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QUALITY CONTROL OF PHARMACEUTICAL PREPARATIONS

The control of the quality of pharmaceutical preparations presents difficulties in many countries, particularly with the increasing number of products and specialties now in international commerce and of pharmaceutical products made locally in the different countries for the internal market. This issue was discussed at the XVII World Health Assembly and a resolution was passed (WHA17.41) calling attention to the need to subject all pharmaceutical preparations, whether produced within a country for national consumption or for export, or whether imported, to an adequate control and to insure that pharmaceutical preparations that are exported from a country will "comply with the same drug control requirements as applied to drugs for its domestic use". This resolution also invited the member states which export drugs to consider whether testing facilities could be made available by arrangement with an importing country which has no such facilities.

A study of the Quality Control of Pharmaceutical Preparations was prepared by the Secretariat of WHO and reviewed by the Expert Committee on Specifications for Pharmaceutical Preparations*. The Committee emphasized the importance of the subject and the necessity for action. It was agreed by the Committee that the establishment of any facility, or the extension of existing facilities for the training at all levels of personnel for the analysis and quality control of pharmaceutical preparations was of primary importance in the interests of public health. Stress was also laid on the need to give Member Governments, on request, assistance in establishing laboratories for pharmaceutical quality control, adequately staffed and equipped, with special reference to countries depending largely on imported pharmaceutical preparations.

*WHO Expert Committee on Specifications for Pharmaceutical Preparations, 1965, Technical Report Series 307

At the XVIII World Health Assembly a report on the control of pharmaceutical preparations was presented by the Director General, pointing out the unsatisfactory situation that exists in regard to the quality control of pharmaceutical preparations moving in international commerce. It was emphasized that a large part of the world population that makes use of these pharmaceutical preparations did not have adequate facilities for quality control. A recommendation that the Member Governments should take the necessary measures to subject pharmaceutical preparations imported or locally produced to adequate control was made by the Assembly, and the Organization was requested to continue to assist Member Governments to develop their own laboratories facilities or to secure access to such facilities elsewhere.

In view of these resolutions of the World Health Assembly (WHA17.41 and WHA18.36) and the great interest expressed by the Governments of this Hemisphere on the importance of having adequate control of drugs and pharmaceutical preparations, the Pan American Sanitary Bureau has taken several steps. Firstly, through WHO, discussions have been opened with the United Nations Development Fund regarding the possibilities of financing such a center or centers. Secondly, the Organization has made a study of the possibility of establishing an international pharmaceutical control and reference laboratory that could serve a number of South American countries in: (1) serving as a training facility for scientists and technicians who may need additional instruction and experience; (2) provision of scientific advice and information to national drug control centers; (3) acting as a center of communication of scientific information in this field, as well as reporting the results of investigations carried out in the international control laboratory itself; (4) assistance as a reference laboratory in the quality control of pharmaceutical preparations.

A report of the need for, and potential value of such an international quality control laboratory was presented at the XVI Meeting of the Directing Council of the Pan American Health Organization. The organization and functions this laboratory could have were examined, as were space requirements, location, personnel and equipment. The XVI Meeting of the Directing Council, bearing in mind this report and recommendation VII.C.2 of the Final Report of the Task Force on Health at the Ministerial Level (Washington, D.C., 15-20 April 1963), adopted resolution No. XII on Quality Control of Pharmaceutical Preparations; it recommended that the Bureau continue studies on the possibilities of establishing international laboratories for the analysis of pharmaceutical products which might serve as reference centers, and that the Director study the possibility of the Organization providing more extensive assistance in the development of projects of this type.

Following this, a team of two special consultants visited Uruguay, Brazil, Venezuela and Panama during June and July of 1966 in order to continue studies of the possibility of establishing an international center of this type and its possible location. The consultants considered a number

of factors with respect to the establishment of such a center. These included: (1) patterns of communication and distance between the capital cities, chief industrial cities and ports of entry of the countries served; (2) the availability and cost of land; (3) proximity to good universities; (4) the climate, amenities and cost of living in the site to be chosen; (5) transportation facilities between the site and the chief cities or port of the countries to be served; (6) the likelihood of recruitment of a competent staff within a reasonable length of time; and (7) the interest of the countries in having the laboratory located in their territory.

In seeking the answers to these questions and other questions related to them, interviews were held with informed persons both in public and private life in each of the above-mentioned countries. The consultants were permitted to observe the operation, teaching programs, and instrumentation of various branches of the universities located in the cities visited (Montevideo, Sao Paulo, Rio de Janeiro, Caracas and Panama City). Special attention was given to the regulatory units for control of drugs and pharmaceutical preparations in the respective Ministries of Health. Several pharmaceutical houses manufacturing a wide variety of drugs were visited. Interviews with scientists in these various institutions were carried out to evaluate the level of their educational experience and ability in the light of the significance of modern techniques in Pharmacology, Analytical Chemistry, Biological Chemistry and Physical Chemistry in the establishment of such a center.

It is the assumption of the consultants that the superior quality of the analytical services which may be performed in a center or centers of the type proposed, and the caliber of the technical advice available from such center(s), will progressively lead most, if not all, of the countries of South America to participate in a project or projects of this kind.

In all the countries visited there was land available that was generously offered by the governments for the establishment of an international center. Health authorities, universities and private industry showed great interest in the possibility of future development of a program of this type. In each country studies of manpower availability were made and existing drug control laboratories were inspected. In view of the limited experience found in the drug control field, it is envisaged that the senior staff of a drug control center such as contemplated will have to be recruited from many areas of the continent.

Although the governments of each of these four countries expressed interest in the establishment of such a project, Uruguay has taken official action to offer facilities for the organization of such a center. It is the feeling of the consultants that in the beginning a center of this type should serve on a national basis with the necessary provisions for expansion that will permit it to be rapidly made a Regional International Reference Center.

