of assistance in favor of countries having motivated and dedicated leadership in charge of their blood safety programs and providing training to competent national specialists to create such leadership; and (**d**) maximization of resources and avoidance of duplication by complementing existing support provided by other organizations and agencies or through bilateral agreements and coordination with the other providers.

Post-Grant Plans

ICBS obtained solid commitments from some ICBS collaborating centers to continue carrying out the activities on behalf of ICBS for several years to come at no cost to ICBS. Despite the post-grant lack of funds there are certain ICBS activities continuing to be made by some ICBS collaborating centers without need to be financially supported by ICBS. The following are the major ongoing activities on behalf of ICBS by some ICBS Collaborating Centers (at no cost to ICBS):

- The Institute for Infectious Diseases at the Free University of Berlin, Germany and the Institute for Diagnostics and Biotechnology, Berlin, Germany:
  - The Institute continues to conduct the international EQAS program on behalf of the German Institute for Documentation and Standardization (INSTAND), ICBS and WHO.
  - Involving the ICBS as partner in activities supported and funded by the German Government to improve blood safety in Russia.

- Excellent activities continue to be conducted by Pró-Sangue/Hemocentro de Sao Paulo:
  - The EQAS of the Fundação Pró-Sangue/Hemocentro de São Paulo continue to conduct on behalf of PAHO, ICBS and/ Pró-Sangue/Hemocentro de Sao Paulo. This EQAS program covers all the Latin American and the Caribbean countries.
  - Implementing the Latin America and Caribbean TTI screening test EQAS Project (2005-2009). The partners of this project are: Fundação Pró-Sangue Hemocentro de São Paulo (FPS/HSP), the International Consortium for Blood Safety (ICBS), Pan American Health Organization (PAHO) and the Caribbean Epidemiology Centre (CAREC). The objective of the project is to advise and monitor the quality of the national External Quality Assessment Schemes (EQASs) conducted at the level of each Latin American country.

- The German Institute for Documentation and Standardization in Laboratory Medicine (INSTAND) continues to contribute to the activities of ICBS by conducting, at no cost to ICBS, the regular INSTAND/ ICBS/ WHO training course on quality assurance.

- The ICBS Evaluation Center in PEI continued evaluating test kits and making data and information available to the developing countries. However the raising of additional funds is necessary in order to maintain the strategy of purchasing test kits from the open market and not donated by the manufacturers to ensure that test kits chosen for evaluation were from normal production runs, thus avoiding a potential selection by the manufacturers, of particular test kits or batches that may reveal a better standard of performance than those from routine production.

- Groningen ICBS Collaborating Center: Dr. Cees Sibinga is conducting on behalf of Sanquin and ICBS, blood safety activities in 3 African countries funded by the President's Emergency Plan for AIDS Relief (PEPFAR). Other blood safety activities have been conducted in Uzbekistan The Academic Institute for International Development of Transfusion Medicine, University Medical Center Groningen, NL, trains fellows from developing countries.

In the light of the experience gained during the course of implementing ICBS' activities and the significant achievements during the short period of this pilot project, it has become evident that in order to achieve its goals to improve blood safety, ICBS would have to expand the project to other needy countries and regions in the developing world. ICBS continues to seek funds and support from potential funding sources.

Other sources of project support and collaboration

During the years of funding by the Bill and Melinda Gates Foundation, the additional support and contributions received were as follows:

1. The Hepatitis Branch, Centers for Disease Control and Prevention (CDC) in Atlanta, GA, U.S.A.
The Hepatitis Branch of the Centers for Disease Control and Prevention (CDC) in Atlanta, GA, U.S.A. provided support (cash and in-kind) towards the establishment of the ICBS Master Panels. It covered the cost of characterization and provided direct and indirect support towards the cost of establishing the ICBS Master Panels.

2. The former Visible Genetics
The in-kind support received over a period of 2 years from the former Visible Genetics towards the characterization of HCV positive plasma units to construct the HCV Panel.

3. In-Kind support from Toshiba General Hospital, Japan
In-kind support has been provided to ICBS by this laboratory to characterize HBsAg positive plasma units to construct the HBV Panel.

