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# Laboratory Support to HIV Diagnosis and Monitoring of Antiretroviral Therapy

*Report of a Regional Workshop  
Pune, India, 27-30 July 2004*

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## 1. INTRODUCTION

The AIDS epidemic continues to spread in the South-East Asia Region. South-East Asia (SEA) is the second most affected WHO region in the world, after sub-Saharan Africa. To date, close to 40 million people throughout the world have been infected with human immunodeficiency virus. Of these, almost 6.4 million are in the SEA Region. The estimated prevalence rates per 100 000 population range from less than 1 in DPR Korea to over 1 200 in Thailand. Over 99% of cases have been reported from four countries - Thailand, India, Indonesia and Myanmar.

The epidemic has affected persons in every country all over the world. The majority of persons living with HIV infection and AIDS are found in the developing world where resources are poor and access to health care and new treatment is limited. Despite the high prevalence rates, care of persons with HIV infection living in these countries has not been given high priority because of the high burden of disease due to other illnesses. In areas where the epidemic is most severe, the provision of health care is further compromised by the rapidly weakening economies, the costs of effective medications and the non-availability of efficient laboratory support services.

Countries in the Region continue to give high priority to the AIDS problem and to fight the epidemic. They are implementing national strategic plans with the involvement of a number of government sectors, the private sector and non-governmental organizations. Priority is being given to scaling up of effective targeted interventions. Realizing the importance of anti-retroviral therapy, WHO has initiated various steps, the most notable being commitment by the Director-General that at least 3 million HIV patients from developing countries shall be provided antiretroviral therapy (ART) by 2005 ("3 by 5" initiative).

The Global Fund for AIDS, Tuberculosis and Malaria has also identified ART as one of the priority area. With huge efforts being initiated to provide

ART, close monitoring of patients on these drugs is also essential to ascertain response. Monitoring includes clinical, immunological and microbiological, the latter two being entirely dependent upon knowledge, skills and infrastructure of the laboratory network. Enumeration of CD4 T lymphocytes is the most sensitive and specific indicator for this assessment. This, and identification of an opportunistic infection, constitute two universally-accepted monitoring tools.

For various issues pertaining to prevention and control of HIV/AIDS, laboratory support is the most basic and fundamental tool. Monitoring of antiretroviral therapy, diagnosis of HIV and associated infections and evaluation of response to therapy in individual and various public health interventions cannot be accomplished until reliable laboratory support is available, both at clinical and public health areas. WHO has developed guidelines to ensure optimal utilization of laboratory support in providing quality care and reliable diagnostic support to various interventions against HIV/AIDS.

To review the status of laboratory support to HIV/AIDS programme in the countries of the Region and to apprise national trainers about the utility of guidelines and mechanism for its implementation, a Regional Workshop on Laboratory Support to HIV Diagnosis and Monitoring of Antiretroviral Therapy was convened at the National AIDS Research Institute (NARI), Pune, India, from 27 to 30 July 2004. Nineteen participants from seven countries of the Region, viz Bhutan, India, Indonesia, Maldives, Nepal, Sri Lanka and Thailand attended this Workshop. Four experts from India, Thailand and WHO facilitated the workshop. The List of Participants is at Annex 1 and the Programme at Annex 2.

## **2. OBJECTIVES**

The objectives of the workshop were as follows:

- (1) To review the status of laboratory support for diagnosis of HIV and antiretroviral treatment in the countries
- (2) To discuss the use of Regional Guidelines on Laboratory Support to Diagnosis of HIV and Antiretroviral Treatment, with National AIDS

Programme Managers and national focal points for HIV/AIDS laboratories, and

- (3) To formulate country-specific draft plan of action for implementation of the Regional Guidelines on Laboratory Support to Diagnosis of HIV and Antiretroviral Treatment.

### **3. INAUGURAL SESSION**

Dr Ramesh Paranjape, Officer In-charge, NARI, welcomed the participants and the facilitators of the workshop. Dr Rajesh Bhatia, WHO Consultant, welcomed the participants on behalf of WHO and read out the inaugural address of the Regional Director, WHO South-East Asia Region. In his address, Dr Samlee emphasized that HIV/AIDS was among the greatest health crisis ever faced by humanity. Already this pandemic had killed 30 million people. Every year 3 million people would die, if not treated. Tragically, every sixth death would be of a child less than 15 years of age. Most of these deaths were preventable with specific antiretroviral therapy. Unfortunately, only a few were lucky to be on treatment. Of a total of 6 million who need this treatment worldwide, only 400 000 were currently receiving it.