In order to continue towards implementation of this project, the Organization has made provisions in the Proposed Program and Budget for 1967-68 (O.D. 67), through a specific project, AMRO-4709, Center for Control of Drugs.

In addition to this specific project, it is worth noting that the Organization has been cooperating since 1964 with the Government of Panama in the establishment and operation of a food and drug control laboratory to serve the needs of Central America and Panama, following the recommendations of the VIII and IX Meetings of the Ministers of Health of the region. This is explained in greater detail under AMRO-4703, Food and Drug Control, Zone III (O.D.67). Further activities of the Organization in this field in support of national programs, through consultant services to Argentina and Chile, and a seminar on Food and drug control in Guatemala, are described in detail in the Annual Report of the Director for 1965. (pp. 54-55 of O.D.70).

22 September 1966

ABRIDGMENT OF REPORT

ON

THE LOCATION OF AN INTERNATIONAL PHARMACEUTICAL CONTROL LABORATORY

prepared by

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LOCATION AND DISTANCE BETWEEN THE CAPITAL CITIES, CHIEF INDUSTRIAL CITIES, PORTS OF ENTRY OF THE COUNTRIES SERVED AND TRANSPORTATION FACILITIES

To deal with these subjects requires several assumptions. We assume that the superior quality of the analytical services performed, the high caliber of the technical advice available and the advanced training in modern chemical, physical and biological analytical procedures will progressively lead most, if not all, of the countries of South America to participate.

Information under this heading was obtained from a number of informed sources, principally the Office of the General Director of Telecommunications and ALALC (Asociación Latinoamericano de Libre Comercio) (Latin American Association of Free Commerce).

Some other inquiries concerning telephone and cable communications were made of these same people.

AVAILABILITY AND COST OF LAND, PROXIMITY TO A GOOD UNIVERSITY

To answer the questions we interviewed Architects of the Chamber of Construction of Uruguay, Architects employed by the City as well as private Architects. We also learned of the experience of pharmaceutical firms who have recently bought land for new plants.

CLIMATE, AMENITIES AND COST OF LIVING

We were informed by the official meteorologists of Uruguay that the climate of Montevideo is temperate. From September through May it is most comfortable. From June through August temperatures are above freezing and there are frequent strong winds. The humidity is high throughout the year.

We observed that Montevideo is a large city with a wide variety of religious, educational and cultural activities. There are also available participating and spectator sports. Its beaches are world renowned.

To learn about the cost of living and salary scales we interviewed various persons ranging from the President of the Association of Chemistry and Pharmacy of Uruguay, the Acting President of the University of the Republic, to the individual citizen, both those engaged in science and commerce. In addition we reviewed statistics prepared by the Government of Uruguay. (II).

RECRUITING OF A COMPETENT STAFF WITHOUT UNDUE DELAY

The majority of the scientists in Uruguay in the scientific disciplines that would staff the Laboratory are graduates of the University of the Republic. In general the scientists' salaries are inadequate. Many find it necessary to

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(II) "Diario Oficial. República Oriental de Uruguay. No. 17357. June 2, 1966"

The assignment given to these consultants was to visit Uruguay, Brazil, Venezuela and Panama to recommend the most desirable location for an International Laboratory to serve those South American countries that wished (1) assistance in the analysis and testing of pharmaceutical preparations for quality, purity, potency and sterility, (2) to provide, on request, certain scientific advice and information to National Control Centers, (3) to serve as a training Laboratory for scientific and technical studies of control procedures and (4) to publish results of worthy investigations carried out in the course of their duties.(I).

In pursuing our task we in general followed the recommendations in the excellent report of Dr. Morrell. (I).

In his report he recommended that in the "Location of Laboratory", "a number of factors must be considered where the Laboratory should be located. These include (1) location and distance between the capital cities, chief industrial cities and ports of entry of the countries served, (2) the availability and cost of land, (3) proximity to a good University, (4) the climate, amenities and cost of living in the site to be chosen and (5) the transportation facilities between the site and the chief cities or ports of the countries to be served."

In addition we have considered (6) the likelihood of successful recruiting of a competent staff within a reasonable length of time and (7) the interest of the countries visited in having the Laboratory located in their territory.

STUDY IN URUGUAY

In seeking the answers to these questions and other questions related to them many interviews were held with informed persons both in public and private life. We were also permitted to observe the operations, teaching and instrumentation of various branches of the University of the Republic (Montevideo-Uruguay). Research Institutions were also included in this survey.

The Drug Control Laboratory of Uruguay was given special attention, as well as the General Inspection of Chemistry, Pharmacy and Drugs.

Several pharmaceutical houses manufacturing a wide variety of drugs were visited. Here the manufacturing and particularly the control procedures were observed in depth.

Interviews with scientists in these various Institutions were designed to learn the level of their education, experience and ability in the light of the application of modern techniques in Pharmacology, Analytical Chemistry, Biological Chemistry and Physical Chemistry.

(I) "An International Pharmaceutical Control Laboratory", C.A. Morrell. June 30, 1965.

occupy two or more positions. Repeatedly individuals expressed frustration to us because of the lack of the expensive, modern instruments essential to the most precise and rapid analysis of samples, as well as adequate teaching and research.

This was particularly true in the case of drugs that require precise quantitative analysis by such modern procedures as infra-red and ultra-violet spectrophotometry, flame photometry, polarography, paper, column, thin-layer and gas chromatography, potentiometric tirations, conductimetry, etc.

If Montevideo were to be seriously considered as the site for the Laboratory, several weaknesses would need to be compensated for. Because of lack of funds scientific library facilities in the area are limited. They would need to be supplemented.

It would strengthen future recruiting possibilities if the University were to be provided with a number of the modern technical instruments. At present students are given a good theoretical knowledge of instrumentation, but because of lack of funds for replacements and repairs they do not operate them but must rely on demonstrations by the professors.

