Technical Assistance to Strengthen the Medical Supply System for HAART and DOTS-Plus Programs in Peru: Final Consultancy Report

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About the SCMS

The Supply Chain Management System (SCMS) was established to collaborate with in-country and global partners to ensure a reliable, cost-effective and secure supply of high quality medicines and health products for HIV/AIDS prevention, care and treatment. SCMS is funded by the President's Emergency Plan for AIDS Relief through the U.S. Agency for International Development.

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- *DISAs/DIRESAs, institutions and hospitals that were visited*
- *SIS*
- *Committee on Prevention and Control of AIDS of the Armed Forces and the Police*
- *EsSalud*

CONTENTS

ACRONYMS AND ABBREVIATIONS

AEM	Specialized Medicines Storage
AIDS	acquired immune deficiency syndrome
ARV(s)	antiretroviral(s)
CD4	T-lymphocytes with surface marking CD4
CMS	MINSA Central Medical Stores
CONAMUSA	National Multisectoral Coordinator in Health
DGSP	General Directorate of Health–MINSA
DIGEMID	General Directorate of Medicines, Supplies, and Drugs–MINSA
DIRESA	Regional Health Directorate
DISA	Health Directorate
DOTS	Directly Observed Treatment, Short Course
ESN	National Health Strategy
ESN-PCITS-VIH/SIDA	National Health Strategy for the Prevention and Control of Sexually Transmitted Diseases and HIV/AIDS
EsSalud	Social Security of Peru
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GPS	Good Storage Practices
HAART	highly active antiretroviral therapy
HIV	human immunodeficiency virus
INS	National Institute of Health
MDR-TB	multidrug-resistant tuberculosis
MINSA	Ministry of Health
NGO	nongovernmental organization
OGA	General Office of Administration
OGEI	General Office of Statistics and Computation
ORE	Office of Strategic Resources of MINSA
PAHO	Pan American Health Organization
PLWHA	people living with HIV/AIDS
PROVIDA	Pro-Vida Medicines Services
SISMED	Integrated Medical Supply System
TB	tuberculosis
UNAIDS	Joint United Nations Programme on HIV/AIDS
USD	U.S. dollar
WHO	World Health Organization

Abbreviations of antiretrovirals

3TC	lamivudine
ABC	abacavir
ATV	atazanavir
AZT	zidovudine
D4T	stavudine
DDI	didanosine
EFV	efavirenz
FTC	emtricitabine
IDV	indinavir
LPV/r	lopinavir/ritonavir
NFV	nelfinavir
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NVP	nevirapine
PI	protease inhibitor
RTV	ritonavir
SQV	saquinavir
TDF	tenofovir, disoproxil fumarate

EXECUTIVE SUMMARY

Medicines constitute one of the key components of the strategies and interventions for the prevention and control of primary problems relating to public health, such as HIV/AIDS and tuberculosis (TB). For these two illnesses, equitable, prompt, and uninterrupted access to the necessary medicines by people who are ill is particularly critical and should be considered a human right. With financial help from the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund), Peru, through the corresponding National Health Strategies of the Ministry of Health (MINSA), has been taking responsibility for the supply of antiretroviral (ARV) and TB medicines.

In April 2006, a mission from the Global Fund, as a condition for the disbursement of funds for the purchase of health products (for both HIV/AIDS and multidrug-resistant TB [MDR-TB]), imposed the requirement that programming and management of stocks of the products financed by the Global Fund be substantially improved no later than October 2006, for purposes of dealing with deficiencies that had been identified by the mission.

To comply with this requirement, an ad hoc committee—composed of representatives of the Multisectoral National Health Coordinator (CONAMUSA, the country's coordinating mechanism); the two National Health Strategies (for HIV/AIDS and TB); the General Directorate for Medicines, Supplies and Drugs (DIGEMID); and CARE Peru (Principal Recipient)—identified as the principal bottlenecks the existence of an excessive number of ARV treatment schemes and the serious difficulties in the acquisition process for medicines for both HIV/AIDS and MDR-TB. CONAMUSA requested technical assistance from the U.S. Agency for International Development to be able to confront the problems mentioned with the support of experts and to secure proposals for optimizing the purchases of ARV and anti-tuberculosis medicines, selecting ARVs and, in general, strengthening the supply system as a whole.

Background

According to the World Health Organization (WHO), HIV/AIDS and TB represent two of the priority problems in public health at the global level. In Peru, national health strategies have been established to optimize actions for the prevention and control of these transmittable diseases.

With regard to HIV/AIDS, national efforts at confronting this problem date back to the end of the 1980s, with the creation of the Multisectoral Commission to Fight AIDS in 1986 and, later, the Special Program for the Control of AIDS.[1] In 1995, the first public policy for confronting the epidemic was defined. Through Resolution 235-96-SA/DM, Manual of Doctrines, Standards and Procedures for the control of Sexually Transmitted Diseases-HIV/AIDS, the National Program for the Control of Sexually Transmitted Diseases and AIDS was established. Later, Law No.

[1] Ministry of Health, DGSP: General Plan for the National Health Strategy for the Prevention and Control of STDs and HIV/AIDS, 2004–2006.

26626[2] (called CONTRASIDA) was approved, which protects the rights of individuals affected by the virus and whose scope was broadened through Law No. 29243.

In 2001, Peru signed the Statement of Commitment at the Special Session on HIV/AIDS of the United Nations General Assembly, which contemplates the implementation in 2003, among other strategies, of mechanisms to guarantee access to ARV treatment by people living with HIV/AIDS (PLWHA). Compliance with this commitment began in a comprehensive fashion with the implementation of the highly active antiretroviral therapy (HAART) program in May 2004.