Dr Samlee added that in September 2003, WHO had declared that failure to provide antiretroviral therapy to patients in developing countries was a global health emergency. Accordingly, WHO announced a new "3 by 5" initiative, i.e. to provide 3 million people in developing countries with treatment by the end of 2005. This was only an interim target, with a long-term goal of universal access to antiretroviral therapy for all those who need it.

In countries that comprised the South-East Asia Region of WHO, 800 000 people who were living with HIV needed ART. However, only 50 000 were presently receiving it. The target to be achieved was 400 000 by 2005 – requiring an eight-fold scale-up in less than two years.

Dr Samlee emphasized that laboratories played a critical role in the successful treatment against HIV, by providing reliable support for the detection of HIV antibody for diagnosis as well as for undertaking efficient monitoring of treatment effectiveness among those receiving ART. While monitoring of patients on chemotherapy was essential in all infectious

diseases, it was of greater importance in HIV because of the life-threatening nature of the illness, and the potential of the virus to mutate and develop resistance to drugs.

Although laboratory support to AIDS programmes was very important, the desired infrastructure, expertise and networking required strengthening in most countries of the Region. In addition, it was important to institute quality systems in the functioning of laboratories since diagnosis, initiation of treatment and proper management of people on antiretroviral therapy depended upon reliable laboratory results. Realizing the need to provide relevant information on utility and infrastructure of laboratory to the national authorities, WHO had developed the Regional Guidelines on HIV Diagnosis and Monitoring of Antiretroviral Therapy. The current meeting would discuss the Guidelines and provide a platform to share experiences, understand the problems in the Region and formulate solutions to improve access to, and the quality of laboratory support to the AIDS Programme. Dr Samlee assured the meeting that WHO would continue to provide all possible technical support to the countries in strengthening laboratory support to national efforts in containing the rapidly evolving epidemics of HIV in the Region.

## **4. WORKSHOP**

### **4.1 Review of HIV Status in the Region**

Dr Rajesh Bhatia presented the global and regional scenario on HIV (see Table), importance of laboratory in the implementation of "3 by 5" initiative and the genesis of the Regional Guidelines. He stressed that access to and availability of reliable laboratory results was a prerequisite for establishing diagnosis of HIV, initiation of antiretroviral therapy and its monitoring. Laboratory evidence was essential to assess failure of treatment in an individual as well as the emergence of resistance to various antiretroviral agents. Close coordination and flow of information between laboratories at various echelons and antiretroviral therapy providers was important for optimal utilization of laboratory services.

**Table. HIV in the South-East Asia Region**

Country	Estimated HIV Infections	Heterosexual	IV drug use
Bangladesh	13 000	+	--
Bhutan	< 100	+	--
DPR Korea	< 100	--	--
India	5 100 000	+++	++
Indonesia	111 000	+	++
Maldives	< 100	+	--
Myanmar	330 000	+++	++
Nepal	56 000	++	++
Sri Lanka	4 700	+	--
Thailand	650 000	+++	++
Timor-Leste	N/A	--	--

The status of HIV and the laboratories support in various countries were presented by country representatives.

### **Bhutan**

Since the detection of the first HIV positive case in 1993, Bhutan has experienced a slow but steady rise in HIV infection. At the end of June 2004, the officially recorded cases of HIV infections were 50. Though the primary mode of transmission is heterosexual contacts, one case of mother to child transmission was reported. The infected individuals mainly fall in the age group of 18-44 years and come from diverse social and professional background. Bhutan at the moment has not been able to either map high-risk groups or geographical areas.

In all the districts and regional laboratories, rapid tests for the detection of HIV-1 and 2 antibodies are available. Public Health Laboratory (PHL) is the only testing centre in the country which confirms a positive test. It is also the only laboratory having ELISA test facility. Bhutan follows the WHO

recommended confidentiality policy of HIV test and, an unlinked anonymous testing policy is employed in all sentinel surveillances. Partner notification policy entails index patient to notify immediate partners.

