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DEVELOPMENT OF THE LOCAL INDUSTRY FOR PRODUCTION AND COMMERCIALIZATION OF HUMAN AND VETERINARY VACCINES AT THE NATIONAL VETERINARY LABORATORY, BOKLE (LANAVET), CAMEROON

SI/CMR/95/801/11-52 and 11-53

REPUBLIC OF CAMEROON

Technical report: Findings and recommendations*

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

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ABSTRACT

A technical mission to Cameroon was undertaken by two UNIDO Technical Experts to support the "Development of the Local Industry for Production and Commercialization of Human and Veterinary Vaccines at The National Laboratory Veterinary Bokle (LANAVET)" project SI/CMR/95/801. The main objectives were to evaluate the current infrastructure at LANAVET for production and commercialization of human and veterinary vaccines and make recommendations for the improvement of these activities in order to boost the control of infectious diseases in the region.

ACKNOWLEDGEMENTS

The consultants wish to express their gratitude to the Deputy Director of LANAVET Dr. Abdul Kadiri Souley and all LANAVET's officers and staff for their co-operation in the implementation of this technical mission.

PROJECT TERMS OF REFERENCE

The UNIDO technical mission to Cameroon project SI/CMR/95/801 was undertaken during August-October, 1995. The focus of the project was to work with the National Veterinary Laboratory Bokle (LANAVET) in Garoua and assist LANAVET in the enhancement of the production and commercialization of human and veterinary vaccines.

The mission Terms of Reference were as follows:

1. To evaluate LANAVET's infrastructure for the production of tetanus toxoid for human use and veterinary vaccines in accordance with international standards of quality.

2. To advise improvements to technical procedures for production and down stream processing of vaccines and evaluate the possibilities for production of other vaccines in the existing facilities.

3. To evaluate human resources for the optimization of production.

4. To evaluate the need for additional equipment which could be procured within the project budget.

5. To set the stage for the implementation of single dose vaccine presentation.

6. To provide complementary training for technical personnel responsible for production and quality control.

7. To prepare a final report on the technical mission with conclusions and recommendations.

ABBREVIATIONS AND ACRONYMS

CBPP	Contagious bovine pleuropneumonia
cGMP	Current Good Manufacturing Practices
GLP	Good Laboratory Practices
FDC	Freeze drying cycle
GMP	Good Manufacturing Practices
HEPA	High Efficiency Particulate Air Filter
i.u.	International unit
Kf	Flocculation time
L	Litre
LANAVET	National Veterinary Laboratory, Bokle
Lf	Flocculation units
mg	Milligram
OIE	International Office of Epizootics
PAHO	Pan American Health Organization
PANVAC	Pan African Veterinary Vaccine Centre
A	Quality Assurance
QC	Quality control
SS	Stainless steel
TCA	Trichloroacetic Acid
UNIDO	United Nations Industrial Development Organization
WHO	World Health Organization

1. LANAVET ORGANIZATIONAL STRUCTURE

The National Veterinary Laboratory Bokle (LANAVET) is an autonomous organization which operates under Cameroon's Ministry of Livestock, Fisheries and Animal Industries. LANAVET's mandate is to provide veterinary support services to Cameroon's animal industry. The services include research in animal health, epizootiology surveillance of domestic animal infectious diseases and manufacture of veterinary vaccines. In addition, LANAVET has a pilot plant for the manufacture of tetanus toxoid for human use.

LANAVET's organizational structure is shown in Figure 1. The laboratory is divided into six service units or departments:

- Maintenance service
- Administration and Finance
- Quality Control service
- Department of Diagnostics and Public services
- Department of Production
- Commercial services

Even though the departments are well differentiated in their activities, all share LANAVET's administration and overhead cost. Personnel, as well, have equal working rules and benefits.

LANAVET does not have an official cross appointment system within their labour force. As a result, in many cases, there are significant differences in the working load and responsibilities among employees.

LANAVET employs a total of 119 people from which only 25% (29) are involved in activities related to vaccine production and their quality control. The current distribution of the staff is presented in Figure 1.

The major source of financing of LANAVET is the Government of Cameroon, revenues generated from the sales of vaccines and some assistance from international organizations, cooperation programs. No significant contributions are generated by other services provided by LANAVET.