With regard to TB, Peru made a significant thrust in the direction of achieving more-effective control over this illness with the restructuring of the National Program for the Control of Tuberculosis in the second half of 1990. Some of the resources destined for the health sector were invested in increasing the effectiveness of diagnosis and in extending free and supervised treatment. In this effort, the technical recommendations of the Pan American Health Organization (PAHO) and the WHO were followed. One central aspect was the implementation of DOTS (Directly Observed Treatment, Short Course) in 1991.

Nevertheless, it was quickly necessary to confront one of the most complicated problems in the handling of this illness: the high levels of TB resistance to first-line pharmaceutical products. Multidrug-resistant tuberculosis has been defined as that type in which the tuberculosis bacilli are resistant to at least isoniazid and rifampicin. This resistance represents a threat to the current efforts in TB control. For this reason, WHO and its partners have established the DOTS-Plus Working Group with the goal of formulating guidelines for evidenced-based policy for treating MDR-TB. DOTS-Plus is an integrated management initiative, based on the five elements of the DOTS strategy. However, DOTS-Plus also considers specific issues, such as the use of second-line anti-TB medicines and the application of treatments in areas where a high prevalence of MDR-TB exists.[3]

Despite the achievements made, TB continues to be an important health problem, requiring strengthening of the strategies established for its control, especially of MDR-TB. In Peru, since 1997, a standardized retreatment has been applied for patients with this variety of the illness, in accordance with the recommendations of WHO's Global Tuberculosis Program.[4]

Since January 1999, the then National Program for the Control of Tuberculosis, with the support of PAHO/WHO; the Program for Infectious Diseases and Social Change of the Harvard University School of Medicine, Boston, USA; and Partners in Health–Peru, has developed the Collaborative Project for Responding to Patients with MDR-TB in Peru.

In 2001, however, the industrialized countries and the main international financial foundations created the Global Fund to Fight AIDS, Tuberculosis and Malaria, aimed at the developing

[2] Archives of the Congress of the Republic of Peru.
[3] World Health Organization. 2002. A Broadened DOTS Framework for the Effective Control of Tuberculosis. Geneva: WHO.
[4] Technical Norm 025 – MINSA.DGSP. Updating of Response to Patients with Multidrug-Resistant Tuberculosis (TB MDR)). RM 162-2005/MINSA.

countries, for purposes of strengthening their national responses to these epidemics. Peru petitioned at the second meeting, obtaining acceptance of the proposal called "Strengthening Prevention and Control of AIDS and Tuberculosis in Peru." In addition, in 2006, within the framework of the fifth Global Fund round, the project called "Closing Gaps: Toward the Achievement of the Millennium Objectives for TB and HIV in Peru" was approved.

In Peru, CONAMUSA is the coordinating mechanism for purposes of the Global Fund, and the Principal Recipient is CARE Peru, which plays an important role in fighting poverty in the country. CARE Peru is in charge of administering the financial resources of the Global Fund and contributes to the achievement of the goals agreed to with the Fund.[5]

The HAART program, which is run by the National Health Strategy for the Prevention and Control of Sexually Transmitted Infections and HIV/AIDS (ESN-PCITS-VIH/SIDA) of MINSA with Global Fund support, was initiated in May 2004, and its goals are treatment at the national level as committed to with the Fund, with regard to both implementation and financing. The proposal presented by CONAMUSA established a goal for the first year (2004) of the project of assigning 7,000 PLWHA to HAART, and, based upon reprogramming established for the second phase, in 2007 this number is expected to reach 9,000 individuals. MINSA's financial participation will become greater and greater and, five years into the program, it is forecast to be sustained completely through the use of Peruvian resources.[6]

The DOTS-Plus program has been under way since September 2003, concentrating on Objective 3 of the Project for Strengthening of Control of Tuberculosis in Peru: "Extending DOTS coverage from 50 percent to 90 percent, and improving the rate of cure for TB MDR patients from 60 percent to 85 percent,"[7] through financing from the Global Fund.

According to CARE Peru, since the beginning of the program, for the HIV component, the sum of 15,965,762.30 U.S. dollars (USD) has been used, representing 41 percent of the investment cost for medicines. For the TB component, USD 22,469,050.52 (92 percent of budget) has been used, with the investment in medications representing 29 percent of that figure.[8]

The Global Fund mission, which visited the country in April 2006 to conclude negotiations and sign the contracts for the second phase of the program, established as conditions for the disbursement of funds for the purchase of health products that the scheduling and the handling of inventories of the products purchased with the resources of the fund (Second Round) be substantially improved no later than October 30, 2006.[9]

[5] Selection of Executive Consortiums for the program "Closing Gaps: Toward the Achievement of the Millennium Objectives for TB and AIDS in Peru." HIV/AIDS Component. Bid 002-2006 Care Peru.
[6] Monitoring and Evaluation Report on the implementation of the UNGASS commitment by Peru. December 2005, page 26.
[7] Technical Norm 025 – MINSA/DGSP. Updating the Care of Patients with Multidrug-resistant Tuberculosis (MDR-TB). RM 162-2005/MINSA.
[8] Care Peru. Annual Report on the HIV-AIDS Component. July 2005–November 2006. "Strengthening Prevention and Control of AIDS and Tuberculosis in Peru" program.
[9] CONAMUSA and CARE Peru. 2006 Request for Technical Assistance to Global Funds Grants: "Technical Support to Strengthen the Medical Supply System for HAART and DOTS-Plus Programs in Peru."

