

PD-ANZ-791

AGENCY FOR INTERNATIONAL DEVELOPMENT PROJECT DATA SHEET	1. TRANSACTION CODE <input checked="" type="checkbox"/> A = Add <input type="checkbox"/> C = Change <input type="checkbox"/> D = Delete	Amendment Number _____	DOCUMENT CODE 3
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2. COUNTRY/ENTITY Worldwide	3. PROJECT NUMBER <input type="checkbox"/> 936-5987 <input type="checkbox"/>
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4. BUREAU/OFFICE S&T	5. PROJECT TITLE (maximum 40 characters) <input type="checkbox"/> Americares <input type="checkbox"/>
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6. PROJECT ASSISTANCE COMPLETION DATE (PACD) MM DD YY 09 30 90	7. ESTIMATED DATE OF OBLIGATION (Under 'B.' below, enter 1, 2, 3, or 4) A. Initial FY <input type="checkbox"/> 85 <input type="checkbox"/> B. Quarter <input type="checkbox"/> 4 <input type="checkbox"/> C. Final FY <input type="checkbox"/> 85 <input type="checkbox"/>
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8. COSTS (\$000 OR EQUIVALENT \$1 =)						
A. FUNDING SOURCE	FIRST FY			LIFE OF PROJECT		
	B. FX	C. L/C	D. Total	E. FX	F. L/C	G. Total
AID Appropriated Total			(800)			(800)
(Grant)	()	()	(800)	()	()	(800)
(Loan)	()	()	()	()	()	()
Other U.S.	1.					
	2.					
Host Country						
Other Donor(s)						
TOTALS			800			800

9. SCHEDULE OF AID FUNDING (\$000)									
A. APPROPRIATION	B. PRIMARY PURPOSE CODE	C. PRIMARY TECH. CODE		D. OBLIGATIONS TO DATE		E. AMOUNT APPROVED THIS ACTION		F. LIFE OF PROJECT	
		1. Grant	2. Loan	1. Grant	2. Loan	1. Grant	2. Loan	1. Grant	2. Loan
(1) HE	U	513	590			800		800	
(2)									
(3)									
(4)									
TOTALS						800		800	

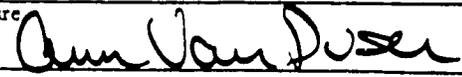
10. SECONDARY TECHNICAL CODES (maximum 6 codes of 3 positions each)	11. SECONDARY PURPOSE CODE
12. SPECIAL CONCERNS CODES (maximum 7 codes of 4 positions each) A. Code BR B. Amount 800	

13. PROJECT PURPOSE (maximum 480 characters)

To contribute of field trials of a new multidrug therapy for leprosy.

14. SCHEDULED EVALUATIONS Interim MM YY MM YY Final MM YY 09 87 09 90	15. SOURCE/ORIGIN OF GOODS AND SERVICES <input checked="" type="checkbox"/> 000 <input type="checkbox"/> 941 <input checked="" type="checkbox"/> Local <input type="checkbox"/> Other (Specify)
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16. AMENDMENTS/NATURE OF CHANGE PROPOSED (This is page 1 of a _____ page PP Amendment.)

17. APPROVED BY	Signature  Title Ann Van Dusen Acting Director, S&T/H	Date Signed MM DD YY 06 13 85	18. DATE DOCUMENT RECEIVED IN AID/W, OR FOR AID/W DOCUMENTS, DATE OF DISTRIBUTION MM DD YY
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Project Authorization

Name of Country: Interregional Project Title: Americares
Project No.: 936-5957

1. Pursuant to Section 104 of the Foreign Assistance Act of 1961, as amended, I hereby authorize the centrally funded project, AMERICARES, involving planned obligation not to exceed \$800,000 in grant funds for fiscal year 1985 subject to the availability of funds in accordance with the A.I.D. OYB/allotment process, to help in financing foreign exchange and local currency costs for the project.

2. The project will provide drugs, technical assistance, and operating expenses to support the conduct of field trials of a new leprosy control and prevention method. This project will be carried out through a grant to the Americares Foundation, a private voluntary organization registered with A.I.D. Field trials will take place in Venezuela with the collaboration of the Venezuelan Government. (Hereinafter referred to as the cooperating country.)

3. The agreement(s) which may be negotiated and executed by the officer(s) to whom such authority is delegated in accordance with A.I.D. regulations and Delegations of Authority shall be subject to the following terms and conditions, together with such other terms and conditions as A.I.D. may deem appropriate.

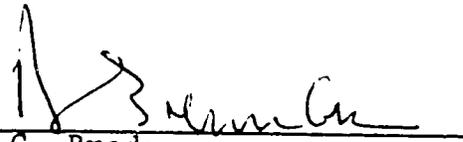
4. Source and Origin of Commodities, Nationality of Services

a. Commodities financed by A.I.D. under the project shall have their source and origin in the cooperating country or the United States except as A.I.D. may otherwise agree in writing. Except for ocean shipping, the suppliers of commodities or services shall have the cooperating country or the United States as their place of nationality, except as A.I.D. may otherwise agree in writing.

b. Waiver Based on the justification set forth in the attached Action Memorandum I hereby approve the waiver of source/origin/nationality from Code 000 (U.S. only) to Code 935 (Selected Free World) to permit procurement of up to \$88,000 worth of the drug clofazimin for use under the project and certify that the exclusion of procurement from Free World Countries other than the cooperating country and countries included in Code 941 of the AID foreign policy objectives and the objectives of the foreign assistance program.

~~CONFIDENTIAL~~

c. Ocean shipping financed by A.I.D. under the project shall, except as A.I.D. may otherwise agree in writing, be financed only on flag vessels of the United States.


for N. C. Brady
Senior Assistant Administrator
for Science and Technology

6/20/85
(Date)

Clearances:

ST/H/CD, J. Erickson	<u>JNE</u>	Date	<u>6/11/85</u>
ST/H, AVanDusen	<u>WJD</u>	Date	<u>6/12/85</u>
GC/CP, S. Tisa	<u>(Draft)</u>	Date	<u>5/8/85</u>
ST/PO, G. Eaton	<u>ZM for</u>	Date	<u>6/17/85</u>

WJD
ST/H:WOglesby:4/22/85/:0827Q
Revised:WOglesby:tns:6/11/85:1453t:X5-8934

AGENCY FOR INTERNATIONAL DEVELOPMENT
WASHINGTON, D.C. 20503

June 17, 1985

ACTION MEMORANDUM FOR THE SENIOR ASSISTANT ADMINISTRATOR
FOR SCIENCE AND TECHNOLOGY

FROM: S&T/H, Ann Van Dusen *Ann Van Dusen*

SUBJECT: Project No. 936-5957, Americares

Action: Your approval is requested to authorize a new project that will support field tests for a new treatment of leprosy, and to approve a source waiver permitting procurement of a drug from a country in Code 935. Life-of-project funding is \$800,000 from the Health account, Section 104 of the Foreign Assistance Act of 1961 as amended.

