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19235

DP/ID/SER.A/1523
13 November 1991
ORIGINAL: ENGLISH

ESTABLISHMENT OF A FORMULATION - FILLING PLANT FOR BACTERIAL VACCINES FOR VETERINARY APPLICATION

DP/URT/86/023/11-51

UNITED REPUBLIC OF TANZANIA

Technical report: Findings and recommendations*

Prepared for the Government of the United Republic of Tanzania
by the United Nations Industrial Development Organization
acting as executing agency for the United Nations Development Programme

Based on the work of Mr. Laszlo K. Nagy
Expert in Veterinary production

Backstopping Officer: Ms. M. Sanchez, Chemical Industries Branch

United Nations Industrial Development Organization
Vienna

* This document has not been edited.

V.91-30742

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MISSION'S RECOMMENDATIONS

1. In view of the importance of the livestock sector in Tanzania and with the objective of reducing the country's dependence on imported vaccines the mission CONFIRMS that a unit for industrial preparation of bacterial vaccines is justified along the Project Document attached (ANNEX 1)

2. To create the necessary conditions for the utilisation of and to provide information for improved and / or new vaccines , prepared at the projected unit, the mission RECOMMENDS that the Government draws up plans for completing :

i. rehabilitation of an adequate infrastructure for storage and distribution of veterinary drugs and vaccines (cold chain).

ii. rehabilitation of veterinary diagnostic services .

3. The mission, having been advised about the introduction of the National Agricultural and Livestock Extension Rehabilitation Project (NALERP) by World Bank backing in 1989 and in view of the plans for completing rehabilitation of the cold chain and the diagnostic services RECOMMENDS that Project Proposal for vaccine formulating unit should be submitted for approval subject to i) inception of those plans concerning the cold chain and the diagnostic services; ii) favourable outcome of a feasibility study of the vaccine formulating unit.

4. Considering that the preparation of vaccines, in quantities justified by the country's requirements , needs to be undertaken on an industrial scale the mission CONFIRMS that UNIDO should be designated as the Executing Agency in the establishment of the projected facility.

5. To draw on the experiences of the Tanzania Pharmaceutical Industries (TPI) and with a view of sharing certain facilities (workshop, preventive maintenance of plant and equipment, canteen, etc...) the mission RECOMMENDS that the site adjacent to TPI in Arusha should be the first choice for siting of this Project.

However, if for other priority reasons, the Government considers this inadvisable, this mission RECOMMENDS, as an alternative site, the land adjacent to the Animal Disease Research Institute, on the outskirts of Dar Es Salaam, where, according to Government officials, about 100 acres are available.

1) Introduction

1.1) Terms of Reference

- To evaluate the existing infrastructure for the establishment of a formulation filling and packaging unit for bacterial vaccines for veterinary use, prepared from imported antigen concentrates.

-To recommend the type of vaccines to be produced, based on the national requirements, indicating their annual production capacity

- To determine the 'cold chain' requirement based on the existing transport and storage system.

- To present the list of necessary equipment for performance of processing and quality control tests indicating their specifications and possible manufacturers.

- To recommend the necessary measures to fulfill GMP requirements during the processing of vaccines.

- To indicate the measures and requirements for the environmental protection in the proposed installation.

- To present the layout of the plant, giving recommendations on civil and archetectural solutions for satisfaction of hygienic requirements.

- To inicate the procedures and equipment requirements for the effluent treatment.

- To indicate the climatisation requirements.

- To prepare a draft project document for the establishment of processing of vaccines.

- To draft the terms of reference for the subcontract of the required services for the establishment of the processing of selected vaccines.

- To present a detailed mission report.

- During the preparatory mission, the expert is expected to follow up the project number DP / RAF / 86 / 012: "Assistance in the Production of Veterinary Drugs in SADCC Countries".

1.2) Mission's Schedule

02.05.91 Thur	Briefing L.K. NAGY at UNIDO Vienna
27.05.91 Mon	UNIDO Consultant (L.K. NAGY) leaves for Dar Es Salaam
28.05.91 Tues	Consultant arrives at Dar Es Salaam at 2pm
29.05.91 Wed	Briefing and discussion at UNIDO office
"	Discussion at National Chemical Industries (NCI) and drafting of work program
30.05.91 Thurs	Discussion of regional projects at FAO office
"	Consultation at UNDP office
"	Discussion at Ministry of Industry and Trade
31.05.91 Fri	Consultation at NCI
"	Discussions at FAO office
01.06.91 Sat	Consulting FAO project documents FAO library
03.06.91 Mon	UNIDO - office
"	Discussions with General Manager at NCI
"	UNDP offices discussion with livestock specialist
04.06.91 Tues	UNIDO Country director
"	NCI - civil engineering
"	UNDP - Assistant Resident Representative.
05.06.91 Wed	Ministry of Industry and Trade / Director of Planning
"	Ministry of Agricultural Livestock Develpment (MALD) / Assistant Commissioner
"	NCI / director of finance and development
06.06.91 Thurs	MALD/Principal Secretary
"	MALD / Assistant Commissioner
07.06.91 Fri	Animal Disease Research Institute / Director
08.06.91 Sat	Planning Commission / Assistant Director
10.06.91 Mon	UNIDO / Director
"	MALD / Assistant Commissioner - NALERP
11.06.91 Tues	Delegation of the Commission of EC / Livestock Service Development Project
"	Ministry of Industry and Trade / debriefing

12.06.91	Wed	MALD / Assistant Commissioner / debriefing
13.06.91	Thurs	FAO / director / debriefing
"		UNDP / Assistant Res. Rep. / debriefing
"		UNIDO / Director / debriefing
14.06.91	Fri	Departure for home
15.06.91		
24.06.91		Home - based: Preparation of :
		1: Equipment List, complete with prices
		2: Mission Report
		3: Project Document
		4: Terms of Reference for sub-contractor

1.3) Persons Met by the Mission:

A Goverment Services

Dr.B.E. Moshi	Principal Secretary/MALD
Dr. G.L. Komba	Assistant Commissioner/MALD
Dr. J.B. Ndunguru	Assistant Commissioner/MALD
Mr. L.W. Nyachia	Director of Planing/Ministry of Industry and Trade
Mr. E.G. Moyo	Assistant Commissioner/ NALERP / MALD
Mr. H.M. Kitilya	Director of Finance and Development / NCI
Dr. J.M.K Hyera	Director, Animal Disease Research Institute
Dr. K.M. Mayaliwa	MALD
Mr. S.M. Kakala	Assistant Director / Planning Commission
Mr. O. Paresoi	General Manager / NCI
Mr. I.R. Khomo	NCI
Mrs. E. Undiri	NCI
Mrs. E.E. Mangesho	Ministry of Industry and Trade

B. External Assistance

Mr. A. Krassiakov	UNIDO Country Director
Mr. T. Vissers	Deputy Resident Representative/UNDP
Mr. R.W. Fuller	FAO Country Director
Mr. P.M. Matovu	Assistant Resident Representative, UNDP
Mr. D.M. Lucia	Program Officer FAO office
Mr. V. Akim	Senior Admin. Assistant - UNIDO office

2) Project Background

In June of 1986 a UNIDO mission visited the SADCC countries to review the situation with respect to the supply - demand gap for veterinary drugs and vaccines in the region.