For purposes of complying with this requirement, an ad hoc committee was established that included representatives of the Executive Secretariat of CONAMUSA, the National Health Strategies for HIV/AIDS and TB, DIGEMID, and CARE Peru. This committee identified as critical problems in the handling of the supply of medications *selection* (the existence of 52 different HAART schemes, which would be very complicated to handle) and *purchasing* (among other problems, the delay in the process, which could take up to six months). In addition, for purposes of optimizing purchases, the government has taken the initiative in applying new modalities, such as the inverse auction, but, for this method to work, technical specifications are required that define in a rigorous fashion the medicines and supplies to be purchased. In the case of medicines relating to the diagnosis and treatment of HIV/AIDS and TB, such information has not yet been prepared.

It is pertinent to add that, at the initiative of CARE Peru, between May and July 2006, several consultancies were carried out to make a technical evaluation of the system for the supply of ARVs[10] and of the management of the stocks of these pharmaceuticals and those used in the treatment of TB[11] within the scope of MINSA.

The present consultancy is oriented toward both a rapid evaluation of changes that have occurred in the last six months with regard to the system for the supply of ARVs and MDR-TB medicines, and a critical analysis of the situation regarding the HAART schemes, so as to prepare proposals for their improvement. In addition, taking into account the lack of technical specifications for some medicines and reagents for the management of HIV/AIDS and MDR-TB, consideration has also been given to the preparation of such documents, which will be used for the joint purchases of the government as well as for updating the National Essential Medicines List.

Objective of the Technical Assistance

To strengthen the supply system for medicines and supplies used in the ESN-PCITS-HIV/AIDS and multidrug-resistant tuberculosis of MINSA.

Expected Products

- *Product 1:* Rapid evaluation of the Integrated Medical Supply System (SISMED) for ARVs and MDR-TB medicines, determining progress over the last six months. In addition, to provide technical assistance for strengthening this system.

- *Product 2:* Evaluation of the HAART regimens of the various health subsectors and a proposal for standardizing and optimizing the Ministry of Health regimens.

[10] CARE Peru. August 2006. *Final Consulting Report: Evaluation of the Management of the ARV Supply in the Context of the HAART Initiative of the Ministry of Health.*
[11] CARE Peru. June 2006. *Final Consulting Report: Management Plan ARVs for MDR-TB Medicines Stock in CARE Peru and the Global Fund.*

- *Product 3:* Preparation of technical specifications and dossiers for medicines, medical materials, and reagents for managing HIV/AIDS and MDR-TB, which will be used for updating of the National Essential Medicines List and the joint purchases of medicines and supplies.

Methodology

This consultancy used various instruments and methodologies for obtaining and processing information. For Product 1, checklists were used in collecting data, as well as direct observation techniques, documentary reviews, analysis of databases, and interviews with individuals connected with the supply of ARVs and medicines for MDR-TB.

For Product 2, bibliographical and documentary reviews were done; visits were made to institutions with interviews of key participants; official HAART reports were analyzed; and comparative evaluations were made of treatment guidelines (including those of five other Latin American countries), among other methods.

For Program 3, the methodologies used included interviews with employees of such institutions as DIGEMID and the National Institute of Health, documentary reviews, standardization of the nomenclature to be used, preparation of models for technical dossiers, and others.

Findings and Recommendations

Improvement of the Medical Supply System

Starting with a rapid evaluation of the system that emphasized the variations observed over the last six months, this technical assistance component was oriented toward improving the management of the supply system for ARVs and MDR-TB medicines and proposing strategies and tools that will contribute to strengthening the capabilities of those responsible for the system at all levels of coordination.

Among the main problems, the following were found: a limited capacity for the management and integration of individuals connected with the supply of ARV and MDR-TB medicines; a fragmented information system that is incomplete and unreliable; weaknesses in inventory management, with no establishment of safety-stock levels; storage practices that do not meet the requirements of Good Storage Practices (GSP), with problems in infrastructure and equipment; a minimum priority assigned to the development of supervision and monitoring activities; and an absence of defined and used management indicators.

With regard to the process of *selection*, as a result of an earlier evaluation in May and July 2006 by CARE Peru, which reported deficiencies in the levels of coordination of DIGEMID and the General Directorate of Health of Individuals (DGSP) (National Health Strategies), an improvement has occurred in recent months, which must still be translated into a clear correspondence between the medicines of the National Essential Medicines List and the

treatment schemes. Currently, treatment guidelines (Technical Norms) for HAART are being reviewed for both children and adults, as well as the guidelines relating to the prevention of vertical transmission of HIV from mother to child, with the expectation that rigorous procedures and techniques as established in the norm for preparing guidelines of clinical practice will be applied. Last, mention should be made that a relatively new pharmaceutical product is being used for treating MDR-TB, financed by manufacturers, that the evaluation under Product 3 of this consultancy concluded lacks the qualities required for its inclusion in the treatment schemes.

The *planning* of ARV and MDR-TB medicine needs is done at the level of the facilities and the Health Directorates (DISA), using technical criteria defined at the central level. However, there is a lack of integration and systematization of the information external to MINSA (nongovernmental organizations [NGOs], Partners in Health, Armed Forces, and the Police, etc.). Also, no comparative evaluation is made between the annual planning for ARV and MDR-TB medicines and the actual consumption for the corresponding period. This evaluation is essential for adjusting the planning criteria, promptly detecting risks of stock-outs of products and of excess inventory that could result in the expiration of products, and ascertaining the need to devote more resources to products that are required.