4. The Institute for Infectious Diseases at the Free University of Berlin, Germany and the Institute for Diagnostics and Biotechnology, Berlin, Germany
The two institutes provided and continue to provide a major contribution at no cost to ICBS, in the areas of external quality assessment schemes (EQAS) and quality assurance programs in general. During the last two years the two institutes provided direct and indirect support towards conducting the EQAS.

5. The German Institute for Documentation and Standardization in Laboratory Medicine (INSTAND)
The German Institute for Documentation and Standardization in Laboratory Medicine (INSTAND) contributed to the activities of ICBS by conducting, at no cost to ICBS, the regular INSTAND/ WHO/ ICBS training course on quality assurance.

6. Paul-Ehrlich-Institut (PEI), Langen, Germany
PEI who agreed to continue hosting the International ICBS Reagent Kit Evaluation Center within its structure provided and continues to provide an outstanding in-kind support by evaluating blood screening test-kits.

7. The Laboratory of Virology, Lindsley F. Kimball Research Institute at the New York Blood Center, New York, U.S.A.

The Laboratory of Virology, Lindsley F. Kimball Research Institute conducted research to support ICBS and its activities especially in developing appropriate technology and economical testing strategies for use by central confirmatory laboratories in developing countries.

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8. The Sanquin Division Blood Bank Northeast, Groningen, the Netherlands

SANQUIN, the not-for-profit Netherlands National Blood Supply Foundation, which bears the authority and responsibility for the National Blood Supply in the Netherlands assisted by training trainers from the developing world, waiving training fees and frequently providing housing at symbolic rent.

9- The WHO Headquarters and WHO Regional Offices

a- WHO Headquarters

ICBS and WHO/CSR/LYO of the Department of Communicable Diseases Surveillance and Response, WHO/Headquarters, Geneva, Switzerland, shared the cost of studies to establish the global and regional burden of chronic hepatitis C, in order to encourage national public health authorities to, in turn, establish their own national burden for the prioritization of public health action.

b- The WHO Regional Office for the Eastern Mediterranean (WHO-EMRO)

As a contribution to ICBS' efforts, WHO-EMRO took care of the cost for the overseas training of two Pakistani scientists whom ICBS had planned to train as per the Memorandum of Understanding signed between ICBS and the Ministry of Health in Pakistan. In addition the training centers waived training fees.

c- WHO Regional Office for Europe (WHO-EURO)

The Blood Safety and Diagnostic Support, WHO-EURO collaborated with ICBS and shared the costs of several workshops for the five countries of Central Asia covering different aspects of quality assurance and blood safety.

d- PAHO/AMRO

The close cooperation between PAHO and ICBS in supporting training activities and the introduction of screening for HCV, of blood collected by the blood banks in countries of South and Central America, resulted in the marked increase of screening for HCV, of blood units collected by the blood banks in Latin American and Caribbean countries. Eleven (of 19) Latin American countries and eight (of 22) Caribbean countries are now testing all blood units collected by public blood banks for HCV. Other countries are partially testing blood units collected and are striving to routinely screen more blood units.

e- WHO Regional Office for Africa (WHO-AFRO)

WHO-AFRO collaborated with ICBS and shared the costs of several workshops.

10- Shanghai Blood Center, Shanghai, China

The Shanghai Blood Center, in its capacity as an ICBS Collaborating Center as well as a WHO Collaborating Center has, on behalf of ICBS and at no cost to ICBS, trained trainers and staff of blood banks from different provinces in China, to enable them to install and maintain quality management systems at their blood transfusion facilities and will continue to do so.

11- The Office of Health and Population-USAID Regional Office for Central Asia (USAID/CAR) & CDC/CAR

In early 2003 the Office of Health and Population-USAID Regional Office for Central Asia (USAID/CAR) provided support in the amount of US$ 400,000.00 towards ICBS's activities to assist the Ministries of Health in the countries of Central Asia to improve their blood transfusion services. CDC/CAR and ICBS established a partnership and jointly executed and implemented the project. The project covered recruitment; motivation and retention of blood donors; strengthening of blood bank laboratory screening capacities; application of laboratory safety principles; establishment of proper waste disposal programs and training in the appropriate utilization of blood, blood components and blood products.

12- ICBS Collaborators providing Plasma to construct panels

ICBS Collaborators from around the world provided the large number of plasma units needed, free of charge to ICBS, from which the necessary specific plasma units were selected after characterization, to construct the ICBS Panels.