Discussion: Leprosy causes severe disability for an estimated 12 million people mostly in tropical LDCs in Africa, Asia and Latin America. Traditional treatment involves long-term therapy with one drug to which resistance has been reported since the mid-1970s. A new medical treatment has been developed that promises to shorten the duration of treatment of leprosy, prevent resistance of leprosy to drugs now used, and interrupt the chain of transmission, thereby eventually eliminating the disease. In 1982 WHO recommended supervised use of the new therapy.

The Biomedical Institute of Venezuela will take the lead in providing overall management and logistical support for the field testing under this project. The Institute is recognized by the Pan American Health Organization (PAHO) as the outstanding center for research and training in tropical diseases in the Americas and is uniquely capable of providing the management and supervision of the leprosy patients in Venezuela which has one of the highest morbidity rates from leprosy in Latin America, second only to Brazil.

In response to an unsolicited proposal, A.I.D. will make a grant to Americares, a U.S. private voluntary organization, to provide technical assistance, the drug clofazimin, and laboratory equipment and services required under the project. PAHO will provide guidance and supervision of the project to assure conformity to the WHO guidelines for the new leprosy treatment. All three organizations -- the Biomedical Institute of Venezuela, PAHO, and Americares -- will enter into an agreement confirming the responsibilities of each before the project activities begin. At the end of the five year project we expect there will be sufficient data and analysis from the field trials to determine the efficacy of the multidrug treatment and whether the treatment can be applied worldwide.

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The project will follow the guidelines for the clinical testing of the drugs established by the World Health Organization. The multidrug treatment proposal has been reviewed and accepted by world authorities on leprosy including Dr. Barry Bloom, Chairman of the WHO Scientific Working Group on Leprosy and Dr. Nordeen, Chief of the WHO Programme on Leprosy, Geneva, and the PAHO Programme, Washington, D.C. Drs. Alfred Buck and James Shelton of S&T/HP have reviewed the design of this project and the role of the WHO/PAHO in the supervision of the trials and they are satisfied that the project, if implemented as anticipated, will comply with AID standards and procedures for testing with human subjects.

We believe that Americares has technical expertise and experience to provide assistance to the activities of the Biomedical Institute of Venezuela. The drug company, Ciba-Geigy, Basel, Switzerland, will provide licensing codes for the drugs to be used.

Based on an unsolicited proposal from and subsequent discussions with Americares, this project will cost a total of \$5.5 million over a five-year life of project. AID's contribution will be an \$800,000 grant to Americares. Americares will contribute \$175,000 from non-AID funds, and the Government of Venezuela (GOV) will contribute staff, organization, one drug and resources of their Ministry of Health and Social Welfare valued at approximately \$4.5 million. The GOV contribution will include six million tablets of one of the drugs, dapsone. The AID grant to Americares will support the following elements of the program:

Drugs	
clofazimin	80,000
insurance/shipping	8,000
Laboratory materials:	
50,000 syringes	5,200
20,000 needles	14,400
Medical consultants	25,400
Field personnel: per diem	
transportation, other	
survey costs	398,769
Medical personnel: per diem	144,000
Supervision at central level:	
training programs, admin	
and data gathering	25,000
Production of soluble antigen	
in laboratory	99,231
TOTAL:	<u>800,000</u>

The Agency's health strategy emphasizes selective disease prevention and control. This project addresses the high priorities of adaptation of medical discoveries and applied research to determine the effectiveness of alternative health improvement measures and field testing in LDC settings. Multidrug therapy, as recommended in 1982 by the World Health Organization, will be tested. Three drugs -- rifampicin, clofazimin, and dapsone -- will be administered by the Venezuelan Ministry of Health and Social Welfare whose Biomedical Institute will carry out the field activities of the project. The results of the project will be disseminated worldwide by WHO to all organizations working in leprosy control and prevention.

Source and Origin Waiver for AID-Financed Commodities: Given the importance to human life and health, AID gives especially careful consideration to pharmaceutical requests. Measures are taken to ensure that only safe and efficacious pharmaceuticals are procured and that they are manufactured in accordance with accepted quality standards. As a general rule, the source of AID-financed pharmaceuticals is limited to the United States, and AID relies on the U.S. Food and Drug Administration for promulgation and enforcement of standards for the safety and effectiveness of pharmaceutical products used in the foreign assistance program. The proposal requests AID funding for \$80,000 (plus \$8,000 for insurance and delivery) worth of drug clofazimin to be purchased from Ciba-Geigy in Switzerland. AID funds will not be used to purchase rifampicin or dapsone.

Handbook IB, Chapter 4C3, permits consideration of source and origin waivers for pharmaceuticals under project assistance if the drug in question does not infringe on U.S. patents and if:

1. the pharmaceutical product is essential to the project;
2. the product, in the same or substantially equivalent form, is not available from the United States, or the delivered price from the United States would be at least 50% more than from another source, and;
3. information is available to attest to the safety, efficacy, and quality of the product, or the product meets the standards of the U.S. FDA or other controlling U.S. authority.

Clofamizin is essential to the project and is not available from the U.S. Physicians in the Office of Health know of the drug and have attested to its safety, efficacy, and quality. Furthermore, the U.S. FDA has judged the Ciba-Geigy operations in Switzerland to be safe and of high quality. Therefore, we believe you should exercise your authority to waive the source and origin requirements for the \$88,000 worth of clofazimin to be purchased by Americares from Ciba-Geigy for use under the project.

Recommendation: That you sign the attached project authorization for this five year, \$800,000 project. The authorization will also waive the source and origin requirement for the drug clofazimin.