With regard to *purchases*, the national experience at corporate purchasing based upon the inverse auction concept (2006), with the joint participation of MINSA, Social Security of Peru (EsSalud), Armed Forces, and Police Forces, has permitted a savings of approximately 10 million new soles (15 percent) and a reduction in process time (to 27 days). Of the 188 medicines scheduled, only 3 were ARVs. Prices were reduced by 16.21 percent for lopinavir/ritonavir, 13.05 percent for saquinavir, and 32.40 percent for ritonavir, as compared with the reference purchase prices. Also, prices were lower by 36.2 percent, 10 percent, and 1.33 percent, respectively, for those medicines in relation to the prices established for the latest purchase made by MINSA through a public bid in 2006.

It has been demonstrated that the planning and purchase of ARVs for patients financed by Integral Health Insurance (children under age 18 and pregnant women) are done by each hospital in an individual fashion. Under this modality, the price is increased by up to 12 times, and in certain cases, no supplier could be found. This situation causes loss of economies of scale and opportunity, which negatively affects the hospitals. The inclusion of these products within the purchasing modality used for adult products seems to be the most appropriate immediate solution.

No improvements have been observed in the various levels of *storage* of ARVs and MDR-TB medicines in comparison with what was reported in the prior consultancy. The MINSA Central Medical Stores (CMS) presents serious deficiencies with regard to the storage of these products. In addition, this warehouse is not registered with DIGEMID and has no GSP certification. The General Office of Administration (OGA) is awaiting an evaluation report from the General Directorate for Infrastructure, Equipment and Maintenance, so as to take corrective actions. However, given that this is not the only storage facility with deficiencies, a comparative cost analysis is recommended between the option of improving this and the DISA storage facilities and establishments and the option of contracting for the services of a logistics operator that

include, in addition to the functions of storage and inventory management, an information system that permits the MINSA managers to have up-to-the-minute information available.

Considering the Joint United Nations Programme on HIV/AIDS (UNAIDS) indicator for evaluating national AIDS programs on the supply of medications—"*percentage of storage and dispensing for ARVs that ran out of supplies in the last six months"*—it was noted that, at the CMS level, the DISA storage facility for Lima, the Second of May Hospital, and the Institute for Child Health, at least one product was out of stock during the period of this study.

With regard to medicines for MDR-TB, isoniazid, streptomycin, pyridoxine, and capreomycin were found to be out of stock at the Lima DISA. It was also found that Partners in Health is making deliveries without distilled water ampoules. Also, some ARVs, such as atazanavir, abacavir, and the combination of stavudine+lamivudine+nevirapine 30/150/200 mg, were out of stock at that same DISA and at the Second of May National Hospital. Nevertheless, attention must be strongly called to the fact that such products were available at the CMS and at the storage facility for Pro-Vida Medicine Services (PROVIDA), which reveals a lack of coordination and of appropriate access to information between the entities at the DISA level, the Office of Strategic Resources of OGA (ORE), CMS, and PROVIDA.

Expired ARVs and MDR-TB medicines were also found at the PROVIDA storage facility (six ARVs, worth USD 90,500); at the CMS (15,380,844 100 mg isoniazid tablets and 71,032 vials of rifampicin, 100 mg/5mg × 60ml, valued at USD 97,663); and at the Lima DISA storage facility (seven ARVs and capreomycin, with a value of USD 10,444 and USD 532, respectively).

It was determined that *basic indicators for managing the supply* of ARVs and MDR-TB medicines have been defined, and that therefore, no information is collected about them (e.g., percentage of products that are out of stock, overstocked products, understock, nonrotation, returns, expired products, redistributed products) at the level of treatment facilities, distribution centers, or storage centers (Specialized Medicine Stores [AEM] DISA and AEM Networks) and at the central level (ORE and DIGEMID).

There are no flow diagrams, chronograms, or procedure manuals for the distribution of ARVs at the DISA and facility levels. The availability of vehicles for the transport of medicines is restricted. No transport units ensure constant and prompt distribution of ARVs and MDR-TB medicines from the CMS to the DISAs, and from there to hospitals. *The medicine may be at the CMS, but because of the lack of transport, it does not reach the treatment center.* Currently, a critical problem exists with the distribution of strategic medicines (including ARVs and those for MDR-TB) from the CMS to the AEMs of DISAs and Regional Health Directorates (DIRESAs), caused by the delay in the process of contracting transport services. Therefore, the latter have to finance the transport of their products.

The average time between the diagnosis of a patient with MDR-TB and the delivery of medicines to the health facility responsible for the initiation of treatment is 20 to 30 days at the level of the Lima City DISA.

Another problem that persists is the preparation of cut dosages of ARV medicines for pediatric patients (hospitals) and the breaking up of doses into capsules for MDR-TB patients younger than one year of age or with low weight (AEM DISA Lima). In the first case, the hospitals do not have the appropriate equipment for preparing such pharmaceutical forms (analytic scales, individual compartments, among others) to guarantee the quality of the medicines dispensed in this form. In the second case, this activity is not one of the functions of an AEM, and it should therefore be done at the hospital level, assuming the presence of improved equipment.