Bhutan is yet to initiate ARV therapy for PLWHA. In the next NHAC (National HIV/AIDS Commission) meeting, the introduction of ARV facility in the country will be discussed.

### **India**

The prevalence of HIV-positive individuals in the country is 0.8% with 6 states reported to be having a higher prevalence. These are Tamil Nadu, Andhra Pradesh, Maharashtra, Karnataka, Nagaland, and Manipur.

As per the estimates, 40 000 cases in the country are eligible for ART. As part of the "3 by 5" initiative, India has started the ART roll-out in April 2004. Currently, 1 500 cases of AIDS are on ART, with drugs being available for a total of 8 000 patients. By December 2005 about 20 000 cases would be under treatment. This is being provided through 8 designated centres spread across higher prevalence areas. It is planned to increase the number to 25.

Blood screening for HIV is carried out in blood banks in all districts of the country. There are over 570 voluntary confidential counselling and testing centres offering services in the country. All ANCs or walk-in patients in labour rooms are offered HIV testing after informed consent and, if found positive, the mother and the child are administered single- dose Nevirapine.

Currently there are 12 reference laboratories at the national level in the public sector equipped with CD4 and viral load testing facilities. HIV resistance monitoring, however, is currently being performed at NARI, Pune, and YRG Care, Chennai. NICD, Delhi, plans to start this facility shortly. EQAS is in operation for HIV antibody testing at present. In addition, individual institutions participate in international EQAS. Internal quality control is also in place at different levels. ELISA facility is available in the microbiology departments of over 200 medical colleges in the country. As part of the diagnostic support, all district and sub-district hospitals have 2-3 rapid tests available.

### **Indonesia**

The estimated prevalence of HIV in Indonesia is 111 000, (90 000-130 000). 1 525 cases of AIDS have been reported from 25 provinces of whom 519 have died. Under the "3 by 5" initiative 4 000 people living with HIV would be provided ART by the end of 2004. The target for end-2005 is 10 000 people who will be provided ART through 25 hospitals. Minimal infrastructure is available in 25 hospitals. CD4 machines are available in 15% of the hospitals that will provide ART. Currently, simple/rapid tests, ELISA immunoassays and Western blot tests are available for HIV diagnosis. Viral load facilities are available in one hospital and resistance study infrastructure is being created.

### **Maldives**

In Maldives, though at the policy level administration of ART has been accepted, there is a strong need to establish the required infrastructure, laboratory support and microbiological monitoring of ART. At present facilities for CD4 count are not available.

### **Nepal**

The first HIV case was detected in 1988 in Nepal. Since then, HIV epidemic has gained firm ground among certain population sub-groups like IDUs, sex workers (SWs) and their clients. Nepal is still a low prevalence country with 0.5% HIV prevalence among the general population but also has "concentrated" epidemic among IDUs (68%) and SWs (17%). Recent estimates show that 60 000 people are infected with HIV AIDS and the cumulative reported cases number 3 905. About 766 AIDS cases have been reported till June 2004. The number of people requiring ART is estimated to be 6 000-9 000. At present Nepal is providing ART for 25 PLWHs against an estimated requirement of 400-600 patients.

The National Public Health Laboratory (NPHL) is a central reference laboratory for HIV diagnosis and ART which is the only place for CD4 cell count facility. If ART has to be expanded, laboratory support needs to be strengthened in terms of infrastructure, training of manpower and supplies. There is infrastructure in all zonal hospitals for laboratory support.

### **Sri Lanka**

In Sri Lanka there are an estimated 7 200 HIV-positive cases. However, as at the end of July 2004 the cumulative total of reported HIV positive cases was 552 with a male female ration of 1: 5.1.

The reported AIDS deaths accounts for 124. Twelve perinatally transmitted HIV infections have been reported to date. The prevalence of HIV among the adult population is less than 0.1%.