2. LANAVET SITE AND BUILDINGS

LANAVET currently occupies approximately 13,000 square metres of buildings divided into three major areas:

A. Main building which includes the administration, diagnostic, research and production of veterinary and human vaccines, quality control and maintenance.

B. Animal quarters, maintenance warehouse and workshops.

C. Living quarters for the staff.

In general, all buildings are of good basic construction. However, most facilities dedicated to production activities require minor repairs of interior wall surfaces.

LANAVET's general layout is shown in Annex 1.

Area A, which includes modules dedicated to specific functions such as administration and senior staff offices; diagnostic and research; veterinary bacterial vaccine production; veterinary viral production; washing and sterilization and media preparation; final processing (filling, capping and inspection) for tetanus toxoid; quality control unit; and maintenance and main mechanical room. An independent single storey building is dedicated to the manufacture of tetanus toxoid for human use. (See Annex A).

In area A, most spaces allocated to existing functions appear to be sufficient with the exception of washing and sterilization and media preparation which is crowded.

Most office space is provided with central air conditioning. All the modular units dedicated to production are equipped with central air system and HEPA filtered air, gas, compressed air, steam and special electrical lines with access to emergency power supply provided by a central stand-by generator. Walk-in cold storage and incubator rooms are present in all vaccine manufacturing units.

Existing cold storage units are in poor running condition and most units need to be upgraded with special attention to surfaces, controls and recording instruments.

Area B, dedicated to animal house and maintenance workshops is sound and appears to be in good order. Currently most of the buildings are under-utilized due to a significant reduction in the animal rearing activities at LANAVET in the last years.

Area C, living quarters , was not reviewed.

3. TETANUS TOXOID PRODUCTION AUDIT REPORT

The inspection has been concentrated on evaluating tetanus toxoid facility and manufacturing process and technical base with respect to their level of current Good Manufacturing Practices (cGMP).

3.1 Facilities

The pilot plant facility dedicated to tetanus toxoid production is a single storey building with approximately 272 square metres of floor space. Layout is in Figure 2.
The building structure is physically separated from other buildings in the complex. The facility is composed of two distinct and separated units:

a) the toxin production unit.
b) the down stream processing unit or toxoid processing area.

Both units are environmentally controlled with independent HEPA filter systems.

The interior of the building dedicated to tetanus toxoid production requires some minor repairs of wall cracks and repainting of all wall surfaces with an epoxy base paint. All areas appeared to be well ventilated, with sufficient lighting and adequate space for the orderly placement of the necessary equipment and accessories required for the production of tetanus toxin.

The area dedicated to toxoid processing, in particular toxoid purification and filtration, is not suitable for these activities because the working environment is crowded with equipment dedicated to tetanus culture media preparation.

The final formulation, filling and capping of the ready-to-use product is conducted in a segregated area in the main production building. The area, in general, is properly maintained. However, it requires minor wall repairs and repainting with epoxy or epoxy like material.

3.2 Equipment and accessories

The facility is furnished with suitable equipment and accessories to produce and process tetanus toxoid. Current equipment and accessories include:

- Major production equipment including the main stationary 150 L fermenter vessel, the stationary formulation vessel and the ultrafilter.

- Minor production equipment including the centrifuge and filtration equipment.

- Laboratory services equipment including steam sterilizers, sterilization oven and cold rooms.

- Laboratory equipment including pH meter, scales, magnetic stirrers, water baths and light microscope.

- Final processing equipment including vial washing machine and filling and capping machine.

The majority of the equipment necessary for manufacture and processing is operational and suitable for the current methodology to manufacture tetanus toxoid. Exception is the stationary formulation vessel which has been out of commission since project start-up.

At present, there is neither a preventive maintenance programme nor validation programme in place for the tetanus production unit.

3.3 Raw materials

The storage and management of raw materials utilized for the production of tetanus toxoid was in general deficient. Materials utilized for manufacture are not kept in proper storage conditions. For example N.Z. case is stored in the washing sterilizing section of the plant exposed to high temperature and humidity, chemicals and reagents are stored in the cold storage used for intermediate production material without proper protection. The identification of suitable storage for raw materials, a dried control environment, requires immediate attention. Most of the materials are not currently been tested and in some cases show deterioration by humidity. There is no comprehensive inventory with information such as date of procurement, testing, etc.