Supervision and monitoring of the various processes of the supply system for ARVs and MDR-TB medicines have not been systematized or established in a regular fashion. Also, problems persist with regard to the *management of information*, such as the problem of partial information caused by failure to deliver information and unregistered providers, the absence of indicators, the absence of feedback, lack of updating (unregistered providers: PROVIDA, Partners in Health, National Penitentiary Institute, NGO, Armed Forces and Police Forces, University Centers, and others), applications without computerized reports, absence of reports on quality control of data, lack of a standard and specific application that includes hospital information, and parallel information systems. Currently, the SISMED application is being used as well as the application that the ORE recently implemented.

In conclusion, it has been found that the supply system for ARVs and and MDR-TB medicines shows deficiencies similar to those presented in the findings for the year 2006. The determinants of these findings are probably frequent changes in personnel at the central and operating levels, reorganization of the functions of MINSA (liquidation of the Program for Administration of Management Agreements, creation of the ORE, transfer of functions), absence of management indicators, lack of financing for supervision and monitoring activities, lack of feedback at the operating levels, and lack of the application of a culture of continuous improvement of the quality of the system.

Despite the preceding, some improvements or strengths of the system have been found, as presented below:

- With regard to selection, higher levels of coordination exist between DIGEMID and the National Health Strategies for HIV/AIDS and TB, as well as the current process, initiated with political backing at higher levels, to integrate requests for bids for medicines from all of the institutions in the health sector, which will assist in joint purchasing.

- The new model for purchasing on the basis of the inverse auction process has shown clear advantages with regard to purchase times, adjudication of the medicines offered, and prices.

- The management of the supply of strategic medicines under a single administration. The ORE is presently responsible for the supply of strategic medicines within MINSA, which includes ARVs and MDR-TB medicines. Because of the short time it has been functioning, ORE should be given the necessary support so that it can take on its task in the best fashion.

- Health personnel are committed to the mission of the National Health Strategies for HIV/AIDS and MDR-TB at the central and operating levels.

- Although the information system presents weaknesses, it also represents a good opportunity; applying the reengineering of processes and introducing the corresponding improvements could lead to the creation of a solid and integrated virtual supply system.

- The quality of the medicines is guaranteed before their delivery to the MINSA storage facilities and the storage facilities of CARE and Partners in Health. The performance of quality tests is now accredited through Test Reports issued by the accredited laboratories of the Network of Official Laboratories for Quality Control, at MINSA.

Finally, based upon the principal problems identified in this evaluation, the following set of actions and measures is recommended for improving the supply system for ARVs and MDR-TB medicines:

- *Problem:* Inefficient management model for the supply of ARVs and MDR-TB medicines

  Recommendation: Revisit all the processes to generate an improvement or substantial change in the model for managing the supply of strategic medicines under the administration of ORE and within the guidelines of SISMED (through consultancy).

- *Problem:* Limited management capacity of ORE in the supply of strategic ARVs and MDR-TB medicines

  Recommendation: Strengthen the technical and administrative aspects of ORE: organization model; hire qualified human resources; develop standards, regulations, and procedures for the management processes relating to the supply of ARVs and MDR-TB medicines.

- *Problem:* Weaknesses in the present information systems for the supply of ARVs and MDR-TB medicines

  Recommendation: Strengthen the information systems through a platform for a "virtual supply chain," permitting the control of information quality, consultations, and online reports, "Balanced Scorecard" indicators (monitoring, evaluation, and control) according to administrative level. This can be developed with assistance from the General Office for Statistics and Computerization (OGEI) at MINSA.

- *Problem:* Storage facilities unqualified with regard to GSP, with serious problems of infrastructure and equipment

  Recommendation:

  - Immediately improve the conditions for storage at the CMS, and develop an investment project for the construction of a model pharmaceutical storage facility at

the central level, in compliance with the GSPs, or evaluate the appropriateness of leasing a GSP-certified storage facility for ARVs and MDR-TB medicines. Implement a model standard for regional storage facilities for medications that ensures GSPs.

- Study the viability and feasibility of contracting a private logistics operator to take responsibility for the storage and distribution process for ARVs and MDR-TB medicines (which could be extended to all strategic medicines). This logistics operator would be responsible for storage and distribution, based upon information from the logistical system regarding inventories. This strategy would relieve MINSA of the responsibility for handling inventories in storage facilities and would reduce operating costs. Therefore, a comparative analysis is required of the costs of the service that presently is provided by MINSA and of the service that would be provided by a logistics company that would perform such functions.

- *Problem:* Restricted and insufficient supervision and monitoring activities

  Recommendation: Develop and implement an annual integrated supervision and monitoring plan at different levels of the system that guarantees the assignment of budgets, tools that are integrated with supervision, subdivided by components according to level (local or regional), training of personnel, feedback, and follow-up.

- *Problem:* The System for Pharmaceutical Care and the Unit Dose System for patients with HIV/AIDS and MDR-TB has not been implemented

  Recommendation: Prepare, implement, and monitor an intervention plan that permits the development of a pharmaceutical care and supply system for unit doses at the level of national hospitals (HAART) and health centers (MDR-TB), on a pilot basis, throughout the country. This plan could be initiated at the Child Health Institute, the Second of May Hospital (HAART) and the health centers in Lima (MDR-TB) within a period of four to six months, with outside help to MINSA.

Analysis and Optimization of HAART Schemes

Analysis of the HAART Schemes at MINSA

This component of the consultancy was oriented toward analyzing the ARV schemes and other aspects relating to the Guidelines for Management of Patients with HIV/AIDS in the different institutions of the health sector, and, based upon the results, preparing a proposal for standardizing and optimizing these schemes at the Ministry of Health.