Attachment:
Project Authorization

Clearances:

S&T/H, A. Buck	(Draft)	Date	_____
ST/H/CD, J. Erickson	(Draft)	Date	_____
S&T/POP, J. Shelton	(Draft)	Date	6/7/85
GC/CP, S. Tisa	(Draft)	Date	5/9/85
LAC/SA, J. Hulehan	(subs)	Date	5/9/85
SER/CM, J. Johnson	(draft)	Date	5/21/85
SER/COM, T. LaFrance	(subs)	Date	5/21/85
ST/PO, GEaton	<i>Kim fw</i>	Date	6/9/85
DAA/ST, D. Brennan	<i>ds</i>	Date	6/20/85

ST/H:WOglesby:4/22/85:1453t
Revised:WOglesby:tns:6/17/85

[Faint stamp]

PROGRAM DESCRIPTION

Purpose of Grant

The purpose of the grant is to support the conduct field trials of a new medical treatment for the control and prevention of leprosy.

Specific Objectives

The ultimate goal of the project is to improve the health of people worldwide by controlling and preventing leprosy.

To this end the objectives of the project are:

1. to lower the burden of the disease caused by leprosy;
2. to cure the patients and prevent disability and handicap;
3. to interrupt the chain of leprosy transmission;
4. to lower the national prevalence of leprosy in Venezuela;
5. to prevent the emergence of drug resistance;
6. to determine the high risk groups and detect early leprosy and subclinical forms through contact follow-up examinations;
7. to evaluate the efficacy of supervised multi-drug therapy in a public health setting. (Finding here will have relevance to leprosy control in public health care settings in other less developed countries;
8. to evaluate the efficiency of leprosy control service and its impact on the disease.

Implementation

This project is designed to treat all active leprosy cases in the country with polychemotherapy and identify high-risk groups and possible subclinical infections with skin and immunoserological tests.

- A. Treatment of leprosy patients with a standardized therapy scheme: supervised multi-drug therapy, a modification of the WHO recommendations. An initial survey of the patients and their close contacts will be carried out. The first year approximately 3000 patients will be examined, followed by approximately 4000 in the second, and about 3000 patients in the third year.

The patients will be examined and reclassified if necessary, according to clinical and bacteriological criteria. A histopathological examination will be done on a selected group.

The patients will be registered at the peripheral level as well as at the central level in a computerized program.

All patients will be treated with multi-drug therapy: rifampicin, clofazimin, and dapsone. Rifampicin and clofazimin intake will be supervised by auxiliary personnel. Dapsone intake will be tested periodically with urine tests. (For more specific details on treatment see Section V: Multi-drug therapy.)

By the end of the treatment period (two years of multibacillary cases and one year for paucibacillary ones), a medical and bacteriological examination will be carried out. It will determine if the patient can be considered as cured and can be released from treatment. Further follow-ups will be necessary to recognize eventual relapses or reinfections.

After five years it should be possible to determine if the new treatment schedules of multibacillary and paucibacillary cases are sufficient.

- B. Survey of the contacts and determination of high risk groups and possible subclinical infections with application of skin tests (soluble-antigen test, Mitsuda test) and immunoserological studies (E.L.I.S.A.)

At the initial survey of the patients, intra- and extradomicillary contacts will also be identified (ca. 20 per patient) and registered. The following tests will be performed:

1. A-48 hour delayed-type skin test with soluble antigen on contacts of 10+ years of age will define the high risk groups (non-reactors), we expect about 20%.
2. A standard Mitsuda-antigen-test (28 days) to further determine true anergy to leprosy antigens.
3. A serological evaluation of the non-reactors (neg SA-test and neg Mitsuda reaction) with a test which measures antibodies towards phenoglycolipid to detect contacts with medium and high antibodies (E.L.I.S.A.).

It is suspected that these individuals with negative skin tests but with medium and high antibody levels have a subclinical infection and are likely to develop leprosy. They will be controlled as follows:

9'

1. One-half will receive a vaccination with a mixture of M. leprae and BCG (immunotherapy) and the other half a one-time treatment with 600 mg rifampicin.
2. They will be followed-up in close intervals to capture an eventual clinical manifestation of the disease.
3. Immunodiagnostic tests for leprosy will be carried out annually.
4. T-cell suppressor cells will be studied in collaboration with Dr. Barry Bloom, Professor and Chairman of the Department of Microbiology and Immunology at the Albert Einstein College of Medicine in New York.

The field research on treatment of leprosy and follow-up of contacts, as outlined above, requires specially trained manpower and changes in the structure of the health services. Short-term training and retraining courses will be held at the central level and in the field. The descriptions of specific activities of medical and auxiliary personnel are outlined in Annex II of the Americares unsolicited proposal.

We expect an important reduction of new cases which will become more evident with time. Over a period of three years, the whole country will be included in the program.

The first year will include six services with 3118 patients and 62,360 contacts; the second year will include 17 services with 4020 patients and 804,000 contacts; and the third year will cover the remaining 8 services with 2855 patients and 57,100 contacts. Geographic distribution of services is shown on Map 1 of the Americares proposal. In addition, about 300-350 rvw cases per year will be expected according to the observation made during the last three years.

SCHEDULE

A. Purpose of Grant

The purpose of the grant is to support the proposal of the Amicare Foundation entitled "Implementation of Supervised Multidrug Therapy and Survey of Contact, Detection, and Study of High Risk Groups and Suspected Subclinical Infections in Venezuela" dated April 16, 1985, which is hereby incorporated by reference, as more specifically described in an attachment to this Grant entitled "Program Description." The Program Description, Standard Provisions, and Schedule take precedence over the Amicare proposal.

B. Period of Grant

The effective date of this Grant is the date of the grant letter. The expiration date of this Grant will be five years from the date of the grant letter.

C. Amount of Grant and Payment

1. A.I.D. hereby obligated the amount of \$800,000 for the purposes of this Grant.

2. Payment shall be made to the grantee in accordance with procedures set forth in Attachment 3 -- Standard Provision entitled "Payment - Federal Reserve Letter of Credit (FRLC) Advance, 7A(c)." See special provisions below for deviation in paragraph 7A(c) regarding the timing of the submission of the Financial Status Report (SF-269).