There is a modern water treatment unit which provides sufficient deionized and distilled water for production. However, during the technical inspection there was no evidence of testing records to assess the performance of the water treatment system. The quality control department is equipped to conduct water testing and monitoring.

3.4 Human resources

The tetanus toxoid manufacturing team is composed of a team leader, a senior technical person and four support technical staff. The technical team leader is a competent professional trained abroad (Hungary) on know-how for the manufacture of tetanus toxoid for human use.

3.5 Product

Tetanus toxoid is a sterile solution of purified aluminum adsorbed tetanus toxoid in physiological saline. The toxoid is prepared by detoxification with formalin of sterile filtrate tetanus toxin obtained by broth cultures of **Clostridium tetani** grown in a fermenter vessel. The toxoid is purified by chemical methods and is adsorbed with

aluminum hydroxide as adjuvant corresponding to not more than 1.25 mg aluminum per single dose, 0.01% merthiolate is added as a preservative.

Each single dose contains 10 Lf of tetanus toxoid with no less than 40 i.u. Vaccination is carried out with two doses of 0.5 ml each at 4-6 weeks intervals. To ensure a long lasting immunity a third dose is recommended 6-12 months after the second dose.

The product is presented in 20 dose glass vials with a rubber stopper and aluminum seal. Product leaflets in English and French are available with the product. (see Annex 2)

The storage facilities for in-process product are adequate. However, the final product quarantine storage does not comply with cGMP. The storage and inventory of production components for ready-to-use tetanus toxoid also do not comply with cGMP. In particular there is a lack of control on product labels and ready-to-use inventory.

3.6 Production process

The tetanus process is carried out in a pilot production facility completely isolated from other production areas and with equipment fully dedicated to this process.

The production process is conducted in the following stages:

- Equipment preparation and sterilization, media preparation, media inoculation with Harvard strain No 49205 Y-IV-4 from Hungary, cultivation and harvest, total 10-12 days.

- Clarification (40x40 Seitz EKS pads), filtration (Pall SLK7002 NRP 0.2u), and detoxification, total 30 days.

- Concentration (10-20 fold), purification (16% TCA precipitation), sterile filtration, total 1-2 days.

- Final bulk preparation (average 80 litres), filling and labelling , total 1-2 days.

The tetanus process is carried out in a pilot production facility completely isolated from other production areas and with equipment fully dedicated to this process.

The toxoid is produced from the strain of **Clostridium tetani** identified as Harvard N° 49205-Y-IV-4, from Hungary. This strain is maintained in a lyophile and cultured in thioglycolate-Surjan media.

The production of tetanus toxoid is summarize in Figure 4.

LANAVET's stainless-steel fermenter is equipped with instruments to monitor mixing, air supply and temperature.

The fermenter is prepared with 100-110 litres of media and seeded with 1300 ml of tetanus culture (10^3 /ml) and incubated at 35°C for 5-7 days. During the cultivation period the vibromixer and aeration are adjusted at 20, 40, 64 and 124 hours. Yield, pH, purity, Lf and Kf are continuously monitored.

The toxin is harvested after 5-7 days incubation. LANAVET yields of tetanus toxin have been relatively low when compared with the recommended averages of 60-80 Lf/ml obtained by other manufacturers. LANAVET'S yields varies between 25-60 Lf/ml with an average of 39 Lf/ml. The culture is filtered and detoxified with formalin at 37°C.

The low toxin yields could be the results of the following factors:

- growth media composition
- strain maintenance (viability)
- cultivation cycle

The critical constituents of the growth media are the digested casein and the beef heart infusion as they provide nitrogen and carbon critical for tetanus culture. N.Z. case is recognized to have batch to batch variations with impact in the yield of toxin. Therefore, only pre-tested material that yields 50 Lf/ml of media or more should be used.

Considerations should be given to charcoal treatment of N.Z. case. Batches of tetanus medium should be prepared with charcoal treated and untreated N.Z. case in order to determine whether charcoal treatment enhances or hinders the production of tetanus toxin. A suggested procedure for the preparation of N.Z. case solution is presented in Annex 4.