Apart from a Terminal Report (DP / RAF / 86 / 012) the mission produced a series of country reports. The report for Tanzania made the following recommendations:

1) An integrated animal disease control should be drawn up, starting with the rehabilitation of an effective diagnostic service, followed by disease monitoring and quantification.

2) The veterinary infrastructure and all aspects of extension services should be built up, paying attention to training, transport, communication, distribution and storage of drugs and vaccines.

3) Within this overall strategy, the plans for local veterinary vaccine and pharmaceutical production should be included so as to come on stream with appropriate quantities and qualities of products in phase with the maximum growth of the animal health market.

3.1 Production of large demand bacterial vaccines should be established through a progression of development phases.

In phase 1 establishment of a formulation/ filling/ packaging unit (utilising imported antigen concentrates) and a quality control laboratory is recommended.

In phase 2 production of bacterial vaccines is established and Quality Assurance, Quality Control Laboratories expanded.

In June 1987 a Project Proposal was prepared and submitted to the Government for comments. The proposed scheme provides for a two - phased approach, as outlined in the recommendations. The vaccines proposed for formulation and filling in the first phase include:

Anthrax
Blackquarter
Haemorrhagic septicaemia
Brucella S 19 vaccines

The Government, in consultation with UNDP, suggested the fielding of Project Development Facility (PDF) mission.

The mission worked in Tanzania in the first half of March 1988 and submitted its findings in a PDF mission report and also prepared a Project Document (PD / URT / 86 / 023), and submitted them to UNDP H.Q. in May of the same year.

The Mission Report confirmed the earlier recommendation of the Project Proposal that the establishment of the bacterial vaccine formulation unit should be implemented with the collaboration of a reputable private firm, specialized in this field, and subcontracted to it.

The subcontractor should provide expert advice on:

1) Functional design of formulation unit and quality control laboratory.

2) On plant and equipment and their installation.

3) Technical experts on vaccine formulation / filling / packaging.

4) Technical experts on Good Manufacturing Practice (GMP), Quality Assurance and Quality Control.

5) Provide bulk antigen concentrates.

6) Train key personnel on subcontractor's premises.

The Project Document (DP / URT / 86/023) stipulated prior obligation and prerequisites.

Prior Obligations:

1. The Government will make adequate budgetary allocations to enable the National Chemical Industries to fulfil its obligations to the project in the form of buildings and related infrastructural facilities.

2. The Government will make adequate budgetary allocations, including necessary foreign exchange elements, for the running costs of the formulation / filling / packaging unit and the Quality Control laboratory after the withdrawal of external assistance.

3. The Executing Agency (UNIDO) will identify a suitable contractor, willing to co-operate in the transfer of industrial vaccine production technology to the relevant Tanzanian Government Services.

Prerequisites:

1. The Government undertakes to rehabilitate the veterinary vaccine storage and distribution services.

2. The Government undertakes to rehabilitate the diagnostic services network to provide the epidemiological information necessary for vaccine formulation.

3. The Government should select national personnel of suitable qualifications for training abroad in the appropriate disciplines of industrial vaccine productions. The CVs of those will be submitted to UNIDO for approval.

4. Subject to satisfactory implementation, the Government will enter into a consultancy agreement with subcontractor to provide post-hand-over trouble-shooting services with respect to production technology and quality control.

The Project Document (DP / URT / 86 / 023) was sent to the Government for comments, through the UNIDO office in Dar Es Salaam in September of 1988. A request for implementation of the project was posponed and the project suspended in recognition of the Government not being able to meet some of the prerequisites of project implementation at that particular time. The present Preparatory Assistance Mission was fielded on the Government's request to UNDP and is concerned with reviewing all components of the Project with particular reference to the prerequisites referred to above. The Mission also follows up aspects of the original Report (DP / RAF / 012) which have bearings on the Project in question.

3) Existing Infrastructure for Vaccine Production

3.1 Mabibo

Located some 15 km from Dar Es Salaam, was established in 1971 for the production of smallpox and BCG vaccines. Production of smallpox vaccine came to an end in 1978 when smallpox was globally eradicated. The production of BCG vaccine to WHO standards never succeeded and was abandoned in 1982.

In 1980, Mabibo was handed over to the National Chemical Industries (NCI) with a view to rehabilitation / reorientation. In 1984 it was considered as the most suitable site for housing the Extended Program of Immunisation (EPI) in Tanzania and in October of that year all but three of the buildings were handed over to the Ministry of Health for the use of EPI.
In July 1986 the remaining three buildings were handed over by NCI for the use of EPI thus Mabibo has not been available for vaccine production ever since.

3.2 Animal Disease Research Institute (ADRI)

Near Dar Es Salaam, is the only establishment where small quantities of two vaccines, for veterinary use, have been produced. On the grounds of ADRI a building was erected between 1971-75 for vaccine production. Between 1975-80 development of two vaccines, Anthrax and Blackquarter, has taken place. Production of these two vaccines started in 1980 and between 1984-91 ca. 0.9 - 1.0 million doses of each of the two vaccines were produced on, what might be called, "improvised bench scale".

At ADRI all aspects of vaccine production, including media preparation, production of cultures, blending and filling of vaccines and quality control are carried out by the same staff. All aspects of production rely on very basic technologies producing small batches in unsuitable buildings consisting of a few "general purpose" laboratories in addition to a media preparation room, a walk-in incubator, small cold room, some offices and a store room.

From a consideration of facilities, production technologies and testing it becomes apparent that it is not only small scale, but also relies on outdated and uneconomical technologies, incapable of assuring quality of products. Thus it requires not so much changes and adjustments, but complete replacement if it is to meet internationally acceptable standards of manufacture and quality of products, at an economical cost.
Although somewhat larger quantities of these vaccines could be produced within the existing facilities and currently used technologies but significant extension of production is bared

by the lack of space for expansion on site. In any case, it is of basic interest of security of vaccine processing/development to be strictly segregated from potential sources of pathogenic microorganisms, such as those present in laboratories and animal houses of diagnosis and research at ADRI and therefore siting of a new facility on ADRI-site should not be admitted. Even though the siting, production facilities and technologies at ADRI are not appropriate for vaccine production in Tanzania, the staff, its experience in vaccine production and quality control and, in a small degree, equipment would have a bearing on future developments of production of veterinary vaccines.

The staff presently consist of a veterinary graduate and four technicians between from 5 to 10 years experience in vaccine production.

3.3 Site Near to ADRI

Although the ADRI site itself is inappropriate for siting of a modern vaccine processing/production facility, it is understood (but to be confirmed) that there are about 100 acres of land, near to ADRI, available for development.

Advantages:

- Vicinity of Central Veterinary Stores (CVS), starting point of distribution of all veterinary drugs and vaccines in the country.
- Vicinity of centres of veterinary services and of diagnostic laboratories.