D. Financial Plan

	<u>Year</u>					<u>Total</u>
	<u>Year</u> <u>1</u>	<u>Year</u> <u>2</u>	<u>Year</u> <u>3</u>	<u>Year</u> <u>4</u>	<u>Year</u> <u>5</u>	
drugs-clofazimin	88,000	--	--	--	--	88,000
lab materials						
syringes	2,000	2,000	2,000	1,200	--	5,200
needles	5,400	6,000	3,000	--	--	14,400
visiting medical personnel costs	5,000	5,000	5,400	5,000	5,000	25,400
Auxiliary personnel: per diem for patient surveys and super- vision of treatment	100,000	90,000	90,769	59,000	59,000	398,769
Medical personnel (local) per diem and expenses for exams on patients	30,000	30,000	25,000	25,000	34,000	144,000
General supervision and computer assist	5,000	5,000	5,000	5,000	5,000	25,000
Production of soluble antigen and fees of lab technicians	<u>18,000</u>	<u>25,231</u>	<u>22,000</u>	<u>22,000</u>	<u>12,000</u>	<u>99,231</u>
Totals	253,000	163,231	152,369	116,000	115,000	<u>800,000</u>

In addition to the A.I.D. schedule of financing cited above, over the life of the project Americanes will contribute \$175,000 from non-A.I.D. sources and the Government of Venezuela will make various contributions including contributions in kind totalling approximately \$4.5 million.

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E. Reporting and Evaluation

The financial status report (SF-269) will be submitted as an attachment to the progress reports, and in return progress reports will be required generally on a six month basis instead of quarterly. The objective of this is to enable the project officer to assess the budget status at the same time one is assessing the over-all status of the project.

1. Progress Reports: The Grantee will submit interim progress reports in four copies to the AID Project Officer stating what has been accomplished to date, including as an attachment the Financial Status Report. These reports are due within thirty days following the reporting periods ending December 31 and June 30 for each year of the grant.
2. Final Report: The Grantee shall submit to the AID Project Officer a final report in 10 copies no later than the completion date of the grant which currently is estimated as September 20, 1990. The report should be sufficiently detailed to substantiate the findings and to permit a scientific evaluation of the project. The principal investigator should share a draft of the final report with the A.I.D. Project Officer for comment prior to the formal submission.
3. The Federal Cash Management Report (SF-272) shall be submitted on a quarterly basis to the AID Controller at the following address:

Agency for International Development
FM/PAD
SA-12
Washington, D.C. 20523

4. A.I.D. Project Officer:

Dr. Alfred Buck
Agency for International Development
ST/Health, S&T
Room 705, SA-18
Washington, D.C. 20523

5. Grantee Project Officer

Kieran V. Malone
Americares Foundation
51 Locust Avenue
New Canaan, CT 06840

F. Special Provisions

1. the Grantee will provide evidence that WHO/PAHO has reviewed the project with a duly constituted professional committee and had determined that the project complies with local and internationally accepted standards and procedures for testing with human subjects;
2. the Grantee will enter into an agreement with PAHO and the Biomedical Institute of Venezuela to establish the responsibilities of each organization within the project;
3. while in the field, the Grantee will keep the U.S. Embassy generally appraised of their work, but will not request administrative support except for the usual in-country introductions as may be appropriate. The Grantee will abide by U.S. Embassy and host government regulations and customs as they apply to A.I.D. supported, in-country activities;
4. international travel between the U.S. and Venezuela as provided for in the project budget is hereby approved subject to Standard Provision 10, "Travel and Transportation."
5. the placement of a subordinate agreement under this Grant is subject to the prior written consent of the A.I.D. grant officer in accordance with Standard Provision 22, "Subordinate Agreements."

G. Overhead Rate

The grantee will assume all overhead and other indirect costs associated with this project.

H. Title to Property

The title to property acquired under this grant will be vested in accordance with Standard Provision 13A.

I. Authorized Geographic Code

The authorized geographic code for procurement of goods and services under this grant is 941 except for the drug clofazimin which may be procured from Switzerland under Code 935.

BUCK

936-5957
Audit
Technical Files

PROJECT OUTLINE

- I. Introduction
- II. Project
 - A. Objectives
 - B. The Treatment of Leprosy: from Monotherapy to Multidrugtherapy
 - C. Venezuela:
 1. Geographic and demographic data
 2. Organization of the Health Service Systems: Ministry of Health and Social Welfare (MHSW)
 3. Leprosy Control System (August 1982):
Administration, case detection, diagnosis, treatment of personnel, control of patients and contacts, training, research activities, evaluation
 4. Statement of the current leprosy problem (June 1984)
 - D. Americares and the Knights of Malta Participation
 - E. Plan of Action
 1. Information visit
 2. Formulation of plan of action with PAHO, government of Venezuela and Americares
 3. Finalization of drug purchase
 4. Implementation
 5. First evaluation visit
 6. Evaluation indicators
 - F. References
 - G. Tables, Organization Charts, and Maps

INTRODUCTION

Americares was established in 1979 as a non-profit organization. Its original objectives have been dedicated to responding promptly and effectively to medical emergencies in countries torn by war, political repression, or natural disasters. These have included Poland, Lebanon, Pakistan, Brazil, Afghanistan, Zimbabwe, Guatemala, Honduras and El Salvador.

Robert C. Macauley, President and Chief Executive Officer of the Virginia Fiber Corporation, is President of the Americares Foundation. Mr. J. Peter Grace, Chairman and Chief Executive Officer of W.R. Grace & Co., is Chairman of Americares Advisory Committee. Mr. Grace is also President of the American Association of the Knights of Malta.

Because of its achievements in rendering humanitarian services to underprivileged people, the Foundation has received the President's Volunteer Action Award in 1984.

More recently, Americares has become interested in the leprosy problem in Latin America. Its objective aims to reduce the burden of illness caused by leprosy. Leprosy, in addition to

causing severe disability, is still considered by many as a serious social stigma, isolating the afflicted persons from normal community life.

The strongest lay Catholic organization in the world, the Sovereign Military Order of the Knights of Malta (SMOM) of North and South America, have been strong supporters of leprosy control. Both Messrs. Macauley and Grace have shared the concerns of the SMOM and have become a driving force for establishing and implementing an effective leprosy control project in selected areas of Latin America.