A number of the professors expressed interest in possible acceptance and employment in the Laboratory. The Dean of Medicine while offering co-operation and assistance evidenced concern about the possible adverse effect on his Faculty if too many were recruited. Care would need to be exercised not to recruit so many professors from the University as to weaken their already too small staff of senior scientists.

Every effort should be made to recruit widely among South American countries so as to obtain the best talent available and to promote scientific interchange among South Americans.

Obviously, the success or failure of this pioneering project will importantly depend upon the abilities and scientific reputation of the Director and his principal scientific assistants. We concur with Dr. Morrell that, if possible, the Director should be the first of the staff selected, so that he can assume an important part in recruiting appropriate personnel.

COMMENTS ON TRANSPORTATION AND COMMUNICATION

Montevideo is served by twenty-one air-lines and has services to all the capitals of South America either directly or by several alternate routes.

There are problems in transportation and communication between Montevideo and the other capitals and principal cities of South America. These serve to cause delays.

It does not appear however that the delays are unique but are equally applicable to the other cities included in our survey.

Samples would be shipped to the International Laboratory by air express, air mail, bus and railroad in the case of near-by countries, and in an emergency by courier.

Cable communication is excellent and for the most part telephone communication is acceptable.

Frequent delays comparable to those of other South American cities are encountered in the delivery of air mail. Investigation shows that there are ways to expedite the receipt of official samples. This will require the cooperation of officials of the various governments involved. It may be desirable to consider contracting for the services of a firm engaged in obtaining possession of and making prompt delivery of air-express packages such as those that would constitute drug samples.

We are advised by the Sub-Director de Correos de la República Oriental de Uruguay (III) (Sub-Director of the Post Office Department) that because of the interest of the Government in the Laboratory and because of the diplomatic status of the Pan American Health Organization special arrangements can be made to hasten the delivery of samples. He suggests that the Laboratory rent a box in the Central Post Office. His Department would receive the samples at the Air Port. They would not go through customs but would go directly to the Central Post Office. He asserted that the samples would be available for delivery within twenty-four hours after the arrival of the air plane. Perishable samples would be held under refrigeration if the Laboratory provides the Post Office Department with a refrigerator and freezer.

INTEREST IN ESTABLISHING THE LABORATORY IN URUGUAY

The National Government and the Department of Public Health in particular assert their interest emphatically by offering much assistance, including providing a site without cost.

CONCLUSIONS

1. The "location and distance between the capital cities, chief industrial cities and ports of entry" of the countries, we assume will progressively be served, is acceptable.

2. "Availability and cost of land".
   Well located sites of an area of some two and one half acres (one hectar) can be purchased for from $1.00 to $2.00 per square foot. Both the National Government and the City Government offer to donate a site of approximately that size. In our opinion either site or a similar one would be most acceptable.

(III) Mr. Antonio A. Sosa

3. Both of the sites mentioned under (2) are within approximately two to four miles of the University and are served by good transportation and other public service facilities.

4. The climate is relatively good.
Cultural and other amenities are available.
The cost of living is low.

5. Transportation facilities between Montevideo and the chief cities and ports of the countries to be served are reasonably good.

6. Assuming that a capable scientific Administrator widely recognized as a scientist and of outstanding stature is appointed as Director, in our opinion, a competent staff could be recruited within a reasonable time.

7. Uruguay is very much interested in having the International Laboratory located in that country.

STUDY IN SAO PAULO, BRAZIL

Our studies in Sao Paulo sought answers to the same questions as those posed in the introduction to this report.

The plan of inquiries was patterned after that employed in Uruguay. It was however changed to take advantage of the experience gained there and because of the necessities of limited time.

We visited the University of Sao Paulo, talked to several key professors and observed the new Laboratory installations. The University was in recess but we were able to discuss its operations, courses and instrumentation. This covered chemical, biochemical and pharmaceutical sciences.

Of special interest were the Drug Control Laboratory of the State of Sao Paulo and The Inspection Service for professional practice of Medicine, Pharmacy, Dentistry, etc. The Institute of Adolfo Lutz was also visited.

Representative drug manufacturers were surveyed.

LOCATION AND DISTANCE BETWEEN THE CAPITAL CITIES, CHIEF INDUSTRIAL CITIES, PORTS OF ENTRY OF THE COUNTRIES SERVED AND TRANSPORTATION FACILITIES

Inquiries to obtain this information were made of a number of informed persons and organizations mainly The Office of the National Association of Exporters of Industrial Products (ANEPI). Information concerning the telephone and cable facilities of the area was also obtained.

AVAILABILITY AND COST OF LAND, PROXIMITY TO A GOOD UNIVERSITY

This subject was discussed generally with a number of the people with whom we discussed other matters. Some of them were particularly well informed about land availability and cost. Our inquiries lead to the conclusion that a plot of land large enough to serve the purposes of the proposed Laboratory could not be obtained near the center of the City except at an excessive cost. There are very few such sites and these are very much in demand.

The most practicable site would be in the vicinity of the new Sao Paulo University buildings. Here land, being developed, can be purchased for some $2.00 to $5.00 a square foot.

There are, however, disadvantages to such a site. The City has grown so rapidly that certain public facilities have not kept pace. For example, the University to date has only one telephone.

A more important handicap is the lack of public transportation in the area. Private firms with a similar problem have found it necessary to provide company buses for the transportation of their employees to and from work.

There are great difficulties in obtaining a telephone for a private home and this would be a deterrent to recruiting.

CLIMATE, AMENITIES AND COST OF LIVING

Daily weather reports for the City and State of Sao Paulo are issued by the Meteorological Service of the Department of Agriculture.

This Service advised that the climate is quite uniform and agreeable. The rainy season is in December, January and February. June and July are usually quite dry. In May, June and July fog is common.

The Director reviewed for us the weather and related statistics for the past five years and pointed out that neither excessive heat or excessive cold is encountered in the City. Humidity is uniformly high. (IV).