At the end of December 2006, 9,427 patients on HAART were reported at the national level, of which more than two-thirds (68 percent) were being treated in a MINSA establishment, 30 percent at EsSalud, and only 2 percent by the Armed Forces and the Police Forces. Because no access was possible to the required information, no evaluation was made of the treatment norms for HIV/AIDS at these military and police institutions, although reports indicated that at some of

these institutions (naval hospitals and the police), official MINSA guidelines were being used. With regard to systematic reports on HAART by ARV regimens and number of patients, with the exception of the Naval Hospital and the Police Hospital (which report in a partial fashion to MINSA), the other institutions (including EsSalud) do not have this type of information.

Among the most significant findings of the present evaluation is a lack of formal reports regarding the processes of preparing and reviewing the guidelines or technical norms for treating patients with HIV/AIDS, involving both adult and pediatric cases; nonsystematic reviews of the literature were made; the methodology used has been that of informal consensus and no rigorous analysis was made of costs. The guidelines for treating adult and child patients present some deficiencies, especially with respect to the precision or specificity of some recommendations.

At the initiative of ESN-PCITS-HIV/AIDS and of the committees of experts, processes for updating these guidelines have been initiated. This fact becomes very relevant, especially in the case of the guidelines for pediatric patients, which date from 2003, because a large gap exists between what is stipulated with regard to the ARVs and authorized schemes, and what is observed in actuality. The committees or networks of experts—for both adult and child patients—have as their principal function discussing complicated cases to make decisions on the most appropriate treatments. From the beginning, these committees have confronted a series of limitations and deficiencies that are an obstacle to optimum performance.

A comparative evaluation of the MINSA guidelines and those of the World Health Organization, the guidelines of EsSalud, as well as those of five other Latin American countries (Argentina, Brazil, Chile, Colombia, and Mexico) shows both concordance and differences. The initial MINSA schemes are in agreement with those proposed by WHO (2 nucleoside reverse transcriptase inhibitors [NRTIs] + 1 non-nucleoside reverse transcriptase inhibitor [NNRTI], not considering protease inhibitors [PIs]), which contributes to a more limited use of ARV combinations.

With regard to the rescue schemes (primary rescue), in contrast to the guides of other countries, those of MINSA and EsSalud agree with the recommendations of WHO with regard to the use, in rescue schemes, of a limited number of standard regimens, which is appropriate and advantageous from the financial and logistical point of view.

However, the initial and rescue HAART schemes for children—of both MINSA and EsSalud—do not agree with the WHO recommendations, which fact should be justified (or questioned) through a systematic and rigorous evaluation of the accumulated experience in the treatment of HIV/AIDS in children.

In the analysis of the HAART schemes used at MINSA, it was determined that 15 different ARVs are included, of which 12 are considered in the 14th WHO Model List of Essential Medicines in 2005. Not included in this list are tenofovir (TDF), emtricitabine (FTC), and atazanavir (ATV), but TDF and FTC are considered in the WHO treatment recommendations. Because of the high cost of these last three pharmaceuticals, ESN-PCITS-HIV/AIDS should apply more rigorous criteria regarding their use, which could include restricted usage; it should be kept in mind that both TDF and FTC will, in the future, have to be financed by MINSA.

As was reported already in the prior evaluation by CARE Peru, no clear correspondence exists between the ARVs of the official schemes for treatment and the National Essential Medicines List (e.g., the latter does not include the three ARVs mentioned previously). Also, the ARV schemes include various fixed-dose combinations, all recommended by WHO, but that are not yet considered in the National Essential Medicines List.

In 2007, 71 HAART schemes for adults are reported (seven of which are not being applied). This number is significantly higher than the figure for eight months ago, which was only 48; that is, an increase of 32.4 percent has occurred, which indicates a growth trend that deserves special attention by ESN-PCITS-HIV/AIDS.

Almost all of the initial schemes for adults (99.5 percent) contain only six ARVs, and the rescue schemes include eight ARVs, numbers that are acceptable from the technical point of view. However, the special schemes consider a total of 13 different ARVs. Moreover, attention is called to the high number of patients with initial treatments that include stavudine (D4T), a pharmaceutical not recommended for use in the initial phase because of its side effects (mainly lipodystrophy and peripheral polyneuropathy). Also, some schemes have been identified that are not in accordance with current international recommendations, and these should be reviewed by the Committees of Experts.

A highly relevant finding is that the majority of adult patients (86 percent) are being treated with an initial scheme, while 9 percent of patients are in rescue treatments and 5 percent in the so-called special schemes. This fact is particularly advantageous with regard to financing and the supply process.

Additionally, another favorable and highly relevant fact regarding the supply system for ARVs has been observed: *almost half (49 percent) of HAART patients receive the initial treatment using zidovudine (AZT), lamivudine (3TC), and nevirapine (NVP) (which is one of the most economical and available agents in a fixed-dose combination), and 82 percent of the patients treated receive only one of five different schemes (four initial and one rescue).*

With regard to pediatric treatments, apart from what has already been mentioned regarding the lack of correspondence of the national schemes with those recommended by WHO, attention is called to *the increase by double of the number of schemes (from 9 to 18 in only eight months), as well as the increase in ARVs used (from 6 to 12 within the same time period).* Also, applying international recommendations for ARV treatment, about 91 percent of pediatric patients are estimated to be receiving initial treatments, 64.8 percent of them with the combination of AZT+3TC+NFW, the initial scheme included in the existing national guideline.