Disadvantages:

-Lack of services and utilities (roads, water and power supplies,affluent disposal, telephone). Provision of these services and utilities on site would require substantial capital investment by the Government.
- At variance with Government policy of decentralisation of industrial development.

3.4 TPI Site in Arusha.

The Tanzania Pharmaceutical Industries (TPI) is situated on the outskirts of Arusha in an industrial complex well served with roads, rail and an international airport.

There is reliable water and electricity supply and consumable materials can be brought by rail from Tonga. Perishable products may be transported by air.

TPI, with the help of ORION (Finland) as a subcontractor.

was established as a drug preparation plant and benefited from continuing support and monitoring by the above firm, under FINIDA bilateral assistance. Its manufacturing standards are in line with those set out in the Guide to Good Pharmaceutical Manufacturing Practise (1983). There is ample space nearby for a separate veterinary vaccine production facility.

Vaccine production as planned under the first phase of this project is, in principle, not very different from drug preparation insofar that the bulk material (chemicals for drug preparation and antigen concentrates for vaccine production) are imported and formulated on site, filled, labelled and packaged for distribution. Because of this similarity, the TPI plant could provide a model and valuable guidance for the industrial vaccine processing/ production facility. The setting of the latter in the immediate vicinity of the TPI plant, therefore deserves serious consideration.

Advantages:

- Vicinity of TPI plant could serve as a model and provide guidance for good manufacturing practice, quality assurance and quality control.
- Availability of about 25 acres of land for expansion.
- Availability of services and utilities (roads, water, mains electricity, telephone, drainage) which may need to be expanded/enlarged before they could be shared with the new vaccine processing facility.
- TPI's workshop and its engineers may be contracted to carry out preventive maintenance and repairs of plant and equipment of vaccine processing facility.
- Subcontracting of quality assurance, validation and quality control is also worthy of consideration.
- Arusha is one of the countrie's most important and progressive livestock production regions.
- Government's policy of decentralisation of industrial development would also make Arusha a good choice for industrial development, away from the capital, Dar es Salaam.

Disadvantages:

- Distance from CVS at Temeke (near Dar as Salaam).
Since CVS is the start point of distribution of all veterinary drugs and vaccines in the country, those produced in Arusha would first have to be transported to CVS in order to get into the established distribution chain.
- Distance from Government offices and from Central diagnostic laboratories.
Problems of communications may arise, which could be resolved by the appointment of a high level official of the Veterinary Services (eg. Deputy Director) to the project area.

4) Size of the Market

A livestock population of about 13 million head of cattle and ca. 10 million sheep and goats (best estimates of Ministry of Agriculture and Livestock Development, for 1991) make the domestic market large enough to sustain a vaccine manufacturing facility.

Furthermore, there are export opportunities in the region for these products (see Report DP / RAF / 86 / 012) if the quality and price are right and payments can be arranged without the use of foreign exchange.

5) Choice of Vaccines to be Produced Based on National Requirements

The choice of bacterial rather than viral vaccines for processing (phase 1) and production (phase 2) is justified by the fact that there is no modern, industrial scale bacterial vaccine manufacture anywhere in East or South East Africa, whereas there is such viral vaccine production in Botswana. The Botswana Vaccine Institute, on the outskirts of Gabarone, is an excellent modern vaccine manufacturing facility, producing Foot and Mouth Disease and Rinderpest vaccines to the highest international standards. There is considerable excess capacity in the FMD laboratory and the Rinderpest vaccine production unit could be utilised for the production of other vaccines on a campaign basis. There is also ample place for additional high - security virus vaccine production on site. The choice of the four bacterial vaccines (Anthrax, Blackquarter, Haemorrhagic septicaemia and Brucella abortus S 19) is based on the country's large demand for these products, (see Table 2 of Annex 1) The 1990 / 91 demands for the four vaccines amounted to 16.16 million doses of which only 1.5067 million doses were secured and used. (Source of information: Ministry of Agriculture and Livestock Development). It is clear from these figures that there would be much demand for these products, were they available.

5.1) Products and quantities.

These are based on the 1986 estimation of national requirements for year 2000 (see Table 2 of Annex 1) and revised in 1991.

5.1.1 Anthrax Vaccine
(Bacillus anhtracis, live, avirulent spores in liquid)

Annual requirement: 8 million doses, 8000 L bulk vaccine prepared in 8 X 1000 L batches

Pack size: 50 X 1ml and 100 X 1ml per pack

Total no. of packs: 80,000 X 50 ml packs (4000L)
40,000 X 100ml packs (4000L)

5.1.2) Blackquarter Vaccine
(Inactivated Cl. chauvoei culture, adjuvanted with aluminium salt)

Annual requirement: 7 million doses, 14000L bulk vaccine, prepared in 14 batches.

Pack size: 50 X 2 ml and 100 X 2 ml per pack.

Total number of packs: 70,000 X 100 ml packs (7000L)
35,000 X 200 ml packs (7000L)

5.1.3) Haemorrhagic septicaemia vaccine
(Inactivated P. multocida type E culture, adjuvanted with aluminium salt.)

Annual requirement: 2 million doses, 4000L bulk vaccine, prepared in 4 batches.

Pack size: 50 X 2 ml and 100 X 2 ml per pack

Total no. of packs: 20,000 x 100 ml packs (2000L)
10,000 X 200 ml packs (2000L)

5.1.4 Diluent
(for lyophilised Br. abortus S19 vaccine)

Annual requirement: for 1.4 million doses,1400L diluent, prepared in 4 batches and 16 filling lots.

Pack size: for 10 doses, nominal 10 ml/pack

Total no. of packs: 140,000 X 10 ml packs.

5.2 Processing and Storage

All processes are implemented on a campaign basis, ie. only one vaccine is handled at any one time, followed by decontamination before beginning a new campaign.

5.2.1 Antigen concentrate

is imported in bulk and stored at 2-8 ^{o}C till required.

5.2.2 Preparation of bulk vaccine

These are prepared from antigen concentrates which are supplied with complete with blending instructions.

2 X 1500 L jacketed blending vessels are installed in the blending room. These are used in parallel, but one lagging 7 days behind the other with respect to the stage of preparation of the same vaccine.
Following preparation of the bulk vaccine (day 1) it is held in blending vessel for 11 days (days 2-11) and kept at 2-8 ^{o}C, using chilled water circulated via the jacket of the vessel. On day 12 vaccine is filled out directly and on day 13-14 the vessel is washed, sterilised and made available for a new batch. One batch of new vaccine is prepared per week.
To calculate a time frame of the blending campaign and occupancy of the blending room each vaccine is considered under the following headings:
Name of vaccine; volume of batch; number of batches; utilisation of blending vessel by each batch; duration of blending/filling campaign using two vessels.

Anthrax vaccine: 500L; 16 batches; 14 days; 18 weeks.

Blackquarter vaccine: 1000L; 14 batches; 14 days; 16 weeks.