Sao Paulo and its environs has a population of over five million people. It is made up of a mixture of races which appear to be well integrated. Cultural opportunities are widely diversified.

Cost of living and salary scale information was obtained from all persons interviewed. These included business men, trade association representatives, professional men, as well as those specializing in the field of economics.

The rapid growth of the City has resulted in major traffic problems. Public schools are very overcrowded. Cost of attending private schools is high.

(IV) Mr. José Alvies de Santana

RECRUITING OF A COMPETENT STAFF WITHOUT UNDUE DELAY

The University of Sao Paulo would be the principal local source of scientists and technicians in the disciplines that would staff the proposed International Laboratory.

Competition from the large and expanding drug and chemical industries in the area might make recruiting difficult. These industries pay relatively good salaries and have attracted many able scientists from the University graduates and staff, as well as from other Government Laboratories.

The remuneration in the University and in other Government Laboratories is so low as to require a large percentage of their staffs to accept only part-time employment with the Government and to supplement their income with part-time positions elsewhere. Some of these scientists would seek employment in a full-time position in an International Laboratory rather than to continue to occupy two or more positions.

The University of Sao Paulo is now in a period of major transition. New buildings have been erected to house the Schools of Pharmacy, Biochemistry and Chemistry. The new buildings are in part occupied. Many of the laboratories and other academic rooms are not completed as yet. Installation of laboratory equipment and other furniture is expected in the near future. At present the complex scientific instrumentation available to the teaching staff is quite limited.

Some liberal grants from the Ford Foundation are, in the opinion of the professors we talked to, likely to improve this situation materially.

COMMENTS ON TRANSPORTATION AND COMMUNICATION

Sao Paulo is relatively centrally located in South America. It is served by all the principal air lines. These total seventeen.

Wire communications in general are good.

THE DRUG CONTROL LABORATORY AND INSPECTION

The pharmaceutical and chemical control Laboratory of the State of Sao Paulo is a part of the Institute Adolfo Lutz. The head of this Laboratory advised us that he preferred simple methods, volumetric, gravimetric, etc., rather than the complex instrumentation techniques which increasingly are included in books of official standards such as the United States Pharmacopoeia and The National Formulary. He hoped that research in the International Laboratory would be directed to the development of methods of this type. The equipment observed in his Laboratory was consistent with this view.

The Director of the Institute Adolfo Lutz displayed to us a large number of the most modern instruments employed in all phases of pharmaceutical analytical procedures. He assured us that these tools are used in examining both foods and drugs when appropriate.

The Director conducted us through practically the entire Institute. We were much impressed with the staff, facilities and scientific excellence of this well-known interamerican Institute. A fifteen-story building is now under construction. We are told that it will be completed in about eighteen months. The Director explained that drug analyses will be substantially increased and that three complete floors will be devoted to pharmaceutical testing.

Most of the employees of the Institute work some six hours per day.

The Inspection Service is also a part of the Government of the State of Sao Paulo.

Both the Inspection Service and the Institute Adolfo Lutz have relationships with the National Government of Brazil whereby they enforce the national public health laws and regulations.

The Inspection Service has a staff of some thirty Inspectors who deal with a variety of health problems. Some ten of these Inspectors are assigned to the inspection of pharmaceutical manufacturers and retail druggists in the City of Sao Paulo. A few additional Inspectors are stationed in the interior of the State. There is a cooperative working relationship between this Inspection staff and the pharmaceutical Control Laboratory.

Obviously ten Inspectors employed on a part-time basis cannot adequately cover the 137 (V) pharmaceutical firms in the area in addition to the several hundred retail drug stores.

INTEREST IN ESTABLISHING THE LABORATORY IN SAO PAULO

Most of the professional people, businessmen and trade association representatives interviewed expressed the hope that the International Laboratory would be located in Sao Paulo.

Mr. Cury of the National Association of Exporters of Industrial Products (ANEPI) stated that his organization is anxious to have the Laboratory in Sao Paulo. He volunteered the statement that he had interviewed several leading local officials who felt confident that land would be provided free if the Laboratory were to be located in that City.

CONCLUSIONS

1. The "Location and distance between the capital cities, chief industrial cities and ports of entry" of the countries we assume will progressively be served, is very good.

(V) "Annual Statistics of Brazil. Brazilian Institute of Geography and Statistics, 110, (1965)."

2. "Availability and cost of land".
Land near the new University buildings now under construction can be purchased at a reasonable price. It is possible that such land would be donated. We cannot forecast whether or when the present lack of such public utilities as telephone and transportation facilities will be corrected. At present the site, in our opinion, is not acceptable.

3. The site mentioned under (2) is adjacent to the University.

4. The climate is relatively good.
Cultural and other amenities are available. Their use is complicated by congestion caused by the rapid growth of the City.
Cost of living is high.

5. Transportation facilities between Sao Paulo and the chief cities and ports of the countries to be served is very good.

6. Recruiting would be difficult but we do not foresee insurmountable problems.

7. Interest was expressed by scientists and industrialists.

STUDY IN RIO DE JANEIRO, BRAZIL

Time limitation led to emphasis of only the most important factors dealt with in Montevideo and Sao Paulo.

We began with an extensive discussion of factors involved in our survey, with the Chief of Zone of the Pan American Health Organization (VI).

We interviewed the Executive Director of The Commission on International Affairs of the Ministry of Public Health of Brazil (VII). He stated his opinions with respect to the questions we were seeking to have answered. He made appointments for us and accompanied us to installations under the direction of the Department of Health of Brazil and to the University of Brazil.

At this University, Department of Pharmacology (VIII), we learned that the University is well equipped with instrumentation to instruct students in the modern techniques of pharmaceutical analyses. Members of the staff interviewed expressed the hope that progress will result in improved fundamental research, particularly the synthesis of new compounds of possible therapeutic value.