As the manufacture of tetanus toxoid is not a continuous activity at LANAVET, it is necessary that all chemicals and raw materials utilized for tetanus culture media should be tested to ensure sustainable high toxin yield production prior to the initiation of a production cycle.

A review of LANAVET's 21 tetanus cultivation cycles between 1990-1994 indicates an average fermentation time of 153.6 hours with no significant variations between cycles. Also, there were neither significant differences in the recorder data of adjustment to the vibromixer nor the air flow during cycles.

Purification and filtration of tetanus toxoid should be conducted in a more suitable laboratory environment within the processing unit. In addition, closed systems should be used to avoid exposure and ensure the integrity of the product during the ultra-filtration and purification process.

3.7 Quality Control

3.7.1 Documentation

The technical information and production records of the tetanus toxoid production unit are in 18 laboratory books and four file folders. However, the records are not easy to follow and need to be improved in accordance with acceptable cGMP procedures.

There is no central master production file for tetanus toxoid production records.

There are technical written procedures for most techniques utilized in manufacture. However, these documents have not been up-dated from the original documents provided by UNIDO technical team at the time of the technology transfer. Therefore these documents were no longer accurately reflecting the current manufacture process in detail as required by cGMP.

3.7.2 Environmental monitoring

There is no environmental monitoring programme for this unit. There are no documentation nor validation records on the HEPA filtered service. The current procedures for gowning, cleaning and disinfection of the facilities require improvement and development of proper SOP's.

3.7.3 Testing

The quality control process for tetanus toxoid is divided into two distinct phases:

- In-process quality control is performed under the direction of the production personnel and includes test for bacterial purity, pH, sterility, Lf and Kf, potency and free formaldehyde.

- Final product container quality control is performed in the quality control unit and includes tests for pH, sterility, innocuity, stability, adjuvant and preservative contents.

Overall quality control conducts all the required basic tests recommended by WHO for tetanus toxoid final container. However, quality control needs to introduce a systematic methodology and recording programme which should include test procedure and standards. The programme should be implemented to include revisions of testing procedures and standards to assure compliance with cGMP and minimum WHO testing requirements.

3.8 Tetanus Toxoid Production

The production of Tetanus toxoid began in 1990 and, to date, 21 production lots of 105 litres each of crude tetanus toxoid have been produced. Since 1990, six final bulk lots have been prepared with a gross yield of approximately 45,714/20 dose vials or 914,280 doses.

However, the net yield was 31,951/20 dose vials or 639,020 doses which indicates a total loss or final processing waste of approximately 30%, equivalent to 13,714 /20 dose vials or 274,284 doses. Losses are due to volume lost (14%) and after filling discards (16%).

Of the production to-date, 14,700 vials (294,000 doses) were distributed to the Cameroon's Ministry of Health and 17,251 remain on stock at LANAVET warehouse facilities. This inventory will have to be re-tested in order to extend the expiry date.

4. SINGLE DOSE PRESENTATION OF TETANUS TOXOID

4.1 Requirements for pregnant women in Cameroon

With a population of almost 11.7 million in 1990 and a growth rate of 3% annually, the projected population for 1996 is estimated to be 13.9 million and 15.7 million for the year 2000.

LANAVET's tetanus toxoid is recommended for immunization of all pregnant women, with recommended 3 doses of LANAVET tetanus toxoid vaccines. The mortality rate to tetanus in Cameroon is very high due to lack of vaccination coverage of pregnant women by trained health personnel. Since tetanus occurs frequently in puerperal period and after septic abortions, the prophylaxis against tetanus by vaccination is deemed an ideal method.

The estimated number of pregnant women is derived by the crude birth rate for Cameroon, estimated to be 4%. As 3 doses are recommended, the number of doses required for 1996 is estimated to be 1.7 million and 1.9 million for the year 2000.

4.2 Single dose presentation

At present, all of LANAVET's tetanus toxoid is presented in a multi-dose (20 doses) vial. Such 20 dose presentations are appropriate for national immunization campaigns, such as EPI, when the tetanus toxoid is combined with diphtheria and pertussis vaccines as DPT.

However, the primary requirement of tetanus toxoid vaccines in Cameroon currently is for use by pregnant women, which is commonly provided in a single or five-dose presentation.