Last, the cost analysis showed, among other more significant results, that while 86 percent of the population of patients in initial treatment receive 49 percent of the budget for ARVs, a very similar percentage (43 percent) is invested for only 9 percent of the patients under rescue schemes. Interestingly, upon analyzing the cost of 32 schemes that are very little used (with only one to three patients) and that give rise to a great dispersion of schemes, the annual cost for these

treatments, aimed at a population of only 44 patients, has only a minor effect with respect to the budget for ARVs, representing only 2 percent of the total.

Proposal for Standardization and Optimization of the HAART Schemes Used at MINSA

The treatment schemes contained in the Technical Norms, Manuals, and Directives of the Peruvian Ministry of Health constitute the basis for the process of selecting ARVs for HAART. Technical recommendations contained in these official documents have permitted a standardization of schemes, although not yet at an optimal level.

It has been suggested that an excessive number of treatment schemes could complicate the supply system, especially with regard to processes for planning and purchasing ARVs, and this could result in excessive costs for planning and purchasing products for unnecessary schemes, a reduction in budget for the purchase of those that are more necessary, an increase in toxicity and adverse reactions for patients, the need for changes in treatment, and the consequent possibility of failure to adhere to the treatment. As a result, the current schemes need to be carefully evaluated to consider only those treatment schemes that are supported by scientific evidence and low toxicity, for each type of treatment (initial, rescue, and special). The fact that at present 64 HAART schemes for adults and 18 schemes for pediatric patients are being used appears to indicate that a review of these schemes would be valuable.

One highly relevant aspect of public health relates to the costs of treatment, which is a determining factor with regard to access to ARVs and the continuity of treatment. The results in this regard are satisfactory because, despite the high number of schemes observed, principally for adults, in 82 percent of the cases only four initial treatment schemes and one rescue scheme were used, and almost half of the total number of patients uses a single scheme only. Also satisfying is that, in the present study, it has been demonstrated that the majority of patients are receiving initial treatment schemes that are the most economical (with the exception of those that contain abacavir [ABC]).

To contribute to the optimization of the HAART schemes used within the Ministry of Health, both quantitatively and qualitatively, the consultants make the following recommendations; they are formulated as a set of strategies or interventions for confronting or improving on concrete difficulties or problems identified, principally at the levels of ESN-PCITS-HIV/AIDS, the treatment guidelines, the committees of experts, the health facilities, and the HAART prescribers.

- *Problem:* Treatment guidelines for patients with HIV/AIDS are imprecise and have gaps; they need to be updated in accordance with current national and international technical recommendations.

  Recommendation: Correct the deficiencies found during this evaluation during the current review and updating process of the HIV/AIDS management guidelines (children, adults, prevention of vertical transmission) that ESN-PCITS-HIV/AIDS is conducting with the Committees of Experts.

- *Problem:* Committees (Networks) of Experts have limited visibility and lack the necessary support for good performance.

  Recommendation: Identify and implement mechanisms/strategies that are effective, so networks of experts can be strengthened and thereby achieve greater recognition, ensuring in a progressive fashion the basic conditions necessary for the adequate functioning of these networks.

- *Problem:* Possibly inappropriate ARV treatment schemes were observed.

  Recommendation: Have the HIV/AIDS network of experts reevaluate schemes that do not comply with current international recommendations, especially those of WHO, so as to consider possible modifications.

  The authors also suggest a progressive reevaluation of the special treatments and the application in the future of a technical guideline aimed at a better systematization of the combinations of ARVs for patients in complicated clinical situations. This guideline must have as one of its purposes the avoidance of an unnecessary increase in the number of schemes.

- *Problem:* Difficulties in the coordination/interaction between ESN-PCITS-HIV/AIDS and the network of experts with respect to some of the health facilities that provide HAART.

  Recommendation: Optimize the communication between the central level and the networks of experts with all of the health establishments (institutes, hospitals, health centers, NGOs, and other institutions) to achieve full and proactive participation by the professionals of the health facilities authorized for HAART.

- *Problem:* The levels of adherence by the prescribers to the technical norms—which level is presently high—could be compromised by the broadening of the HAART program and by the growing number of patients with complex clinical situations.

  Recommendation: Maintain/intensify activities relating to training and regular communication with prescribers, especially with the professionals of facilities in the different regions of the country where HAART has recently been initiated.

  It should be anticipated that, progressively, the prescribers will confront a greater number of patients with complex clinical-therapeutic situations, demanding greater effort and care in choosing adjustments in treatment, with evaluation of the committees of experts.

- *Problem:* Lack of harmonization between the MINSA ARV Treatment Guidelines and those of EsSalud.

  Recommendation: Implement initiatives for making technical recommendations more uniform, bearing in mind that the present moment is propitious, because joint purchasing

of medications is taking place and a technical committee has been established for preparing a proposal for Joint Tendering for Medicines for the Ministry of Health, EsSalud, the Armed Forces, and the Police Forces.

- Other suggestions:

  - Distribute to physicians and pharmacists the updated costs of the ARVs and HAART schemes, a task that should be assumed by the ESN-PCITS-HIV/AIDS and DIGEMID.

  - Correct deficiencies in the monitoring and reporting of treatment schemes versus patients versus facilities (e.g., repeated schemes in two different classes of treatment, special schemes not recognized by the network of experts).

  - Search for financing for the INS to carry out tests of resistance to ARVs, to contribute to the appropriate treatment of some patients with therapeutic failures, requiring a readjustment of the ARV regimen based upon the best possible evidence.