Up to now antiretroviral therapy had not been offered to patients managed in the government sector. However, under a World Bank project it is expected to enroll around 50 patients during the first year. At present there are 26 STD clinics spread throughout the 9 provinces in the country; of these, 15 clinics including the central clinic in Colombo have laboratory facilities. All these STD clinics are capable of performing only the initial screening test for HIV and samples tested positive in these laboratories are sent to the National Reference Laboratory in Colombo for confirmation. In addition, the reference laboratory has facilities for viral load assays and CD4 counts.

Future plans include the establishment of three centres – in Colombo STD clinic, South STD clinic and Kandy STD clinic – with strengthened laboratory support to provide necessary facilities for follow-up and monitoring of patients.

### **Thailand**

The first case of AIDS in Thailand was reported in September 1984. Progressive numbers of AIDS cases as well as people with HIV were reported throughout the following years. Early cases were generally confined to Thai homosexual males. This was followed by an explosive spread of HIV infection among injecting drug users (IDUs) in 1987 and 1988. The virus then spread to sex workers and their clients in 1989 to 1990 with the result that heterosexual transmission became increasingly important. From 1990 to 1991 many provinces reported cases of mother-to-child transmission with increasing numbers of infected newborns reported in the following years.

Various national data sources allow calculation of the cumulative number of reported AIDS and symptomatic cases of 322 565. The cumulative

number of deaths from AIDS cases was 74 359 as of March 2004. Sexual transmission accounts for 82.8% of reported AIDS cases while infection among injecting drug users accounted for 4.7%. Transmission of HIV from mother-to-child was 4.4%. Reports also indicate that more than 78% of the cases are in the age range of 20-39 with a male to female ratio of 3.3 to 1. HIV prevalence in pregnant women rose from 0% in 1989 to 2.3% in 1995, before decreasing to 1.5% in 1998. This rate increased again to 1.8% in 1999 and dropped to 1.18% in the year 2003. HIV prevalence in military conscripts at the national level decreased from 4% in 1993 to 0.6% in 2003. The prevalence rate among intravenous drug users increased from 39% in 1989 to 51% in 1999 and dropped to 33% in 2003 and is considered one of the major challenges to Thailand's efforts to control HIV.

It was estimated that in 2004, out of a total population of 62 million, 1 074 155 persons had been infected with HIV since the beginning of the epidemic. Among these, 572 484 are currently living with HIV and AIDS of which 49 452 would develop serious AIDS-related illnesses. It was also estimated that 19 471 new infections would occur during this year compared to 143 000 new infections in 1990.

National Access to Antiretroviral Programmes for PHA (NAPHA) have been developing to provide free of charge antiretroviral treatment (ART) to medically eligible PHA. The programmes are evolving from an antiretroviral therapy initiative programme called Access to Care since 2001. By the end of 2004, 50 000 PHAs are expected to receive ART. It is also estimated by experts from various relevant organizations that approximately 150 000 PHAs are eligible to receive ART. At different levels in the public health system, NAPHA has been implemented with all major programme components: ARV protocol development, health care professional training, laboratory network formation, pharmaceutical access, logistics and supply management, and monitoring and evaluation which are based on elements of research, pilot projects, training, national guideline development, experience and policy making. A national monitoring system was developed to monitor the progress of programme implementation. The monitoring reports were received monthly, from implementing hospitals. As of May 2004, there were 888 hospitals participating in the programme. Most of the hospitals were under the Ministry of Public Health (MoPH), 60 were under other government hospitals and 11 under private hospitals. There were 37 365 cases receiving ART; of these, 32 735 cases were ongoing. The monthly uptake of eligible PHAs to the programme is 2000 to 4000 cases.

Considering HIV/AIDS laboratory diagnosis in Thailand, anti-HIV testing with various technologies plus voluntary counselling and testing (VCT) is available in all hospitals and some of health care centres, both government and the private sector. All anti-HIV testing reagents have to be approved by Thai FDA before being distributed to the market. Approximately 30 anti-HIV testing reagents are available in Thailand. The average price of an anti-HIV testing is US\$ 2-3.

CD4 cell count is a standard test under NAPHA. It is recommended that CD4 cell count testing be performed at baseline and every six months after receiving ART. There are 54 dual-platform technology CD4 count machines under MoPH service network and approximately 10 machines under the University and the private sector. In general, the price of each testing is US\$ 12. Two in-house technologies on CD4 cell count had been successfully developed. EQAS has been implemented in most of CD4 count centres within the network.