During the mission, several private sector vaccine distribution centres in the region were visited. In these centres the majority of tetanus toxoid products for pregnant women are imported, primarily from France, and are in syringe single dose presentation.

It is likely that the private sector market demands single dose presentation. If LANAVET is to expand sales of tetanus toxoid, it will be necessary to introduce single dose product.

For LANAVET to introduce single dose and/or five dose presentation of tetanus toxoid, the major constraint is the need to acquire the necessary filling equipment.

LANAVET currently has on site an ampoule filling machine. However, this machinery is outdated and lacking essential components for operation.

The equipment and technology for syringe single dose presentation is expensive, sophisticated and costly to operate and maintain. Ampoule presentation is probably better suited to LANAVET's current situation.

If LANAVET is to proceed to introduce single dose it will need to acquire the following :

a)	One precision ampoule flushing, filling and sealing machine up-to 120 containers per minute. Estimated cost F.O.B. plant	US $ 60,000
b)	Accessories and spare parts Estimated cost F.O.B. plant	US $ 10,000
c)	Installation cost	US $ 1,000
d)	Freight	US $ 4,000
e)	Production components (for 50,000 doses)	US $ 10,000
	SUB-TOTAL	US $ 85,000
f)	Contingency 15%	US $ 12,750
	TOTAL	**US $ 97,750**

Expected average filling speed:

- 60-80 ampoules per minute
- 3,600-4,800 per hour
- 18,000-24,000/ vials per day
  (5 hour day)

It is important to note that all tetanus toxoid vaccine tendered to UNICEF and/or PAHO is in multi-dose presentations of 10 and/or 20 dose presentation. If LANAVET could gain WHO recognition as UNICEF supplier, the institute will be required to maintain its current vial filling equipment.

5. VETERINARY VACCINES

LANAVET has the capacity to manufacture 17 veterinary vaccines from which seven (7) are used in livestock, mainly cattle. Of the 7 vaccines with livestock applications, there are two viral vaccines, rinderpest and sheep pox and four bacterial vaccines CBPP, pasteurellosis, clostridiosis and anthrax.

In addition, LANAVET manufactures a wide range of poultry vaccines such as newcastle, fowl cholera, typhoid, gumboro and bronchitis.

In the last three years, production has been concentrated in vaccines for livestock, mainly rinderpest and CBPP.

The production audit was focused on production and quality control of rinderpest and CBPP. These two vaccines constitute over 90% of LANAVET exports.

5.1 Site and Facilities

The facilities for production of viral and bacterial veterinary products are located in the main building, originally constructed in 1982-1983, following a modular concept utilized in France's biological manufacturing facilities.

The facilities are divided into two independent sections which are physically separated from other production activities. However, final processing, such as filling and freeze drying, are conducted in a common area (see Annex 1).

Electricity is provided by the National Electric Power Agency-SONEL through 30 kv high cables from Garoua. At present, about half of the available capacity is being used. In addition, LANAVET has a power generator system of 700 KVA capacity which is activated automatically if the primary power source fails.

LANAVET has its own water supply from a water well and 2 reservoirs of 350 cubic metres each. All water before consumption is passed through an iron purification system and two sand filters. In general, the water is of good quality and quantity, assuring sufficient quantity to supply all current manufacturing activities.

The steam supply is provided from a central generating plant and is sufficient for all production and service areas requirement.

The HVAC (heating ventilation and air-conditioning) equipment is designed to cope with the extreme climatic conditions (45°-48°C and high humidity) and is provided to all required working areas. Supply of cooled air for the sterile areas is filtered through HEPA filters.

5.2 Equipment and accessories

The equipment utilized in the veterinary vaccine manufacturing group is suitable and satisfactory for the production of all current veterinary vaccines.

The bacterial vaccines section has two modern fully automatic 250 L stationary fermenters and two additional small 50 and 20 litres fermenters. The final processing unit is furnished with two large freeze dryers, each with 100-150 litre capacity. In addition, modern steam and dried heat sterilizers are used for sterilization and decontamination activities. Washing of production material and filling and capping activities are conducted manually.

At present, there is neither a preventive maintenance programme nor validation programme for the production equipment.