(VI) Dr. Santiago Renjifo
(VII) Dr. Murillo Belchior
(VIII) Dr. Lauro Solero and members of his staff

We were informed that the University has a strong Department of Microbiology and that this is recognized by the fact that the World Health Organization sends students here for advanced studies in Bacteriology, Virology, Micro-analysis, etc.

Plans have been made to move the Colleges of Medicine, Pharmacy and Chemistry to the new University grounds on a campus near the Institute Oswaldo Cruz.

Because the University of Brazil was in recess and most of the professors are employed on a part-time basis we did not see the Schools in operation and were unable to meet with a number of the Professors.

The Institute Oswaldo Cruz has been in operation for more than half a century. It is distinguished for the contributions it has made and continues to make in the fields of Biological Sciences, Pathology, Experimental Medicine and other medical and health problems, particularly those of tropical and subtropical countries.

The main building houses the administrative staff and a very extensive scientific library that has been described as one of the most complete in South America. Buildings are maintained for research in Pathology, manufacture of Yellow Fever vaccine and to house laboratories dealing with Chemistry, Virology, Physiology and various branches of other biological sciences.

A variety of vaccines are produced and an extensive animal breeding facility is on its grounds. In collaboration with the World Health Organization, the Institute furnishes Yellow Fever vaccine and other protective vaccines to many parts of the world. A new Hospital of five floors has facilities for both bed patients and out patients.

The Institute is located on a main six-lane highway. It is about nine miles from the center of Rio de Janeiro and six miles from the City's principal airport. Bus service to the Institute is described as excellent.

At the "Central Laboratory for the Control of Drugs and Pharmaceuticals" we met the staff, discussed their problems and observed the laboratory facilities available to them.

The Director of the "National Inspection Service for Medicine and Pharmacy" informed us of the activities and responsibilities of his office.(IX).

Information of value was obtained from the directing staff of a principal pharmaceutical manufacturer.

(IX) Dr. Lucio Costa

LOCATION AND DISTANCE BETWEEN THE CAPITAL CITIES, CHIEF INDUSTRIAL CITIES, PORTS OF ENTRY OF THE COUNTRIES SERVED AND TRANSPORTATION FACILITIES

This information was obtained from "Exprinter", a local travel agency.

AVAILABILITY AND COST OF LAND, PROXIMITY TO A GOOD UNIVERSITY

Dr. Raymundo de Britto, Minister of Health and Dr. Murillo Belchior, Executive Director of the Commission on International Affairs of Brazil, considered this problem. The Minister described land on the campus of the Institute Oswaldo Cruz and on other property nearby that he thought would be desirable for the International Laboratory. This land is owned by the Ministry of Health. At present a number of public health service installations are there and it is planned to successively move the entire Ministry of Health and other related activities to this location. The Minister expressed the interest of his country in having the International Laboratory located in Rio de Janeiro. He offered without cost a choice of sites in the areas described.

Dr. Belchior stated that he had discussed the legal possibilities with their Consul. He was advised that there would be no obstacles to grantint the World Health Organization a ninety-nine year lease.

CLIMATE, AMENITIES AND COST OF LIVING

Detailed information concerning temperature, humidity and rainfall was obtained from the Assistant Director of the Meteorological Service of the Ministry of Agriculture. (X).

The temperature of Rio de Janeiro ranges from warm to hot throughout the year. The nights are frequently cool during June, July and August. Temperatures near the beaches and on high elevations are cooler than inland locations. The relative humidity is high. May through October is dry while the remaining months have higher precipitation. There are periods of haze during September, October and November.

Cultural opportunities are ample. The beaches are particularly attractive.

We discussed salary scales and cost of living figures with representative citizens.

RECRUITING OF A COMPETENT STAFF WITHOUT UNDUE DELAY

The several Universities in Rio de Janeiro and vicinity graduate annually a number of scientists trained in the disciplines that will be

(X) Dr. Leandro Riedel Ratisbona

sought by the International Laboratory. Like other principal cities in South America, the Laboratory will necessarily compete with Industry for its staff. If salaries are competitive with Industry, it is our opinion that the challenging nature of the International Laboratory's work and the facilities that will be made available to its professionals will attract local scientists as well as some from other nations.

COMMENTS ON TRANSPORTATION AND COMMUNICATION

Rio de Janeiro is centrally located on the East Cost of South America. The nineteen airlines that serve the City include all of the principal ones. Cable and telephone communications are quite good.

THE DRUG CONTROL LABORATORY AND INSPECTION

The "Central Laboratory for the Control of Drugs and Pharmaceuticals" is well housed. Its permanent laboratory fixtures are adequate and well-maintained. The staff is provided with many of the modern tools of Analytical Chemistry, Microbiology and Pharmacology. They employ eight chemists, three pharmacologists and five bacteriologists.

The duties of the Laboratory include not only drug analysis but it also serves as a consulting Laboratory to a wide variety of governmental and other agencies who may submit samples to be analyzed. All of the professionals serve on a part-time basis. The staff is not large enough to handle their heavy work-load assignment. Since the establishment of the Laboratory some ten years ago their competence has progressively improved. For example, at least three members of the staff have had graduate training in North America.

We learned at the "National Inspection Service for Medicine and Pharmacy" that the duties of this Office are now limited to the registration of drugs, the collection of pharmaceutical samples on the market and registration of Physicians, Dentists, Pharmacists and Vetinarians.

Firms wishing to register a new drug submit an application accompanied by data designed to demonstrate the safety, therapeutic value and composition of the article. The labeling and other literature used in its promotion is included. This data together with related material is submitted by the Director of the "National Inspection Service for Medicine and Pharmacy" to a Board of Experts for appraisal.

This Board, which serves without remuneration, consists of one clinician, two pharmacologists, one pharmacist, the head of the "Central Laboratory for the Control of Drugs and Pharmaceuticals" and a representative of the pharmaceutical industry.

If the Board regards it as necessary it submits a sample of the drug for analysis before passing upon the application. In most instances no analysis is made.