Haemorrhagic septicaemia vaccine: 1000L; 5 batches; 14 days; 7 weeks.

Diluent for S19 vaccine: 400L; 4 batches; 24 days; 8 weeks.

5.2.3 Filling and closing

To save on storage vessels (ca. $ 16000 for a 250L vessel) and cold storage space for bulk vaccine, pending on test, calculated risk is taken and vaccine is filled out directly from the blending vessel after a provisional sterility test at 11 days. To save on cost of quality control of filling lots the aim is to fill out the batch in a single day.
One person feeds containers to automatic filling machine with a capacity of 1000-1200 packs per hour. A team of three people is required. Work in two shifts may need to be considered..
Vaccine containers are glass bottles of 25, 50, 100 and 250 ml capacity which are sterilised on site.
Good quality glass bottles for vaccines need to be imported unless the quality of those available locally is substantially improved. Similarly good quality rubber closures, caps and closing rings need to be imported. They may be available from Zimbabwe.

Packaging materials, labels, direction for use labels can be printed locally.

To calculate the time frame for filling campaigns and occupancy of filling room, these are considered under the following headings:

Name of vaccine; volume of bulk vaccine for filling; pack volume; number of packs filled out per day; occupancy of filling room in each working week; duration of each filling campaign.

Anthrax: 500L; 50 ml; 10,000; 1 day; 8 weeks
500L; 100 ml; 5,000; 1 day; 8 weeks.

Blackquarter: 1000 L; 100 ml; 10,000; 1 day; 7 weeks
1000 L; 200 ml; 5,000; 1 day; 7 weeks.

Haemorrhagic septicaemia: 1,000 L; 100 ml; 10,000; 1 day 2 weeks
1,000 L; 200 ml; 5,000; 1 day; 3 weeks.

Diluent for S19 vaccine: 400 L; 10 ml; 40,000; 4 days; 4 weeks.

Filling room is thus occupied one day per week for 35 weeks (for Vaccines) and for 4 days per week for 4 weeks for diluent, 39 weeks in all.

5.2.4 Inspection and packaging

Applicable for all vaccines and diluent originating from one batch.

Number of packs for inspection: 5,000-10,000

Number of packs for packaging: 5,000-10,000.

Time taken by one person in each working week: inspection and packaging 2-3 days.

5.2.5 Storage of filled products pending on tests (2-8 ^{o}C)

Each batch of a product requires storage whilst pending on tests for its release for use. Since several batches are produced during the time of testing of the firs batch, these batches accumulate until the first batch is released. Stocks, pending on tests for release, stabilise at that level before depleting after the production of the last batch.

For storage space of filled products three times its bulk volume was taken, allowing for passage (eg.: 1,000 L = 1 m^3 requiring 3 m^3 storage space). For calculating floor area, products are stored 1.5 m high.

Before-release storage space requirements of products is sequential in time, (because of campaign production) with some overlap.

Anthrax vaccine must be adequately segregated in storage from all other products.

Time frame of occupancy and storage space requirements in cold store is considered as follows:

Duration of storage for each batch; total storage time for each product before release; storage space per batch; maximum storage space for each product; maximum floor area for each product.

Anthrax: 5 weeks; 21 weeks; 1.5 m^3; 7.5 m^3; 5 m^2.

Blackquarter: 6 weeks; 20 weeks; 3 m^3; 18 m^3; 12 m^2.

Haemorrhagic septicaemia: 3 weeks; 8 weeks; 3 m^3; 9 m^3; 6 m^2.

Diluent for S19 vaccine: 2 weeks; 6 weeks; 0.8 m^3; 2.4 m^3; 2 m^2.

Since the cold storage requirement of vaccines, before release, is sequential in time, maximum demand is determined by the most voluminous product, in this case Blackquarter vaccine, occupying 12 m^2 floor area. The 5 m^2 area for Anthrax, segregated from other products , is additional.

5.2.6 Storage of released products

Released products require the same storage space as before release. However, their requirements are not likely to be sequential in time. For maximal safety, cold storage facility is planned for concurrent storage of all products, requiring a total floor area of 58 m^2. (Anthrax: 16 m^2; Blackquarter: 28 m^2; Haemorrhagic septicaemia: 10 m^2; Diluent: 4 m^2).

6) Choice of Technology

Utilisation of industrial technology is called for because it is the only type capable of delivering the dosage of vaccines required and manufactured to internationally acceptable standards for a reasonable and competitive price. Recent changes in the government's policy of pricing of drugs and vaccines to the end users, who are expected to pay economical prices for these products, should make vaccine production self - sustaining, if not profitable.

7) Phased Introduction of Technology

Because of the complex nature of vaccine production and the acute shortages of skilled manpower in this field of activity, transfer of technology must be accomplished by stepwise progression, over a relatively long period of time. It is therefore recommended that the project should start with the formulation of vaccines from imported bulk antigen concentrates to enable national staff to gain experience at industrial technology, up to date quality control and to get acquainted with the principles of good manufacturing practise. This would represent phase I of the project.

When phase I is well established and the economy of the activities can be appraised, consideration should be given to expand activities.

In phase II production of bacterial vaccines would be established and Quality Assurance and Quality Control laboratories expanded.

8) Transfer of Technology

In view of the complexities of establishing a new plant and transferring the relevant technologies it is not possible to accomplish these by ad - hoc experts. It is therefore necessary to sub - contract most aspects of the project, including expert advice on design of the buildings and its infrastructure, technologies and expertise, training and equipment to a single company of good international reputation in this field of activity. Subcontracting to a single company would also ensure that the technologies and equipment, required, would be compatible.

9) Possible Licensors for Veterinary Bacterial Vaccine Technology (alphabetical)

Hoescht A.G. Pharma Fabrik
Postfach 800320
D-6230 Frankfurt am Main 80
Federal Republic of Germany.

Phylaxia
Veterinary Biologicals
Budapest, X Szallas u. 5.
Hungary.

Pitman-Moore Ltd.
Berkhamsted Hill
Berkhamsted, Herts.
United Kingdom.

Rhone-Merieux
17, Rue Bourgelat
69002 Lyon
France

10) Manpower, Training, Ex-patriot Technical Assistance

10.1) Government Personnel

- Head of Filling Unit / Technical Manager should preferably be a Chemical Engineer with the necessary background for training in industrial manufacturing procedure.
- Head of Quality Control and Quality Assurance Unit should preferably be a graduate in Microbiology suitable for training in the technical aspects of industrial vaccine production.
- The two senior laboratory technicians, one heading the team of 6 technicians in the blending and filling unit, the other in Quality Control with two technicians, should also be suitable for receiving training at the premises of Contractor
- Instrument technician and maintenance engineer are key personnel in the smooth operation of equipment and plant and each should be suitable for training abroad.

10.2) Contractor's Personnel

- Expatriate Technical Manager should be experienced in all aspects of bulk vaccine preparation, filling and regulations affecting these activities. His understudy (Head of Filling Unit / Technical Manager), a microbiologist, should have received six months training prior to commissioning of the Facility at the premises of the Contractor. They should work in parallel for six months in all during and after commissioning of Filling Unit.