5.3 Raw materials

The storage of raw material utilized for the production of veterinary vaccines was, in general, deficient. Storage conditions were similar to those described in Section 3.3.

5.4 Human Resources

Bacterial vaccines production unit is operated by a staff of 9 people including the Head of Bacteriology, Mr. Fokou Samuel.

Viral vaccines production is conducted by a team of 5 people including Dr. Soyem, team leader.

The staff are adequate in number and are skilled in the production processes and procedures, as well as operation of all equipment including the fermenters.

To increase motivation and enhance input of both professional and labour staff, training programmes in new laboratory techniques, good manufacturing procedures and good laboratory practices need to be organized and conducted on a continuous basis.

5.5 Production process

5.5.1 Rinderpest vaccine

Presently, LANAVET produces rinderpest virus using VERO cells (continuous African Green Monkey Kidney), as recommended by the OIE / FAO standards.

Monolayer is sub-cultivated for not more than 20 passages after removal from the seed stock. Cells are grown for 24 hours in 150-200 square centimetres tissue culture containers, either glass (Roux) or plastic(Falcon).

Infection is achieved by adsorption of the Virus Seed to the monolayer for 1 hour at 37°C. Five days after infection, when cultures are showing about 60-70 % CPE, virus is harvested by scraping the remaining attached cells, with glass beads. Harvested bulk is stored at -75°C to -80°C until used.

5.5.2 Contagious bovine pleuropneumonia (CBPP)

At present, two strains T1 and KH3J of **Mycoplasma mycoides** are available for use for the manufacture of vaccines.

LANAVET's CBPP vaccine is produced with T1 strain which was originally isolated in 1951 and attenuated in 44 egg-passages.

The vaccine is a freeze dried product produced in culture media. The working seed is produced by two successive passages of the master seed in medium F-66 at 37°C. A 10 litre bottle, equipped with a magnetic stirrer and containing five litres of pre-warmed F-66 medium, is inoculated with 500 ml. of the culture in logarithmic phase and incubated at 37°C.

The broth is not stirred during the first 24 hours.

The harvest is conducted prior to the end of the logarithmic growth phase.

The harvested material is cooled down in the ice bath and the vaccine is stabilized with skimmed milk (45g per litre of broth). Since the Streptomycin-resistant strain is being used, streptomycin at 200 mg/ml is added.

The vaccine is filled immediately in 50 or 100 dose units and freeze dried. After 36-38 hours, vials are capped and quarantined until quality control tests are completed.

5.6 Rinderpest and CBPP production

LANAVET manufactures 50 and 100 dose freeze dried presentation of rinderpest and CBPP vaccines. The formulation criteria depends on the final potency of the ready to use vaccine product. Both rinderpest and CBPP vaccine are presented to the market with different commercial names:

- Bovipestovax (rinderpest vaccine strain Kabete-O)
- Perivax (CBPP vaccine strain T1 SR)
- Bivax (rinderpest vaccine strain Kabete-0 and CBPP vaccine T1 SR)
- Thermovax (rinderpest vaccine strain kabete-0 and CBPP vaccine T1 SR, thermostable product)

It is important to mention that LANAVET does not produce vaccine diluent for their freeze dried products.

The production capacity for the manufacture of rinderpest and CBPP vaccines is determined by the freeze drying capacity to lyophilized final product.

The estimated installed production capacity for CBPP and rinderpest vaccines are shown in Table 1 below.

Table 1

LANAVET PRODUCTION OF READY TO USE RINDERPEST AND CBPP VACCINE 1993-1995 (millions of doses)

	1993		1994		1995	
	Dp		Dp		Dp	
	50	100	50	100	50	100
BIVAX	1.13	-	.74	.36	1.16	1.48
THERMOVAX	2.24	-	-	-	.89	-
BOVIPESTOVAX	2.04	1.45	-	10.34	1.27	.82
PERIVAX	2.30	.75	-	2.55	1.09	2.74
TOTAL	**7.71**	**2.20**	**.74**	**13.25**	**4.41**	**5.04**
Doses Produced		**9.91**		**13.99**		**9.45**
Dose Discard		**1.96**		**1.39**		**0.27**
Available doses		**7.95**		**12.60**		**9.18**

Dp= Dose presentation (50 doses, 100 doses)

LANAVET's 1993 to 1995 production output of rinderpest and CBPP is presented in Table 2 below. The data in Table 2 indicates that the total output and production output of each vaccine varies widely from year to year, with no consistent level of output nor systematic scheduled output decrease or increase.