After having explored different options, including visits to leprosaria, the Advisory Committee of Americares concluded that they would like to assist Venezuela in their efforts to control leprosy. Venezuela has one of the highest morbidity rates in leprosy, besides Brazil, and is the country with the best organized and efficient antileprosy program in South and Central America.

PROJECT

A. OBJECTIVES

The project outlined proposes to implement supervised multidrugtherapy (MDT) in Venezuela over a period of five years with the objectives to:

1. Interrupt the chain of transmission
2. Cure the patient
3. Prevent the emergence of drug resistance
4. Evaluate the efficacy of supervised multidrugtherapy over a period of time
5. Support (re)training of staff at all levels of the public health structure to implement the new strategy.

The project is applied field research for optimal utilization of expensive drugs and patient compliance.

B. THE TREATMENT OF LEPROSY: FROM MONOTHERAPY TO
MULITDRUGTHERAPY

Until an immunoprophylactic method, primary prevention with a vaccine, can be applied worldwide, chemotherapy is the only effective means to treat leprosy, prevent the disabilities and stop the chain of transmission. The traditional treatment: long-term, possibly life-long therapy with dapsone, has been

introduced in 1943 and applied worldwide. However, since the mid-1970s Dapsone resistance, secondary as well as primary, has been reported more and more frequently.

This situation asked for a new control strategy: in 1982 a study group of WHO recommended the implementaiton of supervised multigrugtherapy¹ with rifampicin, clofazimin, and dapsone, (more details see Table I). The objectives of the new treatment are (1) to prevent further development of drug resistance, (2) shorten the duration of treatment, and (3) improve patient complience.

Judging the present situation, the WHO study group believes that "further delays in implementing well-planned and well-executed programs of combined chemotherapy could result in a catastrophic situation [sic], with further increase in the prevalence of dapsone resistance and the development of multidrug resistance."

The introduction of MDT in a leprosy control program requires a more complex mechanism for drug delivery and follow-up of patients. Training and retraining of all categories of staff, including personnel of the primary health care system, is necessary. Evaluation (more details -- see plan of action) of the new treatment over a peroid of time is important to measure efficacy, safety, and patient complience.

C. VENEZUELA (Some background information)

1. Geographic data:

Venezuela has a land area of 916,490 km², of which 913,990 km² are continental land and 2500 km² are insular territory. It is divided into four geographic regions: the Maracaibo Basin, the flatlands of the Venezuelan Guayana where the predominant climate is hot and humid, the Andes, and the Northern Range where the climate is temperate. The Orinoco River irrigates most of the Venezuelan territory.

There is an extensive network of paved and unpaved roads which covers more than two third of the territorial area, in which more than 95% of the population lives.

Demographic data: The official estimate of June 1980 was 13,913,218 inhabitants out of which 75% of the population resides in urban areas. The uneven distribution of the population is characteristic in Venezuela: the coastal mountain region, which represents 20% of the territory, has 77% of the population, while the region that feeds the Orinoco River with 80% of the national area, has only 23% of the population.

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2. Organization and Structure of the Health Service System: .The Ministry of Health and Social Welfare (MHSW):

The health sector comprises a public and a private subsector. The ultimate responsibility for supervision, coordination and inspection, which corresponds to institutions of the health sector, lies with the Ministry of Health and Social Welfare (MHSW) for national, state, municipal and private entities in all matters relating to the promotion, preservation and restitution of health. (See Organization Chart I.)

The MHSW is organized on three levels:

- a. Central level: It is directed by the Minister and composed of the Office of the Minister, the General Bureau of the Ministry and the four health sector General Bureaus in addition to the Bureau of Social Welfare, the Bureau of Planning, Budget and Information, and the Bureau of Administration.
- b. Intermediate level: It is made up of 8 Regional Health Bureaus which comprise several Federal States as Subregions. (See Map 1.)

- c. Peripheral level: This level is constituted by a system of executive units of extensive complexity ranging from regional hospitals with specialized services and equipment to primary health care units.

3. Leprosy control program as of 1982:

Administration: The ultimate responsibility (technical and policy-making) for the leprosy control program lies with the Department of Sanitary Dermatology of the MHSW which falls under the jurisdiction of the Bureau of Public Health.

At the applied level control activities are under the responsibility of the Public Health Dermatology Services, which fall under the jurisdiction of the local health authorities, or subregional Health Bureau for each Federal Agency.

The program is carried out through thirty services located in 20 Federal Agencies. These services are under the responsibility of the dermatologist-leprologist and each of these services has an inspector, a variable number of field auxiliaries, depending on the epidemiological needs, secretarial personnel, and in most of them, auxiliary nursing personnel and social workers (Organization Chart No. 2).

Through these Public Health Dermatology Services the basic activities of epidemiological surveillance and leprosy control are carried out, in particular those of detecting new cases, treatment and control of the patients and their contacts, vaccinations, and health education.

There are two hospitals for leprosy patients which deal with acute social problems and serious clinical situation. These two institutions have a total of 460 beds budgeted.

Specialized human resources (1982)

- Dermatologists and dermatologists-leprologists	34
- Public health physicians	7
- Pathologists	4
- Other professional and technical personnel	10
- Graduate nurses	40
- Nursing auxiliaries	164
- Inspectors I, II, and III	242

Case detection: Different methods are used with varying results depending on the endemicity of the disease in each region: reference of patients with suspected symptoms, examination of special population groups, systematic examination of contacts from the same household, general examination of high prevalence areas.

Diagnosis: There are precise diagnostic guidelines that include clinical, bacteriological, immunological, and histopathological criteria. (See also Research Activities below.)

Treatment: Venezuela is in the process of implementing supervised MDT. During the last two years, however, there has been a shortage of medicines, especially rifampicin and clofazimin, mainly due to lack of funds.

Control: The medical examination for control of patients is done semiannually in the multibacillary and annually in the paucibacillary cases and in household contacts.

Training of Personnel: Training is given at the central level, for medical and paramedical personnel.

Research Activities: Different research activities are performed at the central level. Among others, clinical studies in immunology, a vaccination trial with BCG and armadillo derived killed M. leprae, new skin and immunodiagnostic tests for early diagnosis are performed.