- Expatriate Head of Quality Control should be experienced not only in the technical aspects of various tests, but all aspects of regulations affecting Quality Control and Quality Assurance. The understudy, a graduate in microbiology, veterinarian or biologist, should receive nine months training in all aspects of quality control and quality assurance at the premises of supplier of bulk antigens before taking up the post at the new Facility. They should work in parallel for up to six months following commissioning of Filling Unit.

- Expatriate Engineer should be experienced in all aspects of installation of plant and equipment and of plant and equipment used in association with processing of vaccines and quality control.

11) Cold Chain Requirements Based on Existing Transport and Storage System.

In order to maintain the indicated shelf life of veterinary biologicals they have to be stored at a specified range of temperatures. For most of the live and inactivated bacterial vaccine and for some of the viral vaccine, the recommended storage temperature is in the range of 2 - 8oC. for other viral vaccines the recommended storage temperature is -20°C.

11.1 Distribution of Drugs and Vaccines

The Central Veterinary Stores (CVS), on the outskirts of Dar Es Salaam at Temeke, issues drugs and vaccines to the 20 Regional Veterinary Stores (RVS) and also to some Parastatals.
From the RVS drugs and vaccines are distributed to some 116 District Veterinary Stores (DVS) and hence to the 451 Livestock Development Centres (LDC) who deliver these products to the end users.

11.2 Numbers and Condition of Cold Chain Equipment in the 20 Regions*

Item	Condition			Total
	Good	Fair	Bad	
Deep - freezers	17 (90%)	1 (5%)	1 (5%)	19
Refrigerators	135 (40%)	117 (34%)	88 (26%)	340

11.3 Numbers and Conditions of Various Classes of Transport in the 20 Regions

Vehicle	Condition*				Total
	A	B	C	D	
Lorries	7(11%)	17(27%)	23(37%)	15(24%)	62
4WD Vehicle	6(6%)	25(24%)	43(41%)	39(29%)	104
Motorcycles	5(6%)	23(29%)	19(24%)	31(40%)	78
Tractors	6(32%)	0 (0%)	3(16%)	10(52%)	19
Bicycles	54(41%)	22(17%)	22(17%)	33(25%)	131

* Condition: A = Good, usable 300 days a year
B = Fair, usable 200 days a year
C = Poor, usable 100 days a year
D = Unusable

*Soutce of information: Project Preparation and Monitoring Bureau, MALD.

11.4 Additional Requirements of Equipment in the 20 Regions*

Lorries:	18
4 wheel drive vehicles:	83
Motorcycles:	435
Bicycles:	1133
Deep - freezers:	6
Electric Refrigerators:	20
Non - electric refrigerators:	407

Following the EC funded Rinderpest Control Programme there are adequate deep freeze units in all but six regions for vaccine storage. Of the 407 non - electrical refrigerators 175

Kerosine refrigerators are supplied by the National Agricultural and Livestock Extension Rehabilitation Project (NALERP), thus 232 non - electric refrigerators are required mainly for the Livestock Development Centres.

*Source of information: Project Development and Monitoring Bureau, MALD.

11.5 General Comments on the Present State of the Cold Chain

Central Veterinary Store at Temeke: the building has no internal ceiling or insulation so that drugs are kept at unacceptably high temperatures. There are two cold rooms for vaccine storage one of which is non - functional. There is no deep - freeze for storage of freeze - dried vaccines. CVS requires complete rehabilitation and reequiping.

- Many of the Regional and District Veterinary Stores are in need of some rehabilitation. About half of the District Veterinary Stores lack electricity supplies. Bottled gas supplies are limited so they need kerosine or solar - powered refrigerators.

- In the worst conditions are the Livestock Development Centres. Most of the buildings are in poor structural condition and have no water and electricity supplies. They are the worst off for transport, staff are under - utilised for want of facilities and transport. In the rehabilitation program it will be necessary to provide secure stores for the storage of drugs, vaccines, microscopes, etc..

11.6 Rehabilitation of the Cold Chain

From the foregoing it is clear that in order to deliver any locally produced vaccine to the end user, without unacceptable wastage, the cold chain needs to be rehabilitated.

- In 1989, NALERP was financed* with the objective of rebuilding an extension service, capable of formulation and delivery of profitable agricultural / livestock techniques to farmers and livestock owners.

Under NALERP, the separate crop and livestock extension services shall gradually be merged into a multidisciplinary extension system.

During the first four years of NALERP, which began in 1988, 12 of the regions will be affected, containing ca. 10.2 million of the 13 million heads of cattle and most of the 10 million sheep and goats in the country. NALERP, however, does not provide all the inputs required for the rehabilitation of the cold chain. It is providing mainly for the retraining of personnel in the extension services. It also provides for 175 kerosine refrigerators in the 12 regions covered by the project.

*International Development Bank: US $18.4 mill.
African Development Bank: US $ 8.8mill.
Government of Tanzania: US $ 3.2 mill.

Another project with a bearing on the rehabilitation of the cold chain is the "Livestock Development Service" project, supported by the European Community in the form of a grant of 3.7 million ECU. The financial agreement was signed in March of 1991. The objectives of the project include, among others, the eradication of rinderpest by mass vaccination campaigns in two consecutive years, covering that part of the country North of the Central railway line and districts of Southern Tanzania along the Malawi - Zambia borders.

Inception of operations is expected upon finalisation of the Plan of Operation which should be completed within three months of signing the financial agreement (i.e by June of 1991). What exactly it shall provide for the cold chain in terms of transport, communications and equipment is still under consideration. However, it is understood that items of transport and equipment should be substantial and that the Central Veterinary Store at Temeke will be completely rehabilitated, re-equipped and computerised stock control system will be installed.

These items of transport and equipment together with those obtained through NALERP are significant contributions to the rehabilitation of the cold chain and to a lesser degree to the veterinary diagnostic services. However, it still leaves a substantial balance of outstanding requirements for vehicles of various types, cold chain equipment, and structural improvements to Livestock Development Centres requiring financial support.

In addition to the physical rehabilitation of the cold chain, training program for the staff for its operation and preventive maintenance of all equipment, including all classes of vehicles, is vital to be incorporated in the rehabilitation program of the cold chain to enable it to function efficiently and to prevent physical deterioration of buildings and equipment. Without these items of equipment, improvements to buildings and training of personnel the cold chain cannot operate adequately to deliver drugs and vaccines to the end user.

12) Equipment for Processing and Quality Control

The list of equipment is appended (ANNEX 2) indicating specifications and budget prices. For planning purposes a total of US$ 600,400 should be allocated for equipment.