Inspection of pharmaceutical houses, collection of samples and review of the practices in retail pharmacies in Rio de Janeiro is carried out by one Inspector who is employed on a part-time basis.

INTEREST IN ESTABLISHING THE INTERNATIONAL LABORATORY IN RIO DE JANEIRO

The Government of Brazil seeks the establishment of the International Laboratory in Rio de Janeiro.

CONCLUSIONS

1. Rio de Janeiro is well located to serve the countries of South America.

2. Desirable land is available without cost.

3. The site offered is near a University and a research Institute. It is midway between the center of the City and the principal airport.

4. The climate is tropical.
   Cultural and other amenities are available.
   Cost of living is relatively high.

5. Transportation facilities between Rio de Janeiro and the chief cities and ports of the countries we assume will be served, is very good.

6. There will be competition in recruiting a competent staff.

7. The interest of the Brazilian Government was clearly expressed by the Minister of Health.

STUDY IN CARACAS, VENEZUELA

Discussion with the Chief of Zone I of the Pan American Health Organization led to the planning of our itinerary. (XI).

In an interview with the Director of The Office of International Health, arrangements were made to discuss the International Laboratory with the Minister of Health and Social Assistance at a later time during our week in Venezuela. The Executive Director made suggestions as to places we should visit and people we should see.

At the Central University of Venezuela we visited the President and Vice-President. At the School of Pharmacy we saw the Dean, the Professors of Pharmacology, Biochemistry and the Professor of Instrumentation.

(XI) Dr. J.L. García Gutiérrez

At the Faculty of Medicine we were particularly interested in the work of the School of Tropical Medicine. This School receives clinical specimens from all areas of the Republic. It makes diagnoses which are returned to the source where the physicians on the basis of the diagnoses decide what treatments to institute. The School also conducts an extensive educational program. They receive public health officials from all parts of the Republic and give them extensive training in modern Laboratory techniques used in analyzing clinical specimens. A third function of the Institute is to give broad overall advice that is available from the staff of outstanding experts whom they employ. These functions in the field of tropical medicine are comparable to the objectives of the International Laboratory in the field of drug analyses. (XII).

At the National Institute of Hygiene we visited several Laboratories but gave particular attention to the Sections of Chemical, Pharmacological and Microbiological Analysis of Drugs.

The Chief of the Division of Pharmacy and his staff provided us with detailed information concerning their activities. He also arranged for us to meet with the "Board of Pharmaceutical Review".

We visited the Venezuelan Institute of Scientific Research (IVIC) where we explained our mission to the Director and his staff and toured the extensive facilities of the establishment. (XIII).

At the City Planning Office, District of Sucre, State of Miranda, Metropolitan Zone of Caracas, we examined maps of Caracas and vicinity in the light of the Director's suggestions of possible sites for the International Laboratory. (XIV).

We discussed a number of matters with pharmaceutical manufacturers.

AVAILABILITY AND COST OF LAND, PROXIMITY TO A GOOD UNIVERSITY

Dr. Domingo Guzmán Lander, Minister of Health and Social Assistance; Dr. Luis González Herrera, Director of Public Health and Dr. Daniel Orellana, Director of The Office of International Health, discussed at length the possible establishment of the International Laboratory in Caracas. Dr. Jorge Ernesto Atkins of the local Pan American Health Organization office accompanied us.

The Minister and his associates expressed enthusiastic interest in the project. They explained that a site of the size needed for the Laboratory is not available in the center of Caracas or nearby. They pointed out that building sites of this size are very scarce even at some distance from the City. This is because of the mountainous nature of the terrain and the tremendous industrial growth in Caracas and vicinity during the past several years.

(XII) Dr. Félix Pifano and members of his staff
(XIII) Dr. Marcel Roche, Director. Dr. Gabriel Chuchani, Head of Chemical Department
(XIV) Dr. Aquiles Esté Salas

The Minister explained that his Department had found it necessary to locate the Venezuelan Institute of Scientific Research (IVIC) on a mountain top some twenty miles from the downtown office of the Department. He stated that a large area of land in the vicinity of this Institute was controlled by his Ministry. He offered this land without cost. The Minister said that he would recommend to the President of the Republic that if the Laboratory were to be built in Venezuela, a small contribution be made toward the cost of the Laboratory's construction. He made arrangements for us to visit the site suggested.

The City Planning Office pointed out on their maps, lands currently being developed by private investors. Some of this land is in an area where light industry is being located. Other plots are between light industrial and residential areas. This land in the opinion of the City Planner could be purchased for about $.75 per square foot. He pointed out however that land values are rapidly increasing and he could not give us a firm price estimate. The availability of such land is conjectural because the private owners have not made their plans for the several areas known.

CLIMATE, AMENITIES AND COST OF LIVING

Caracas is located near the 10th parallel North. Most of the City has an elevation of approximately 3,000 feet. March through August are the hottest months. November through February is relatively cool and dry. The rainy season extends from June through August and precipitation is frequently heavy. Humidity is high throughout the year.

There are recreational facilities available as in most large cities.

It is generally recognized that the cost of living in Caracas is quite high.

RECRUITING OF A COMPETENT STAFF WITHOUT UNDUE DELAY

The Central University of Venezuela has a student enrolment of more than 20,000. Their various Colleges include instruction in all of the disciplines which will be needed in staffing the International Laboratory. Salary scales in Industry, in the University and Government are relatively high. Competition for the most competent graduates and experienced scientists is keen. It should nevertheless be possible to recruit that portion of the International Laboratory staff that would come from the local educational institutions.

COMMENTS ON TRANSPORTATION AND COMMUNICATION

Caracas is in the northern most part of South America. Seven air lines connect Caracas with the other Capitals of South America. Cable and telephone communications are essentially equal to those of other principal cities of the Continent.