Viral load testing is also available in approximately 20 centres over the country, both government and the private sector. It is not included as a standard test under NAPHA. Four in-house technologies are under development. The cost per test varies from US\$ 50-75. A central validation process for viral load-testing is being implemented.

Three viral-resistant testing centres were established under the University, with connection to MoPH. Five in-house technologies are under development for clinical use.

## **4.2 HIV Diagnosis and Monitoring of Antiretroviral Therapy**

### ***HIV diagnosis***

Dr Suniti Solomon (VHS-YRG Care) presented various diagnostic and screening laboratory tests for HIV that are available currently. Laboratory tests are targeted to assay antibody to HIV, detect specific HIV antigen, as well as viral nucleic acid. The types of test that are available include dot blot and Mac-ELISA, immuno-chromatography, Western Blot, and polymerase chain reaction (PCR). Dr Solomon emphasized the importance of quality in the testing procedures and the need for proper regulation of the private

laboratories. A wide variety of test kits are now available for HIV diagnosis. The selection of appropriate test kits/assays/reagents is critical to ensure quality in laboratory services. Every country or laboratory must therefore define a policy for selection of the most appropriate kit. Kits/assays with high sensitivity and specificity are desirable for use in HIV testing laboratories. A test with maximum sensitivity is desirable when it is to be used as a screening test, while high specificity is desirable for a test that is to be used as a confirmatory test.

### ***Enumeration of CD 4 lymphocytes***

Professor Kovit, Siriraj Hospital, Bangkok presented utility and techniques of enumeration of CD4 lymphocytes. CD4 T cells are the primary target of HIV. These are preferentially depleted during the course of the disease. The utility of CD4 T cell measurements involves clinical considerations for HIV disease classification and AIDS definition, assessment of prognosis, and designing of clinical trials. It is well recognized now that accurate and reliable enumeration of CD4 T cell counts is very crucial for monitoring the rate of progression to AIDS, both for initiating prophylaxis for opportunistic infections as well as monitoring the impact of antiretroviral therapy (ART).

The methods of enumeration of CD4 T cells include immunofluorescence analysis by flow cytometry (FCM) which is the gold standard for CD4 T cell measurements. To obtain an absolute CD4 T cell count, two concepts are utilized: dual-platform (DP) approach and single-platform (SP) approach.

The DP approach uses two instruments to generate absolute CD4 T cell counts: a FCM for generating a percentage CD4 T cells among lymphocytes and a haematological analyzer to enumerate the absolute lymphocyte counts. An absolute CD4 T cell count is derived by multiplying %CD4 T cells by the absolute lymphocyte count.

The single-platform (SP) approach enables absolute CD T cell counts to be derived directly without the need for a haematological analyzer, i.e., the use of volumetric counting, microfluorometry and, most commonly, the addition of a known density of reference fluorescent beads to the sample (FACSCount).

For countries and settings where infrastructure is not available for such FCM technologies, a number of accepted alternative assays have been developed and some that are commercially available are microscopic-bead assay and ELISA-based assay,

In case where CD4 testing cannot be assessed, the presence of a total lymphocyte count of 1200 cells/uL or below may be used as a substitute indication for ARV treatment in symptomatic HIV-infected patients. While the total lymphocyte count correlates poorly with the CD4 T cell count in asymptomatic patients, in combination with clinical staging, it is still a useful marker of prognosis and survival.

### ***HIV and TB***

Dr S.P. Tripathy, NARI, Pune discussed the issue of co-infection of TB and HIV. The South-East Asia Region bears 40% of the global TB burden and ranks second after sub-Saharan Africa in the estimated number of people living with HIV/AIDS. Each year, nearly 3 million cases of TB and 750 000 TB deaths are estimated to occur in the Region. Of the estimated 6 million adults living with HIV in the Region, about half are likely to be infected with TB. The extent to which HIV will contribute to the TB epidemic depends on the degree of overlap between the population groups infected with TB and those with HIV.