13) Measures Recommended to Meet GMP Requirements During Processing

- Quality Control of all raw materials and consumables.
- Adherence to processing protocols on the basis of Standard Operating Instructions.
- Judicious use of process - monitoring tests.
- Strict adherence to work disciplines in sterile and other areas of work.
- Blending and filling should be carried out under Class 1 conditions and over pressure with constant monitoring.
- Constant monitoring of temperature in cold rooms.
- Refrigerator plant of cold room connected to stand-by generator with automatic switch to activate it in case of power failure.
- Segregation of in - process and finished products in cold rooms.
- Segregation of Anthrax vaccine from all other vaccines in cold room.
- Clear identification of all products in cold rooms.
- Verification of equipment and sterile areas.
- Quality control of finished products by internationally recognised standards.

14) Requirements for Environmental Protection

- Kill tank for effluents from blending vessel for Anthrax and for animal testing facility handling virulent Anthrax bacilli.
- Closed drainage system from equipment and animal testing facility to kill tank.
- Full shower and changing facilities for personnel handling virulent Anthrax bacilli in Testing Facility
- Negative pressure in blending and filling rooms during processing of Anthrax vaccine with terminal filtration of exhaust air.

- Incinerator for the safe disposal of suitably bagged bedding and other contaminated materials and carcases from animal testing facility handling virulent Anthrax bacilli.

15) Layout Plan of Facility, Recommendations for Meeting Hygienic Requirements in Working Areas.

15.1 Layout plan of the buildings

incorporating the blending / filling unit, and the Quality Control and Animal Testing facilities are appended as: Annex 3 Layout A and Layout B respectively.

15.2 - Recommendations for meeting hygienic requirements in working areas

- Cloakrooms should be separated from processing areas.
- Toilets should be well ventilated and not open directly to processing areas.
- Floors in processing areas should be made of impervious materials and laid to an even surface. They should be free from cracks and points and should allow prompt and efficient removal of any spillages.
- Walls should be sound and finished with a smooth, impervious and washable surface.
- Ceilings should be constructed and finished so that they can be maintained in clean condition.
- All surfaces must be formed to prevent erosion by water and disinfecting agents.
- Covings of junctions between walls, floors and ceilings in critical areas is recommended.
- The doors and frames should be made from anodised aluminium.
- Pipework, light fittings, ventilation points and other services in manufacturing areas should be sited to avoid creating uncleanable recesses.

- Services should preferably run outside the processing areas and should be sealed into any walls or partitions through which they pass.

- Drains should be of adequate size and should have trapped gullies.

- Air intakes and exhausts and associated pipework and trunking should be sited to avoid product contamination hazards.

- Animal house should be well isolated from processing areas.

16). Procedures and Equipment for Effluent Treatment

- Effluent treatment is required from blending vessel, handling Anthrax spore vaccine, and from rooms from animal testing facility handling virulent Anthrax bacilli.

- Closed drains from this equipment and from the rooms to the kill tank is required.

- Pit, brick lined to accommodate 1000-2000 L plastic tank, the formalin kill tanks, (1% concentration of formalin). Following inactivation, contents to be discharged into public drain system or soakaway. Sample at regular intervals for verification.

17) Climatization Requirements

- For all but the sterile areas, window box type climatization is required, including rooms in animal testing facilities used for animals under test.

- For the sterile rooms (blending / filling) sterile air supply is needed with an overpressure. Temperature between 18 -20°c, relative humidity 35 - 65%

Mission's Main Conclusions

1. The mission is of the opinion that rehabilitation and re-equiping of the vaccine production unit on the ADRI site, so as to comply with GMP requirements, cannot be supported in view of its layout, construction and a lack of suitable land for expansion.

2. However, in view of the livestock population of the country and the demand for a total of over 16 million doses of the four most important bacterial vaccines (Anthrax, Blackquarter, Haemorrhagic septicaemia, and Brucella abortus S19) establishment of a modern vaccine production facility is justified.

3. Utilisation of industrial technology is called for since it is the only type capable of delivering the required dosage, manufactured to internationally acceptable standards at a competitive price.

4. Due to the complex nature of vaccine production and the acute shortage of skills in this field of activities, transfer of technology must be accomplished by stepwise progression beginning with formulation and filling of products, and at a later stage, full production can be considered.

5. External assistance is required in most aspects of the project including design and infrastructure of buildings, technologies and expertise, equipment and training.

6. External assistance should be provided in terms of subcontract with an industrial manufacturer of good reputation in this field of activities.

7. The mission, however, realises that in order to make good use of the vaccines and assure continued utilisation of the plant there are certain prerequisites to be met before the project could be implemented. These include:

i. rehabilitation of the transport and storage system (cold chain) especially in those nine regions included in the first three phases of the NALERP programme.

ii. rehabilitation of the diagnostic services to provide information necessary for improved or new vaccine formulation and usage.

iii. assurances that the project remains viable after withdrawal of external assistance.

8. In respect of rehabilitation of the cold chain and the diagnostic services the Mission was pleased to learn that a good start has been made. However, much remains to be accomplished. Finalisation of plans for the complete rehabilitation of the cold chain and the diagnostic services and inception of these plans, together with favourable outcome of a feasibility study of the vaccine formulation project,(which has not as yet been done), should activate implementation of the vaccine formulation project.

9. For the aforementioned reason the vaccine formulation project should be closely co-ordinated with the rehabilitation of the cold chain and the diagnostic services.

10. The mission is updating the project document so as to provide the planners of the rehabilitation of the cold chain and the diagnostic services programme to take it into consideration and to ensure smooth coordination of activities at home and with external organisations.

11. The mission in the meanwhile is drafting the Terms of Reference for the subcontract of the required services for the establishment of the formulation/ filling unit.

LIST OF EQUIPMENT

Annex 1

Description	QTY	Specification	Justification	Estimated cost US$
Blending vessel	2	1500L stainless steel jacketed, steam sterilizable blending vessel, complete with stirrer	For blending of bulk vaccines and for their storage pending on tests.	135,800
Filling Line	1	Fully automatic filling, stoppering, closing and labelling machine for glass bottles for vaccine packs of 100 - 600ml capacity. Operated under laminar flow cabinet.	For filling out bulk vaccines and vaccine diluent into final container. For closure of final containers of vaccines and diluent with stopper and cap. For labelling of final containers of vaccines and diluent with appropriate labels.	90,000
Washing machine for bottles and ampoules	1	Electronically programmed industrial glass washing - drying machine. Electrical power 10.5 kw, water per cycle 18L.	For washing of glass containers for vaccines and diluents and rinsing in sterile pyrogen-free water ready for sterilization	12,000
Sterilizer (Hot air oven)	1	Heraeys STUH 100 / 150 Vol. 1.4 m^3 (1400L) 5 - 10 shelves. Connected load KVA:15.	For sterilization of final containers for vaccines and diluent for filling unit.	10,800
Water de-ionizer plant complete with automatic regenerator	1	Output 500 - 3000L/h depending on water hardness. Effluent purity: .05 ppm, silica and oil ppm CO_2 pH6. 57.	To demineralize water for distillation (required in vaccine production), generation of steam and use of rinsing of glassware.	17,000
SUBTOTAL				265,600