THE DRUG CONTROL LABORATORY AND INSPECTION

Drug control from an analytical stand point is divided between three principal Sections of the National Institute of Hygiene. These are the Chemical, Pharmacological and Microbiological Sections. All are housed in a modern well-equipped Laboratory building which also houses a number of Sections that employ similar scientific disciplines.

The Central Library serves the entire Institute and is well stocked with books and scientific periodicals. Modern instruments of chemical, pharmacological and biological utility are available. Some of these are shared by the different Sections. The scientific staff has been carefully selected and most of them have served for a number of years. The work load is greater than the staff can currently handle but the analyses that are made generally include precise quantitative determinations. These Laboratories systematically seek opportunities to give their employees advanced training in institutions outside of Venezuela. From time to time they conduct training courses not only for their own people but for scientists in Industry who operate pharmaceutical manufacturing controls.

The Director and four Inspectors visit all of the pharmaceutical manufacturing firms in the Country at least once a year to conduct an inspection. There are 62 such firms in the Country. 29 are in Caracas and 33 are in the rest of the Country. Five Inspectors assigned to the various zones regulate the retail drug stores.

The process of registering drugs involves a submission to the Division of Pharmacy of comprehensive data concerning the chemistry, composition, labeling, analytical methods and therapeutic value of the articles. In addition, samples are required. These are submitted to the National Institute of Hygiene for analyses and the petition for registration is reviewed and summarized by various scientists in the National Institute of Hygiene for consideration by the "Board of Pharmaceutical Review". The application may be accepted, rejected or the applicant may be asked to submit more data.

The Division of Pharmacy Inspectors routinely collects samples during factory inspections of pharmaceutical firms and from the market. These are submitted for analyses by the different Sections of the National Institute of Hygiene. Appropriate action is taken on the basis of the facts developed.

INTEREST IN ESTABLISHING THE INTERNATIONAL LABORATORY IN CARACAS

All members of the scientific community with whom we talked, as well as representatives of the Venezuelan Government, expressed interest in having the Laboratory established in Venezuela.

CONCLUSIONS

1. Caracas is reasonably well located geographically to serve the countries of South America.

2. Land is available without cost. The site offered is adjacent to the Venezuelan Institute of Scientific Research (IVIC). It is some 20 miles from Caracas. The Institute is on the top of a mountain. It is dependent on its own electrical generating system. There is no sewage system except lines connected to septic tanks. The site is remote from established telephone lines. No public transportation is available. The Institute must provide transportation to and from the city for its own employees and transportation to school for the children of those employees who live on the Institute grounds in housing owned by the Government. The site offered presents all of these difficulties. In addition, it is comprised of mountainous land that would need to be leveled, roads would have to be built and all other facilities would need to be established. Later maintenance would be very expensive.

3. The site is adjacent to a Nuclear Research Institute. In our opinion it is not acceptable for the International Laboratory.

4. The climate is tropical
   Cultural activities are readily available.
   Cost of living is very high.

5. Transportation between Caracas and the countries we assume will be served is good.

6. Competition in recruiting a staff may be anticipated.

7. The Venezuelan Government and scientific community would welcome the establishment of the Laboratory in their Country.

STUDY IN PANAMA CITY, PANAMA

Accompanied by the Panamanian Director of Pharmacy, Food and Drugs we visited the "Special Laboratories of Analysis" (LEA) of the University of Panama. The Laboratory Director (XV) informed us that his Laboratory was started six years ago with the help of a $20,000 grant from the "A.I.D." under their point 4 program. He reviewed its development and progress in the intervening years.

(XV) Dr. Jeronimo O. Averza

The Director and Sub-Director of The Office of Pharmacy, Food and Drugs informed us of the responsibilities of their organization and the relationship with the Analytical Laboratories of the University. (XVI).

We learned from the Office of the City Planner about the availability and cost of land.

We interviewed the President of the University, the Director of the School of Chemistry as well as other professors of the Schools of Chemistry and Pharmacy.

Accompanied by the PAHO Representative and the Director of Pharmacy, Food and Drugs we visited Mr. Abraham Pretto, Minister of "Labor, Social Assistance and Public Health".

Some pharmaceutical manufacturers were helpful in acquainting us with matters pertaining to commerce in drugs in this area.

LOCATION AND DISTANCE BETWEEN THE CAPITAL CITIES, CHIEF INDUSTRIAL CITIES, PORTS OF ENTRY OF THE COUNTRIES SERVED AND TRANSPORTATION FACILITIES

This information was obtained from the Pan American World Airways.

AVAILABILITY AND COST OF LAND, PROXIMITY TO A GOOD UNIVERSITY

Acting on advice of the City Planner we visited the Panama Golf Club and other sites within reasonable proximity to the University. These lands would probably be available and they would be acceptable. The cost however in our opinion would be excessive. The City Planner's estimate was that a site of around 2 acres would cost about $300,000.00.

The President of the University of Panama asked us to visit him. He expressed interest in having the Laboratory established on the grounds of the University and offered a choice of several sites without cost to the PAHO.

The Minister of "Labor, Social Assistance and Public Health" stated that the Government of Panama would cooperate fully in finding a site without cost to the PAHO. He discussed some lands too far distant from the University to be desirable. He spoke favorably of the University location but said that if Panama were to be seriously considered he would have additional sites surveyed in depth.

(XVI) Lic. Octavio A. Sosa and Lic. Maria Teresa Zebes

CLIMATE, AMENITIES AND COST OF LIVING

Facts about the climate are summarized from a publication of the Government of Panama. The weather is tropical and near sea level. From December through April there is practically no rain. From may through August there are heavy rains and high temperatures. The humidity is high, ranging from an average of 70% in the dry season to 80% in the rainy season. The hottest month is April and coolest is November.

A variety of participating and spectator sports are available. Educational opportunities are reasonably adequate. Some cultural activities may be had and others are in a developmental stage. Salary scales vary but appear to be generally below average. Cost of living is rather high.