Pulmonary tuberculosis accounts for more than 90% of total tuberculosis manifestation in HIV patients. Before the AIDS pandemic, non-tuberculosis mycobacteria rarely caused serious illness, even in immunocompromised individuals. The prolonged immunosuppression of the cell-mediated immune system caused by HIV provided the opportunity for these relatively virulent organisms (non-tubercular mycobacteria) to cause disease.

Tuberculosis in HIV-infected persons may occur with different manifestations. All these forms, except when cavitations occur in pulmonary tuberculosis, are paucibacillary in nature. Depending upon the form of disease manifestation, several specimens, such as sputum and/or gastric lavage, bronchoalveolar lavage, (BAL), lymph nodes and other biopsy specimens, pus, ascetic fluid, pleural and cerebrospinal fluid should be examined. If delay is anticipated, biopsy specimens may be collected in a suitable transport medium for sending them to the laboratory.

### ***Viral monitoring of ART and surveillance for drug resistance***

Dr Madhuri Thakkar, NARI, Pune discussed the utility and techniques for measuring HIV load in a patient. She also introduced possible approaches for surveillance of drug resistance. HIV1 viral load measurement is useful for monitoring treatment. A baseline plasma viral load is established before starting ART. Periodic monitoring is essential. It is predicted that with successful therapy a fall of 1.5 to 2 log in plasma viral load occurs within 4-6 weeks. With successful ART, it should become undetectable in 4 to 6 months of therapy. Viral load is measured using a variety of commercial kits which can detect upto 50 copies of viral nucleic acids.

A real time PCR is being tested in some laboratories. The cheaper cost of the test and the advantage of avoiding batch testing are some of the plus points. The test uses primers and probe set specific for the LTR region of the HIV genome, which is conserved across subtypes. The virological assays are useful tools in monitoring for the emergence of resistance in HIV against antiretroviral drugs.

The increase in the use of ART is expected to lead to the emergence of drug-resistant mutants of HIV1. The inherent mutability of the reverse transcriptase (RT) gene of HIV allows for drug resistance to emerge under selection pressure. A survey of drug resistance of indigenous HIV strains is essential to ascertain the usefulness of the antiretrovirals, especially in public health programmes. Drug resistance should be suspected if the plasma viral load does not show a greater than 1 log fall within 8 weeks of therapy.

Two types of antiretroviral drug resistance assays are available. The phenotypic assays and the genotypic assays detect changes in the sequence of the relevant HIV1 gene.

### ***Monitoring of opportunistic infections***

Dr Arun Risbud, NARI, Pune introduced the subject of monitoring of opportunistic infections (OI) in patients who are administered antiretroviral therapy. Morbidity and mortality in HIV is due to the occurrence of life-threatening opportunistic infections (OIs) during the natural course of the disease. These are the direct consequence of a decline in CD4 count. A wide variety of opportunistic infections are encountered in patients with AIDS

which are caused by various micro-organisms. Very often these represent reactivation of organisms that have been dormant in the host for several years. The incidence of these diseases increases as the patient's CD4 count declines. The pattern/repertoire of opportunistic infections may vary in different geographic areas. The knowledge of important OIs specific for particular areas/countries is useful for correct diagnosis and management of OIs. Infrastructure facilities should be established based on the level of the set-up required. Although intermediate laboratories have sufficient facilities, further identifications and confirmations may be done by the central laboratory. The flow of specimens should be worked out from low to higher level and the flow of technical, scientific information and quality assurance procedures should be higher to lower levels.

All presentations were followed by group discussions in which the participants identified the constraints being faced by them and their possible solutions.

### ***Quality system in ART***

Dr Rajesh Bhatia introduced the concept of quality and key elements of a quality system. Quality is defined as meeting the standards or match between expectation and realization of the customer who is the user of the laboratory results. The quality system refers to the organizational structure, procedures, processes and resources needed to implement quality. The key elements of the quality system are: organizational structure and management, standards, training, documentation and assessment. The assessment can be man-driven or material-driven. Man-driven assessment is also known as quality audit and is a part of accreditation process. Material-driven assessment is achieved through distribution by an organizer to a large number of participants of samples of known but undisclosed contents. On the basis of the results obtained, the quality system of the laboratory is assessed and suggestions made to improve it.