Next Steps

The following technical assistance activities relating to HAART schemes and, in general, to the guidelines for treating patients with HIV/AIDS are proposed.

- Accompaniment of the process for the optimization of ARV treatment schemes with a consultancy, especially in reviewing proposed new guidelines for treating HIV/AIDS. One or two experts in infectious diseases and in guidelines for clinical practice (for HIV/AIDS) should assume this responsibility. A good part of this consultancy could be carried out by e-mail (April–September 2007).

- A rigorous technical evaluation of the group of patients whose treatments were observed or technically questioned in the present consultancy, as well as those with special or individualized treatment, and the preparation of a methodology or guideline for systematizing the future handling of this type of patient. (Consultancy with an expert on infectious diseases with broad international experience with HIV/AIDS, public health, and mastery of the principles of the selection and rational use of medicines, for two weeks in April or May 2007.)

- Consultancy regarding the preparation of a common or integrated guideline for treating HIV/AIDS for all institutions in the health sector, with leadership provided by MINSA. This activity will depend upon a prior decision by the higher-level authorities at each of the institutions involved. This should be done through consultancies with one or two experts with technical profiles similar to that described for the first of these three activities.

Preparation of Technical Specifications and Dossiers to Be Used in Purchasing Medicines and Reagents for the Diagnosis and Treatment of HIV/AIDS and MDR-TB

At the end of 2006, the Peruvian government carried out the first corporate purchase of medicines for the public sector through the new modality of inverse auction, with very advantageous results. For this type of purchase, the corresponding technical specifications for the medicines and supplies are required, and these should be prepared by expert professionals. These files should contain all of the technical specifications of the products to be purchased. It was for this reason that the decision was made to prepare the technical specifications for five laboratory kits prioritized by ESN-PCITS-HIV/AIDS.

Also, as a way of contributing to the concordance between ARVs and MDR-TB medicines included in the National Essential Medicines List and those considered in the treatment schemes instituted by the national strategies, it was regarded as appropriate to prepare technical dossiers based on the best available evidence, for five medicines (four of them ARVs)—pharmaceuticals which, despite being used in the treatment of patients, are not presently included on the National Essential Medicines List. These dossiers would constitute the basis for supporting the inclusion or exclusion of such medicines in the list in question.

Technical files were prepared for the following laboratory kits—

1. Complete kit for recounting of lymphocytes CD4/CD8, including buffer and controls
2. Kit for recounting of lymphocytes CD14-CD4C/lisis-bynabeads solution
3. PCR (polymerase chain reaction) test kit for HIV viral load in human plasma
4. Kit for viral load (chemical luminescence)
5. Kit for viral load of HIV-1 by the PCR technique in real time

Technical dossiers for the following medications were prepared—

1. Moxifloxacin tablet
2. Atazanavir tablet
3. Saquinavir tablet
4. Abacavir tablet
5. Stavudine+lamavudine+nevirapine tablet (fixed-dose combination)

In the case of the technical specifications, a review was made of official texts and works (American and British pharmacopeias; the Merck Index; DIGEMID legal norms and those of the official daily, *El Peruano*); pharmaceutical product registration dossiers (DIGEMID); databases and other documents through the Internet. For the preparation of the technical dossiers, use was made of the PERUDIS (DIGEMID) data, FDA, EMEA, price catalogs (e.g., Kairos, MSH), and Lists of Essential Medicines (of MINSA and the WHO model list). There was also a review of tertiary sources (BNF, USP-DI, pharmacological texts), secondary sources (Cochrane Library, PubMed, Medline, IDIS, among others), and primary sources (various journals such as the *Lancet, BMJ, JAMA, NEJM,* accessed electronically).

The structure or format of the technical dossiers for medications included the following items: introduction, general and pharmacological aspects, evaluation of efficacy, evaluation of safety, cost evaluation, availability in the national market, conclusions, recommendations and bibliographical references.

Important Findings

- *Problem:* The register of laboratory materials in the DIGEMID database does not use international technical denominations. The register comprises brand names or descriptions using the titular criterion of the registry. This system makes the identification of products registered within the country difficult.

  Recommendations:

  - Prepare an Official Catalog of Laboratory Materials, with international technical descriptions.

  - Improve the technical terms used by DIGEMID for pharmaceutical product registration, so that they are standardized. Catalogs should be prepared with standardized descriptions in which the individual who wants apply for product registration selects the terms or descriptions from the catalogs in question.

- *Problem:* No database exists of reference prices for strategic medicines that permits an analysis of reliable costs for treatment schemes with different therapeutic alternatives.

  Recommendations:

  - Update the laboratory materials product registration database at DIGEMID.

  - Coordinate with international entities periodically to receive a list of updated reference prices for strategic medicines.

- *Problem:* Information on clinical studies of moxifloxacin at the national and international levels is insufficient for its use as a pharmaceutical in treating MDR-TB. Alternatives such as levofloxacin and ofloxacin should be considered.

  Recommendation: Prepare a procedures manual so that users at hospital centers can prepare technical dossiers on laboratory materials; the manual should include instructions, basic information, participants, responsibilities, flows, and entities responsible for the approval of such technical dossiers.

- *Problem:* In terms of antiretroviral medicines, the National List for Essential Medicines does not agree with the recommendations of the Technical Norms prepared by the National Health Strategy for treating patients with HIV/AIDS.

Recommendation: Strengthen the coordination between DIGEMID and DGSP to achieve agreement between the Technical Norms prepared and approved for treating patients with HIV/AIDS and TB (with regard to the medicines included) and the National List of Essential Medicines.