Description	QTY	Specification	Justification	Estimated cost US$
Fully automatic water still	1	Electrically heated, fully automatic still requiring softened or deionised water. E.g: Finn Aqua 75 E-4. Capacity: 75 kg/h, conductivity: 0.5-2.0 us/cm, consumption of electricity /h: 15.6kw, feed water at 15°C 100kg	To provide pyrogen-free distilled water for vaccine preparation and for rinsing of vaccine bottles.	32,000
Water storage tanks (complete with insulation)	2	1000L, each, stainless steel tanks complete with absolute filters at in and outlets. Temperature maintained at 80°C.	Preparation of bulk vaccines from antigen concentrates requires the use of pyrogen-free sterile diluent water requiring defined storage conditions. To provide pyrogen-free glass containers for vaccines and diluents, these need to be rinsed in pyrogen-free water.	15,000
Heaters for water tanks	2	Thermostatically controlled immersion. Type electric.	To maintain sterility of stored water in 1000L tanks.	600
Stirrers	2	Electrically propelled stirrers	To aid maintenance of even temperature of water in storage tanks.	1,800
Sectional pre-fabricated cold room	1	Two chambers fitted with two sets of refrigeration equipment each capable of providing 60% of required duty. Area: ca 80m^2 - 200m^2. Duty: 2 - 8°C within chambers.	To hold antigen concentrates and vaccines requiring a storage temperature of 2 - 8°C.	38,000
SUBTOTAL				87,400

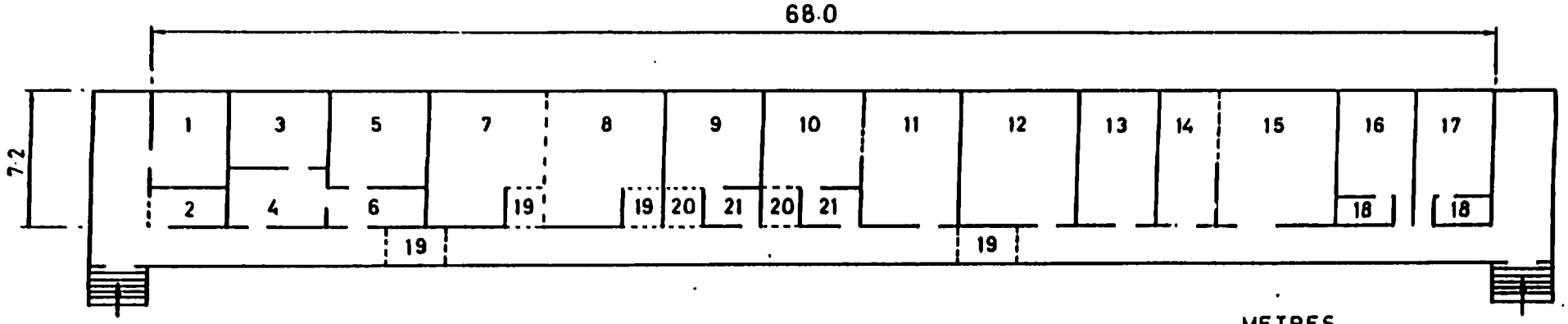
Description	QTY	Specification	Justification	Estimated cost US$
Water Chiller	1	Cooling capacity: to reduce temperature 1000L water from 80°C in 20h and to maintain it between 2 - 8°C. Refridgerator capacity: BTU/HLx1000:12 KCAL/ HRX 1000:5. Example: Acro-Kool, model RTC 150.	To supply chilled water for cooling diluent (sterile dist. water at 80°C to 10-15°C) for vaccine dilution and to maintain temperature of bulk vaccine (stored in jacketed blending vessel prior to filling) at 2-8°C.	15,000
Boiler	1	Oil fired, water tube, steam boiler fed with deionized water, capable of generating 200kg/h particulate matter-free steam per hour	Steam is required for sterilization of blending vessel (150kg/h) and operation of water still	29,900
Oil Tank	1	1000L mild steel tank.	For storage of fuel to boiler.	1,500
Incubators	2	Electrically heated thermostatically controlled, 250L, shelf area 1m^2. Temp. range 5-80°C (1) and -10 to 50°C (1).	For incubation of samples and cultures used in quality control. Two different incubation temperatures are required.	5,400
Refridgerator (2 - 8 °C)	3	General purpose, front loading, electrical, adjustable thermostat, push button defrost. Capacity 215L	To maintain temperatures of samples and vaccines, adjuvants, diluents and for reagents, antisera, etc. awaiting testing, or used in Q.C. Laboratory.	900
SUBTOTAL				52,700

Description	QTY	Specification	Justification	Estimated cost US$
pH meters	2	Fully automatic temperature compensated. Accuracy to 0.01 pH. Range pH 0 - 14 For redox work: range 0 - 1999v. Resolution 1uv.	For measuring and adjusting pH of liquids and vaccines at Filling Unit and Quality Control Laboratory.	1,000
Centrifuges	2	Laboratory type MSE. Super-minor max. RCF x g from 2460 to 6990.	For bench-scale sedimentation of particulate matter in liquids and vaccines at Filling Unit and Q. C. Laboratory.	1,900
Microscope	2	Zeiss.	For use by Q.C. Laboratory and Filling Unit to assess morphology, purity, etc.. of microbiological specimens.	--- Present at ADRI
Autoclave	1	Sterilising temp. to 160^{o}C Max. pressure 21 kg / cm^{2}. Vertical depth 100cm, diameter 62cm.	For steam sterilization of materials and equipment used in Animal House.	--- Present at ADRI
Autoclave	1	Electronically managed, quadrangle, double door, steam autoclave. Chamber size 80 x 80 x 125cm. Horizontal sliding door at each end. Capacity 800L. Demand for steam: max 120kg/h, ave 65 kg/h. e.g: Fedegari F03	For sterilization of solids, liquids. Filtering systems used in relation to production and quality control of vaccines.	60900
SUBTOTAL				63800

Description	QTY	Specification	Justification	Estimated cost US$
Balance	1 1	Sartorius (Germany) Type 2462. Max. 200g. Min 0.1g. Type 2742 Max. 160g. Min 0.01g.	For weighing chemicals for preparation of reagents, buffers, etc. in Q.C. Laboratory and Filling Unit	5,100
Water bath	1	General purpose. Temp. range upto 100 ^{o}C. Capacity 15L. Power rating: 500W. Temp. variation 0.1^{o}C.	For the incubation of serological reactions in Q.C. Laboratory	500
Deep freezer	1	Top loading, min. temp. -20 ^{o}C. Capacity: 260L.	For safe storage of some of the Biological reagents, serum samples of test animals in Q.C. Laboratory.	800
Laminar Flow Biological	2	Bench mounted, Class II. MDH Model No. 20229. Working area: 120 x 64 x 86 cm.	To aid aseptic handling of specimens, media inoculation in Q.C. Laboratory.	13,000
Environmental Control System	1	Purpose made environmental control system providing accurate temperature, humidity, filtration and pressurization control for ca. 80m^2/200m^3 working area.	For providing clean and aseptic environment for blending and filling of vaccines	30,000
Spectrophotometer	2	Solid dtate, wavelength range 340 - 1000, 220 - 240v, 50 - 60Hz, Single phase supplies.	For assessment of bacterial suspensions in Q.C. Laboratory and filling unit	5,100
SUBTOTAL				54500