### **4.3 Visit to National AIDS Research Institute**

Participants visited the National AIDS Research Institute, Pune to observe all three major areas of laboratory support viz. virological, immunological and microbiological including tuberculosis. They also observed the functional

quality system. The participants were taken around to all the areas of the institute to observe the technical work and held discussions with the facilitators as well as the staff of NARI.

### ***Operational research issues***

Dr R.S. Paranjape highlighted the need for continuous operations research to address various issues that confront ART. He emphasized the importance of drug resistance surveillance through a carefully developed protocol and undertaken under strict quality assurance systems. The study can generate valuable data which can be shared by all countries. The use of a new technology which may provide better results at much less cost will require validation and studies to ascertain their fitness in developing countries.

### ***Development of plan of action for implementation of quality system***

Dr Rajesh Bhatia briefed the participants on the need for planning and the method of development of an action plan with specific activities. Various parameters that need to be considered and included in the action plan were activity, time-frame, type of activity, person designated to undertake the same and resources required to accomplish the activity. The participants developed generic action plans in group works and presented them at a plenary session.

Several issues that need to be considered by the participants in the implementation of laboratory support to HIV diagnosis and monitoring of antiretroviral therapy in their own settings were thoroughly discussed at a plenary session on last day. The technical problems raised by the participants were addressed by the faculty. Extensive discussions led to the formulation of the recommendations described in Section 5.

## **5. RECOMMENDATIONS**

### **5.1 To Member States**

- (1) Member States should strengthen the laboratory infrastructure for efficient support for HIV diagnosis and immunological, virological and

microbiological monitoring of antiretroviral therapy on the basis of the Regional Guidelines for HIV Diagnosis and Monitoring of Antiretroviral Therapy.

- (2) Member States should develop a functional network of laboratories to promote access to laboratory support to ART, optimal utilization of existing infrastructure and ensure quality and smooth working of laboratories at various levels.
- (3) Member States should make use of WHO AIDS Medicine and Diagnostic Services to obtain information and technical support on procurement of equipment and reagents.
- (4) Member States should strengthen quality systems in all laboratories which are supporting ART programmes. National External Quality Assessment Schemes should be initiated. The organizers of NEQAS should participate in International External Quality Assessment Scheme.
- (5) Member States should orient/train all staff members on technical aspects of HIV diagnosis and monitoring of ART as well as good laboratory practices especially biosafety and waste disposal measures.

## **5.2 To WHO**

- (1) WHO should convene a meeting of national regulatory authorities of Member States in the South-East Asia Region to create a formal mechanism of sharing information on evaluation of HIV diagnostic kits and ART monitoring reagents to facilitate the availability of quality reagents in all countries.
- (2) WHO should initiate a Regional External Quality Assessment Scheme for CD4 enumeration with the participation by selected/national HIV laboratories. WHO should subsequently provide technical support to the national laboratories to enable them to initiate NEQAS in their respective countries.
- (3) WHO should organize a regional training course for national trainers in CD4 enumeration techniques with the participation of all countries. The

training course should also emphasize on procurement, maintenance and upgradation of equipment.

- (4) WHO should facilitate multicentric studies to understand the dynamics of emergence and spread of resistance in the South-East Asia Region.
- (5) WHO should disseminate the Regional Guidelines for HIV Diagnosis and Monitoring of Antiretroviral Therapy to all policy-makers and National AIDS Programme Managers. Subsequent developments in the field of HIV, specially those that pertain to laboratory technologies, should be regularly provided to national laboratories and National AIDS Programme Managers, preferably through a Newsletter.

## **6. CONCLUDING SESSION**

The concluding session was chaired by Dr R.S. Paranjape. He thanked the organizers and the facilitators for making the workshop a success and hoped that the participants would be able to translate the knowledge gained in strengthening quality assurance practices in their own settings.