Table 2

LANAVET INSTALLED CAPACITY THE PRODUCTION OF READY-TO USE RINDERPEST AND CBPP FREEZE DRIED VACCINE
(millions of doses)

Freeze dried unit	Current		Optimize		Maximized	
	Dp		Dp		Dp	
	50	100	50	100	50	100
Unit 1	18	36	46	92	69	138
Unit 2	27	54	69	138	103.5	207
TOTAL	**45**	**90**	**115**	**230**	**172.5**	**345**
ADDITIONAL CAPACITY			**+70**	**+140**	**+127.5**	**+255**

Dp= Dose presentation (50 doses, 100 doses)

In order to estimate LANAVET's installed capacity for rinderpest and CBPP vaccines the following points have been considered:

a) LANAVET has two freeze driers: unit-1 (U-1) with a capacity of 10,000/5ml vials and unit-2 (U-2) with a capacity of 15,000/5ml vials.

b) Each 5ml/vial of product can represent 50 or 100 doses of vaccine depending on the final potency of their components (rinderpest and CBPP).

c) One lot of either product is considered as one freeze dried product cycle of ready-to-use vaccine.

d) Currently LANAVET phases annual production over a 36 week or 9 months period.

e) Current capacity calculations considered the potential production with present parameters in a continuous operation over a 9 month period.

f) Process optimization calculations considered increase of the freeze dried cycles (FDC) in both units U-1 and U-2 and increase in annual production period to 48 weeks.

g) Process maximization calculations considered increase in the production of CBPP and rinderpest bulk vaccines could be obtained by,

- reduction of the FDC to 48 hours
- implementation of up to three FDCs per week in both freeze dryers, units U-1 and U-2
- Increase of production period to 48 weeks per year.

Neither the process optimization nor the process maximization would require additional capital expenditures nor hiring additional technical personnel.

Either the recommended options, optimization or maximization, would significantly reduce production costs due to increase of overall productivity of the vaccine manufacture operation.

5.7 Freeze drying vaccines

The technique of freeze drying (FD) is widely used for the preservation of the antigenic characteristics of viruses and bacterias. The problems associated with FD can be divided into three basic stages: 1) the preparation of the material;
2) the temperatures and rates of freezing and drying;
and 3) the rehydration of the FD product.

The advantages of using FD to preserve viruses lie in its ability to produce suspensions that are extremely stable when storage.

If a viral vaccine starts with suspensions of viruses having high titre, degradation during storage will be retarded in FD preparations.

It is assumed that biological preparations of FD viruses dried to a low residual moisture, less than 1%, lose little of their activity when exposed to adverse temperatures, which justifies use of relatively high temperatures during the final stages of the FD cycle (secondary drying). The average losses in virus titre over a FD cycle averages 0.5 of a log.

In general FD is conventionally divided into three stages:

- pre-freezing
- primary drying (sublimation)
- secondary drying (humidity is reduced to an optimum value.

A typical freeze drying cycle is shown in Figure 5.

During the pre-freezing, the material must be frozen to induce crystallization. Due to the salt content of the virus suspensions the eutectic point for these products is below -21°C. Concentrations exceeding 10% of sugar may supercool some tens of degrees below freezing point. It is recommended that the pre-freezing should reach minus -40°C or lower.

In order to optimize the FD cycle studies of the eutectic point of LANAVET's FD vaccine menstruums are necessary.

LANAVET's current procedure for pre-freezing FD products is conducted in two stages:

1. During filling, the product is placed in a -20 degree chamber until the filling is completed.

2. Upon completion of filling, the product is transferred into the FD chamber and the pre-freezing starts.

The duration of the first stage varies in accordance with the duration time of the filling procedure.

LANAVET should consider direct pre-freezing in the FD chamber. The freeze dryer should be on 1 hour prior to the initiation of the filling process with the shelf compressor on the shelves set to its maximum freezing capacity. Filled product should be placed directly onto the FD shelves as the filling process is conducted.