Evaluation:

1. Epidemiology: In the thirty year period from 1957-1980 there has been a decrease in the incidence, accompanied by important changes of the epidemiological patterns, of the disease. While prevalence rates have decreased, there has been an increase of the proportion of the severe multibacillary form. The average age of onset of the disease has changed to older age groups. However, it must be understood that leprosy is acquired early in childhood and that it becomes clinically overt only after a very long incubation time (4-10 years). Only recently, it has been recognized that children under 10 years of age constitute a significant proportion of all cases. The disease is much more frequent in poor areas than among economically more affluent parts of the population. (Situation 1981, see table 2, Map 2).

2. Operations: The program objectives are: clinical assessment, medical monitoring of contacts and family health education. There is a uniform information system for the collection of all data in the Public Health Dermatology Service of the entire country.

4. Statement of the current leprosy problem (June 1984)

As of June 1984, the Central Registry of Patients in the Department of Sanitary Dermatology had a total of 24,294

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patients registered, of which 12,216 or 50% were active. They have the following distribution: 8,469 multibacillary and 3,747 paucibacillary forms. Estimates suggest that the actual number of cases is about 25% higher, which means 15,270 active patients of which 10,586 multibacillary and 4,683 paucibacillary. Since 1980, about 370 new cases have been detected each year.

During the last years, multidrugtherapy (MDT), as recommended by WHO with rifampicin, clofazimin and dapsone has been progressively introduced in Venezuela. As mentioned before, for the last 2-1/2 years, a serious shortage of medicines has been reported, especially for the essential drugs rifampicin and clofazimin. This is mainly due to a lack of funds and makes the proper control of leprosy extremely difficult.

For this reason bi-lateral assistance in this essential activity of leprosy control in Venezuela would be of great importance.

D. AMERICARES FOUNDATION AND THE KNIGHTS OF MALTS PARTICIPATION

The Amicare Foundation in close cooperation with the Knights of Malta proposes to assist Venezuela in the implementation of supervised leprosy control by modern multidrugtherapy.

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Americares will expedite the procurement of the necessary drugs at an extremely favorable price from the manufacturer the Ciba-Geigy Co. Basel, Switzerland. Americares will organize regular shipment, delivery, and distribution of the drugs. The professional organization and evaluation of the impact will be the responsibility of a qualified physician, who is a staff member of the Foundation. A detailed plan of action will be prepared after a three-week visit to Venezuela in collaboration with the Government of Venezuela (GOV) and PAHO. Bi-annual visits are planned with a written annual evaluation report about the progress of the project.

During the first year, Americares will provide drugs for the high-prevalence areas where the control services already exist to assure MDT and its evaluation. The areas include the three states of Apure, Tachira and Merida, where the vaccination trial is to be carried out. The vaccination trial and MDT complement each other, as the population exposed to leprosy is carefully examined and will receive either immunoprophylaxis, or if clinical evidence of infection exists, proper medication.

During the ensuing years (five-year program), the MDT program will be extended progressively, so as to include areas where control activities are not yet well developed.

In those areas, the general and the public health care system can serve as the infrastructure to implement MDT. At the end of the five-year period, the project should cover all areas affected by endemic leprosy.

The Knights of Malta have approximately 60 members in Venezuela, all are of prominence and distinction. They will supervise and assist locally to administer the continuous distribution of the drugs. The dollar amount of the contribution of the Knights of Malta within and outside Venezuela, for this program, cannot be estimated precisely at this time. However, the impact of the success of the project through public relations and better communication with the local people, including the coordination with the public sector, should not be underestimated.

Americares through its international experience rendering emergency aid, including medications for treatment to different countries in the world, offers unique experience and flexibility in making the project a success.

E. PLAN OF ACTION

1. Information visit to Venezuela of one of Americare's medical staff members, to determine quantity of drugs, timetable

of drug supply, logistics of delivery and in-country distribution with support of the Knights of Malta.

2. Organize an informal committee between Americares, a representative of GOV and PAHO for establishing cooperation in the implementation of supervised MDT. A detailed plan of action will serve as a guideline over the five year project. Annual meetings for evaluation and new adjustments of control activities as needed.

3. Finalization of coordination with drug manufacturer Ciba-Geigy in Basel to purchase drugs as Americares has already negotiated at extremely favorable conditions.

4. Implementaion of the drug-supply-plan in Venezuela with the support of the Knights of Malta who will secure proper delivery and distribution.

5. First evaluation visit after the first year of operation with submission of a progress report to AID including semiannual visit by Americares is planned.

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6. EVALUATION INDICATORS

The evaluation will provide data for the following aspects:

1. Evaluation of the efficiency of supervised multidrugtherapy over a period of five years.
2. Epidemiological evaluation of the efficacy of old and new leprosy control methods.

For evaluation, the well-established and organized infrastructure of Venezuela will provide the necessary competence for evaluation. The OMSLEP² recording and reporting system will serve as a basic guideline.

The following indices for operative and epidemiological evaluation have been defined:

Operational indices at case finding.

- (i) The proportion (ratio) of multibacillary cases among the total number of patients detected from year to year.

- (ii) The proportion of disabled among new cases detected.
- (iii) The proportion of children (0-14) among new cases detected.

Operational indices after case finding.

- (i) The treatment attendance rate
- (ii) The annual treatment defaulting rate
- (iii) The annual rate of release from treatment
- (iv) The annual incidence and prevalence rate
- (v) Duration of treatment of multibacillary cases until considered as cured

Epidemiological indices

- (i) The annual incidence
- (ii) The annual proportion of patients becoming bacteriologically negative

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- (iii) The annual proportion of patients becoming clinically inactive
- (iv) The annual relapse rate
- (v) The estimated contact rate

By the end of the five year period, a significant decrease in the prevalence and incidence of leprosy in Venezuela can be expected.

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3. Leprosy in Children.
4. Leprosy Control, Bolivars Bicentinnial Seminar Report, 1983, PAHO.
5. II Andean Workshop, Republic of Venezuela Leprosy Control Program August 16-20, 1982.
6. A Guide to Leprosy Control.
7. Report of a Coordinating Meeting on Implementation of Multidrugtherapy in Leprosy Control, New Dehli, February 24, 1984.
8. Statement of the Current Leprosy Problem in Venezuela, June 1984.