## Annex 1

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## Annex 2

### PROGRAMME

#### Day 1, 27 July 2004

0830-0900 hrs	Registration
0900-1000 hrs	Opening ceremony Welcome address RD's address Objectives and mechanics of the meeting Introduction of participants Election of chair Approval of agenda Administrative announcements
1000-1100 hrs	Introductory lectures ( <i>Dr Rajesh Bhatia</i> ) "3 by 5" Initiative of WHO Laboratories in HIV Programme Genesis of Regional Guidelines
1100-1300 hrs	<b>Country Presentations (Participants)</b> <ul style="list-style-type: none"><li>• Number of people on/requiring ART</li><li>• Status of laboratory support</li><li>• Infrastructure available</li><li>• Tests done for diagnosis and ART monitoring</li><li>• Future plans</li><li>• Constraints</li><li>• Support expected from WHO</li></ul>
1400-1530 hrs	<b>Country presentations</b> (contd)
1530-1600 hrs	Development of plan of action ( <i>Dr Rajesh Bhatia</i> )
1600-1630 hrs	Synthesis of country reports ( <i>Rapporteur</i> )
1630-1700 hrs	Major constraints and support areas ( <i>Chairman</i> )

## Day 2, 28 July 2004

- 0900-0945 hrs      **HIV-Diagnosis** (*Dr Suniti Solomon*)
- Various strategies/algorithm
  - Current status
  - New technologies
  - NAT v/s ELISA v/s Rapids
  - Infrastructure required and networking
  - Quality assurance
  - Constraints
  - Areas requiring improvements
  - Discussions
- 0945-1200 hrs      **Group Work No 1 (Participants to be split in two groups)**  
**HIV Diagnosis**
- Problems encountered
  - Practical solutions
  - Group presentations
- 1200-1300 hrs      **Immunological support to antiretroviral therapy**  
(*Prof Kovit*)
- Importance
  - Current tests, principles, technology and quality assurance
  - Common pitfalls and troubleshooting for CD4 count
  - Sample preservation and transport
  - Utility in developing countries
- 1400-1530 hrs      **Group Work No 2 (Participants to be split in two groups)**  
**CD4 enumeration**
- Problems encountered
  - Practical solutions
  - Group presentations
- 1530-1615 hrs      **Challenges in diagnosis of opportunistic infections**  
(*Dr Arun Risbud*)
- Importance
  - Current tests, principles, technology and quality assurance
  - Common pitfalls and troubleshooting for diagnosis
  - Sample preservation and transport
  - Utility in developing countries

1615-1730 hrs	<b>Group Work No 3 (Participants to be split in two groups) Diagnosis of opportunistic infections</b> <ul style="list-style-type: none"><li>• Problems encountered</li><li>• Practical solutions</li></ul> Group presentations
<b>Day 3, 29 July 2004</b>	
0900-1000 hrs	<b>Virological monitoring of ART (Dr Madhuri Thakkar)</b> <ul style="list-style-type: none"><li>• Importance</li><li>• Current tests, principles, technology and quality assurance</li><li>• Common pitfalls and troubleshooting for diagnosis</li><li>• Sample preservation and transport</li><li>• Utility in developing countries</li></ul>
1000-1200 hrs	<b>Group Work No 4 (Participants to be split in two groups) Diagnosis of Opportunistic Infections</b> <ul style="list-style-type: none"><li>• Problems encountered</li><li>• Practical solutions</li></ul> Group Presentation
1200-1300 hrs	<b>HIV and TB (Dr SP Tripathy)</b> <ul style="list-style-type: none"><li>• Importance</li><li>• Laboratory tests</li><li>• Interpretation</li><li>• Biosafety in laboratory</li></ul>
1400-1445 hrs	<b>Infrastructure for lab support to HIV and ART (Dr Suniti Solomon)</b> <ul style="list-style-type: none"><li>• Good laboratory practices</li><li>• Biosafety</li><li>• Waste disposal</li></ul>
1445-1530 hrs	<b>Quality system (Dr Rajesh Bhatia)</b> Discussion
1530-1615 hrs	Operations research issues (Dr RS Paranjape)
1615-1700 hrs	Brief for laboratory visit (Dr Madhuri Thakkar)

**Day 4, 30 July 2004 Visit to NARI LABS**

0900-1100 hrs	Virological diagnosis
1100-1300 hrs	Immunological monitoring
1400-1500 hrs	Open session for trouble shooting
1500-1600 hrs	Presentation of country draft PoA
1600-1700 hrs	Recommendations
	Closure