Description	QTY	Specification	Justification	Estimated cost US$
Holding tank for de-ionised water	1	2000L polypropilane tank.	For storage of deionised water	3,200
Electricity generator	1	3 phase, 420v, 50Hz, 160Kw, Diesel generator set with standard control panel.	To serve as standby generator	58,200
Air compressor	1	Hydrovein air compressor complete with dryer/filter, 3HP, output: 210L/min.	To provide compressed oil-free dry air for vaccine blending/filling	4,000
Vehicle	1	Four-wheel drive	Project vehicle	15,000
Installation of plant and equipment		20% of cost of plant and equipment	Estimated cost of installation of plant and equipment	121,480
SUBTOTAL				201,880
GRAND TOTAL				725,880

ADMINISTRATION - FILLING UNIT - STORAGE - PREPARATION.

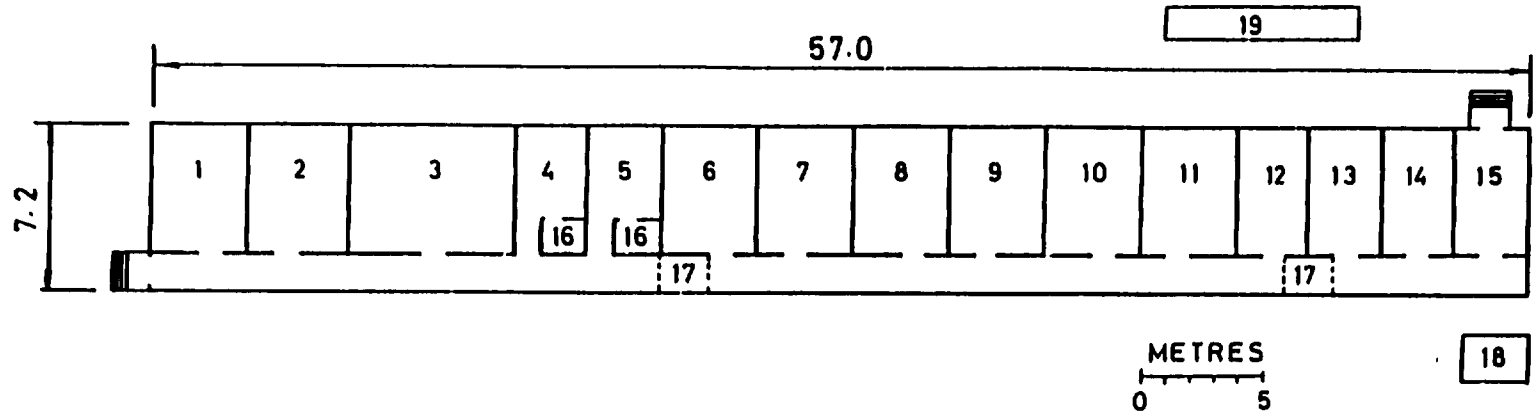


1. ACCOUNTS
2. RECEPTION
3. MANAGER
4. SECRETARY
5. ADMIN-OFFICE REGISTRY
6. TYPIST
7. COLD ROOM QUARANTINE
8. COLD ROOM
9. BLENDING
10. FILLING
11. LABELLING PACKAGING
12. STORE
13. WATER TREATMENT AND STORAGE
14. STERILISATION
15. WASHING
16. FEMALE SHOWER AND LOCKERS
17. MALE SHOWER AND LOCKERS
18. W.C.
19. AIR LOCK
20. FORMALIN LOCK
21. PERSONNEL AIR LOCK

Layout A

ANNEX 3

QUALITY CONTROL ANIMAL TESTING.



1. GENERAL OFFICE Q.C.
2. HEAD OF Q.C.
3. QUALITY CONTROL (Q.C.) LABORATORY
4. MALE LOCKER ROOM
5. FEMALE LOCKER ROOM
6. GUINEA-PIG ROOM
7. MOUSE ROOM
8. RABBIT ROOM
9. INOCCULATION ROOM
10. CAGE CLEANING AND STERILIZATION
11. FOOD STORE
12. GOAT ROOM
13. GUINEA-PIGS (ANTHRAX)
14. SHEEP ROOM (ANTHRAX)
15. PERSONNEL AIR LOCK AND SHOWERS
16. W.C.
17. AIR LOCK
18. INCINERATOR
19. CHEMICAL TREATMENT

Layout B

Annex 4

UNIDO comments on Mr. L. Nagy's technical report
DP/URT/86/023

There is a growing mass of cattle, sheeps and goats in the country which requires specialized medical care and veterinary attention for the satisfaction of the necessities of the population on high quality food and to fulfil the requirements of the international market.

As a conclusion of DP/RAF/86/012 - Assistance in the Production of veterinary drugs in SADCC countries, it was already recommended to establish the production of several types of vaccines in different countries in the region.

The main result of the recent concluded mission to Tanzania under DP/URT/86/023 was the certification of the urgency on the establishment of the production of bacterial vaccines in Tanzania based on the real existence of contageous diseases among the livestocks existing in the country.

The expert suggested the sorts and quantities of vaccines to be produced in the country based on the living animal stock and its annual growth rate.

The establishment in Tanzania of the necessary filling and packing lines for the production of bacterial vaccines based on the imported antigents, followed by the production of the antigent during the second phase of the project is absolutely justified and should be implemented immediately.

The prepared report presents the equipment requirements and equipment costs for the establishment of the first phase of the project.

The rehabilitation of the cold chain system including the upgrading of the maintenance facilities in order to guarantee the proper transportation and storage of the vaccines as well as the rehabilitation of the veterinary diagnostic services are two activities which should be developed in parallet with the establishment of the first phase of the industrial production of vaccines.

The facilities for the establishment of the quality control laboratory for the performance of the quality control test of vaccines should be created attached to the production line. The proper qualification of the personnel is considered one of the most important aspecs, thus during the negotiations of the conditions for the establishment of the formulation plant, it is absolutely necessary to define the training programmes for the plant personnel in activities like sterile water production; filling processes; operation of different equipment; cleaning procedures; validation of plant, equipment and processes; quality control processe, etc.

The assurance of the proper training programmes will permit the personnel to perform the running and production activities of the plant and guarantee the right quality of the end product.

Upon completion of the plant, the installation could be utilized as a training centre for professionals and technical staff of the region.

One important aspect that should be defined in some step is whether the necessary sterile polyethylene containers for vaccines packing will be imported or locally produced. The local production of the polyethylene containers will increase the initial investment cost of the plant but will permit to diminish the operational costs of the plant and could create possibilities for export of the containers to neighboring countries.

The expert drafted a project proposal for the establishment of the filling line which is attached to the mission report and was utilized by UNIDO substantive area to prepare the final project document to be presented to UNDP for analyses and approval.