RECOMMENDED CHEMOTHERAPEUTIC REGIMENS FOR LEPROSY

Treatment of multibacillary leprosy

Rifampicin 600mg once -- monthly, supervised

Dapsone 100mg daily, self-administered

Clofazimine 300mg once-monthly, supervised and 50mg daily self administered

This regimen should be given for a minimum of two years and be continued wherever possible, up to smear negativity.

Treatment of paucibacillary cases

Rifampicin 600mg once a month for 6 months, supervised.

Dapsone 100mg daily for six months.

Rifampicin shall be administered under direct supervision. It secures continuity, regularity, and completion of chemotherapy.

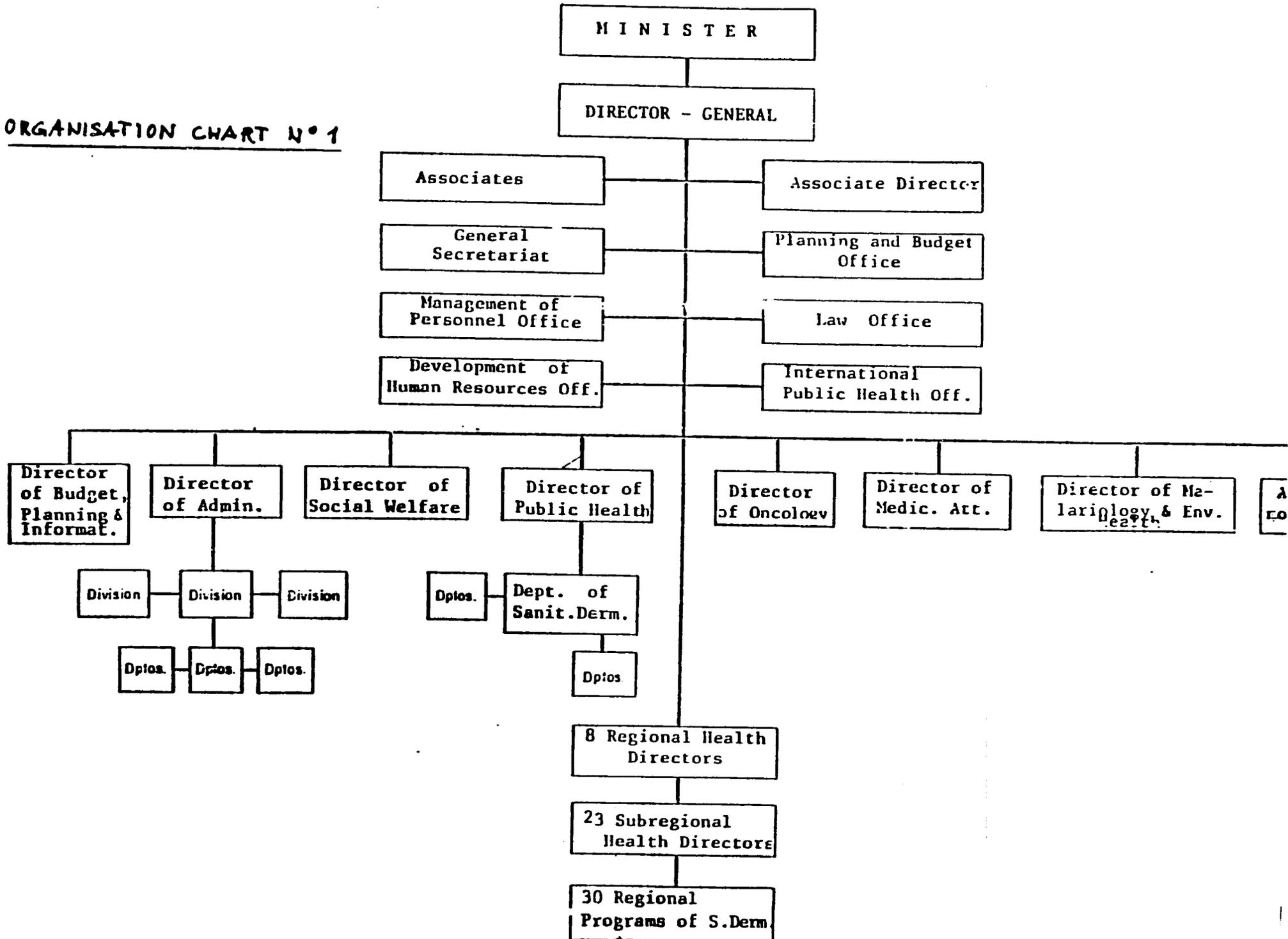
Table No. 2

VENEZUELA: Situation of the total leprosy patients diagnosed as of 31 December 1981.

REGISTERED PATIENTS		23.427
DISCHARGED		3.662
DECEASED		4.782
ACTIVE	}	TOTAL 14.983
PATIENTS		UNDER CONTROL 10.265
		WITHOUT CONTROL 4.718
		PREVALENCÉ 1,026
		BASED ON ESTIMATED POPULATION 14.602.480