RECRUITING OF A COMPETENT STAFF WITHOUT UNDUE DELAY

A School of Pharmacy has been in operation for several decades. Five students graduated last year and no substantial increase is currently foreseen.

Until two years ago science courses in the University were planned to provide teachers for secondary schools. Beginning then the curriculum was changed to permit students to take courses leading to Bachelor of Science degrees in Chemistry, Biochemistry, Bacteriology and a number of biological sciences. There will be no graduates with these degrees until completion of the 1968 academic year.

The scarcity of scientists trained in the disciplines required by the International Laboratory would seriously complicate recruiting.

COMMENTS ON TRANSPORTATION AND COMMUNICATION

Panama, of course, is located on the isthmus between Central and South America. While it has important relations with the countries both to the North and South, its closest affiliations and community of interests appear to be more with Central than South America.

Ten air lines serve the City and make connections to all the Capitals of South America. Cable and telephone communication facilities are adequate.

THE DRUG CONTROL LABORATORY AND INSPECTION

The "Special Laboratories of Analysis" (LEA) is housed in buildings which were not constructed for its purposes. They give the appearance of temporary quarters. Plans are being made for new Laboratories that would be larger and more suitable. A wide variety of modern instruments used in chemical, pharmacological and biological testing is available. The Director estimates that the instruments cost about $250,000.00. The Laboratory does

the analytical work for the Division of Pharmacy, Food and Drugs. The Division receives samples of drugs with each application to register a medicinal product. Fees are charged for the analyses of these samples. They range from $28.00 to $155.00. There are cases where the cost of complex analyses is higher.

The Laboratory also serves a number of Central American countries. It is available to analyze samples of both food and drugs. During the past three years 455 such samples have been analyzed. About 70% are drugs and the remainder are foods. El Salvador and Guatemala have provided practically all of the samples. A few samples suspected of causing food poisoning were submitted by Costa Rica. The University Laboratory charges the Central American Governments one half the fees which they charge Industry.

The total annual budget of the Laboratory is approximately $150,000.00. This income is largely derived from fees. They employ a scientific staff of 28; six chemists, two food technologists, two pharmacologists, three microbiologists, two botanists, one biochemist, two doctors of Vetinary Medicine, two physicists and eight professional assistants. The senior professionals have undergraduate and graduate degrees from a wide variety of educational institutions in a number of different countries. The Laboratory consistently sends members of the staff for advanced training in North America and elsewhere.

The arrangement for paying the staff is unusual. Many receive salaries as members of the University Faculty. They are also paid on a sliding scale fee basis depending upon the number and complexity of the analyses that they make. Samples are analyzed at such times as the members of the staff have available.

The Laboratory serves also a number of government agencies as well as private industry. During the past 3 years a total of 1200 samples from all sources have been examined.

The plans for construction of new Laboratory facilities on the University campus involve obtaining new buildings and equipment including expensive instruments. The present instruments will be retained by the University for teaching purposes. Financing this program would be accomplished by enlarging the service features for private industry. This would importantly involve supervision of control procedures for pharmaceuticals including the analysis of drugs on a fee basis. We asked the Director if serving both Governmental enforcement agencies and Industry might not involve a conflict of interest. His view was that this could be avoided by dividing the Laboratory into sections so that the same section would not serve the regulated industry and the regulatory agencies.

The Division of Pharmacy, Food and Drugs employs a Director, a Sub-Director, six Inspectors, in addition to a small clerical staff. Their annual budget is $45,000.00. They regulate canned foods, certain other non-perishable food items as well as drugs and cosmetics. They estimate that

some 50% of their work is on drugs. The Law requires all drugs and cosmetics to be registered before their sale is allowed. Registration involves submission by a pharmacist of samples, specimens of labeling and full information concerning the quantitative composition of the product. The applicant must also provide methods of analysis including techniques for examining the finished products. A certificate of free sale in the country of origin must be attached. This certificate may be signed by an official in the originating country who has little or no knowledge concerning the distribution of the drug. One application which we examined contained the certificate of general sale throughout the United States signed by a county clerk in the interior of one of the States.

As previously stated the samples are submitted to the Laboratory in the University for analysis. After the analytical fee is paid to the University, if the analysis shows the product to be worthy, a certificate is issued upon the payment of a $25.00 registration fee to the Government.

The registration is effective for five years after which it must be re-registered following the same procedure.

The plan of procedure calls for the collection by the Inspectors of samples from lots on the market to check against the sample submitted by the manufacturer. Budgetary limitations have prevented the collection of any substantial number of such samples.

The Division of Pharmacy, Food and Drugs is responsible for the inspection of the approximately 230 Drug Stores in the country. This includes special attention to the records and physical inventory of narcotic drugs.

The Division is seeking funds to employ more Inspectors. No provision is made for the transportation of these employees in their work. At present they use their own cars which are operated at their expense.

INTEREST IN ESTABLISHING THE INTERNATIONAL LABORATORY IN PANAMA

The scientists interviewed in the University expressed enthusiasm in having the International Laboratory located on their campus. The President offered such a site without cost. The Minister of "Labor, Social Assistance and Public Health" expressed interest, offered every cooperation and said that he was sure a satisfactory site could be made available.

CONCLUSIONS

1. Panama City is the further-most north of the cities surveyed. From a geographical standpoint it is the least desirable site.

2. Land would be made available without cost.

3. The University site would be within walking distance of the principal University buildings.

4. The climate is typical of the tropical sea-level area.
Some cultural activities are available.
Cost of living is rather high.

5. Transportation between Panama City and the countries we assume will be served is adequate but the Capitals in the southern part of South America are distant.

6. Local scientists to staff the Laboratory in part are few. The local University will not graduate a substantial number of scientists for some years. The quality of the early graduates will probably be adversely affected as is usually the case in newly-organized Universities.

   Climatic conditions would probably make recruiting from outside the country difficult.

7. The Panamanian Government and university professors expressed interest in having the International Laboratory in their country.