Source: REGISTRO NACIONAL DE ENFERMOS Y CONTACTOS DEL DEPARTAMENTO DE DERMATOLOGIA SANITARIA

ORGANISATION CHART N° 1

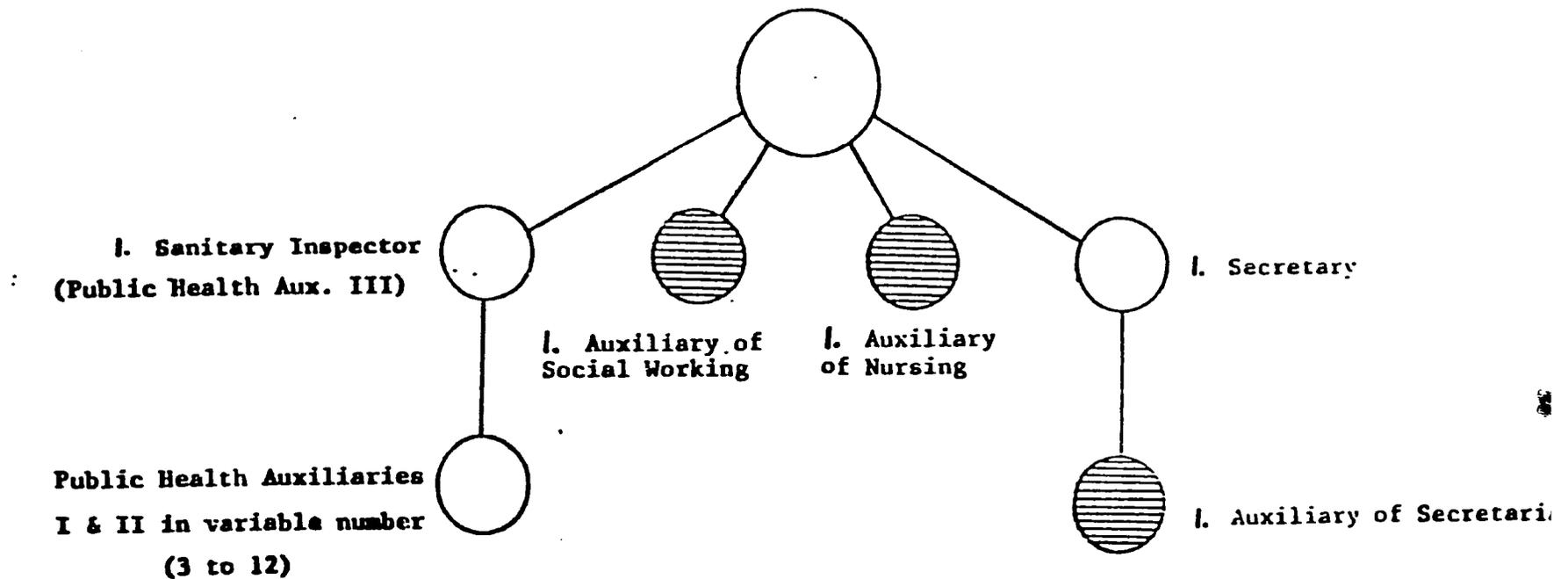


ORGANISATION CHART N° 2

VENEZUELA

Personnel of an Epidemiologist Service of Sanitary Dermatology

I. Dermato-leprology Physician

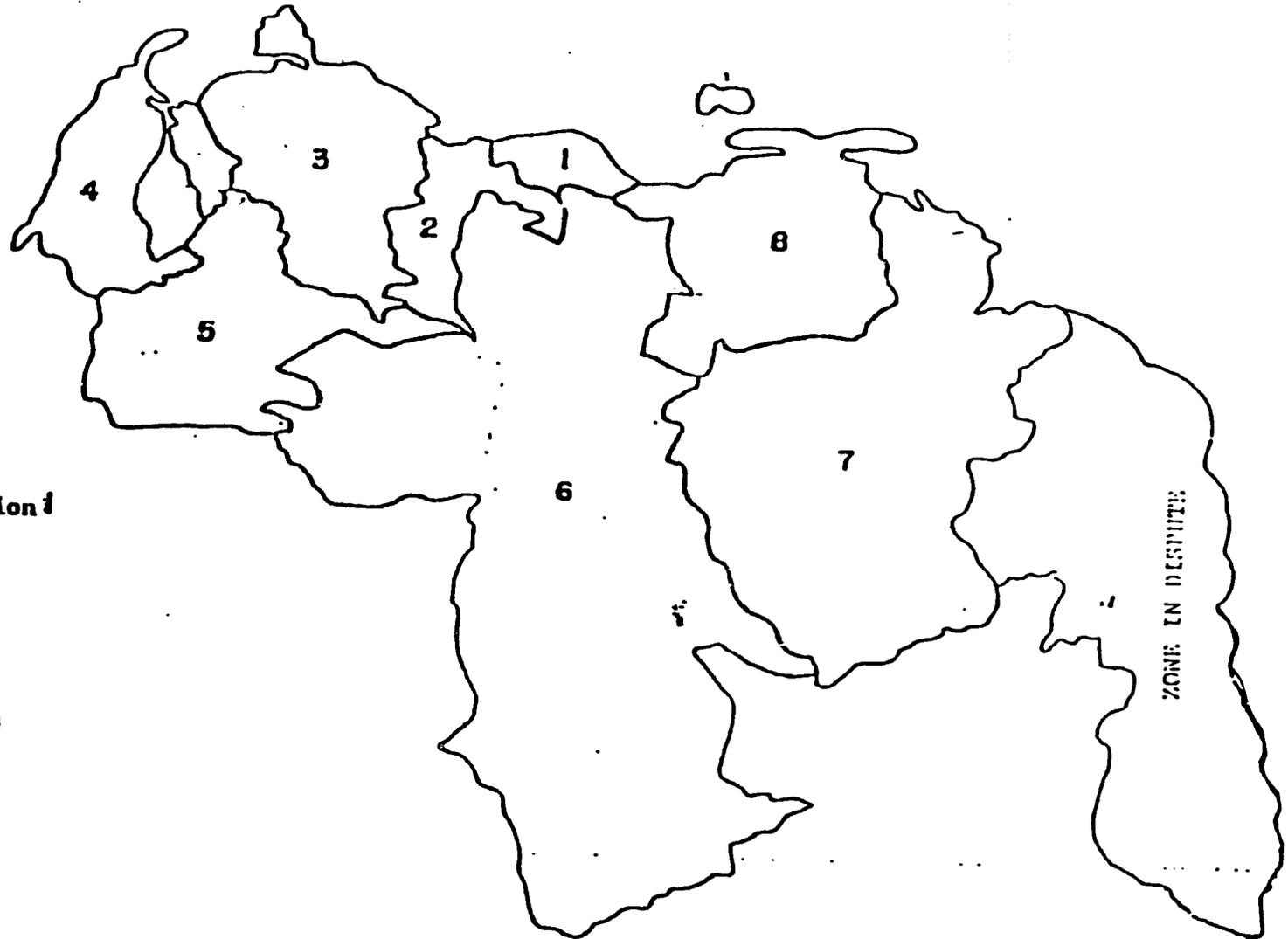


-  Personnel in all Services
-  Personnel in some Services

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MAP 1

SANITARY REGIONS OF VENEZUELA



- 1 Capital Region
- 2 Central Region
- 3 Central-Western Region
- 4 Zuliana Region
- 5 Andean Region
- 6 Region of the Llanos
- 7 Guayana Region
- 8 North-Eastern Region

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MAP No. 2

EPIDEMIOLOGICAL REGIONS OF VENEZUELA, ACCORDING TO THE
LEVEL OF THE LEPROSY ENDEMICIA