The FD trays could be redesigned to ensure that the vials have full contact with the FD shelves to maximize temperature transfer.

Upon completion of the filling, the FD should be closed and the condenser compressor directed to freeze the shelves overnight. In the early morning of the second day, condenser should be chilled by the condenser compressor. When a minimum differential temperature of 10°C has been established between the condenser and shelf, the vacuum should be established. When at least 100 microns has been reached the primary cycle is started.

The primary drying should be started when the product temperature is at a minimum of -45°C. Usually primary drying is equivalent or proportional to the thickness. Under typical conditions the ice boundary recedes from the surface of the dry cake at an average rate of 1 mm an hour.

The duration of LANAVET's primary drying appears to be long. Using the automatic FD cycle rather than manually or semi-automatic as is currently done, could reduce the drying cycle to no more than 10-15 hours.

LANAVET's secondary drying should also be reduced to no more than 6 hours at a temperature not exceeding than 38-39°C.

Currently LANAVET experiences potency losses of their FD rinderpest, particularly in the thermostable vaccine (Thermovax). Quality control test results on accelerated stability studies (14 days at 45°C).

The average potency of LANAVET's virus harvest is 10 x 6.5 log/ml. This virus harvest is further diluted 1:2 with the current stabilizer (lactose-gelatine or lactose-peptone) at a ratio of 1:1, resulting in potency of 10 x 6.2 log/ml. With an average loss of 0.7 log during the FD cycle the potency of the vaccine at the end of the FD cycle averages 10 x 5.5 log/ml.

Retrospective studies indicate an average loss in vaccine titre of 1.6 log/ml during accelerate stability test, resulting in a final potency of 10 x 3.9 log/ml, slightly 0.3 log below the minimum required potency.

As indicated previously improved potency of LANAVET FD products could be achieved by increasing the initial virus titre, improving the currently used stabilizer and modifying the current process for filling and freeze drying cycle.

Particular attention should be given to the standardization of the final product container (vial) and the stoppering activity. These constitute critical parameters for the FD cycle, such as evaporation and heat transfer during the drying cycle.

Differences in dose presentations necessitate that control experiments will be required to identify the most effective FD cycle for the different LANAVET's FD vaccine products.

5.8 Quality Control

The recent reorganization of the quality control department discussed in section 3 and implementation of the Quality Assurance programme should benefit the overall quality control of veterinary vaccines.

Quality control testing of CBPP and rinderpest is conducted in accordance with the guidelines established by PANVAC.

Moreover, the overall system of quality control will improve as the quality assurance programme is implemented.

6. QUALITY ASSURANCE TRAINING PROGRAMME

A Quality Assurance training programme was prepared and delivered to LANAVET senior professional and key technical personnel involved in vaccine manufacturing and quality control.

The training programme had three primary objectives:

a) To enable LANAVET technical personnel to update technical knowledge and basic skills needed to establish an effective core quality assurance programme for the manufacture of human and veterinary vaccines.

b) To enable LANAVET technical personnel responsible for the quality control of vaccines to perform comprehensive quality control testing of vaccines manufactured by LANAVET in accordance with internationally recognized standards and to assure the quality of the production processes.

c) To assist LANAVET in the reorganization of the quality control department as a primary step to meet recognized international standards of quality control for biological products.

The training programme outline and materials are presented in Annex 6. The programme included lectures on quality assurance concepts, terminology, techniques and methods utilized to establish a basic core quality assurance program for biological manufacture.

The programme also reviewed systems for the standardization of laboratory techniques and procedures to set-up the necessary data base for monitoring GMP achievements.

An internal audit programme was also established and hands-on training audits conducted as the first step for implementation. A LANAVET internal audit team was appointed, organized and trained for this purpose.

The training programme was implemented over a one month period with an average of 2.5 hours per week of classroom sessions and an additional 6-8 hours of laboratory demonstrations and experiments. The programme was attended by 15 professionals and key technical personnel. Special sessions were set-up on writing SOPs utilizing sterility and moisture testing as practical examples.

6.1 Standard Operating Procedures

Standard Operating Procedures (SOP's) are essential to the Quality Assurance process. The SOP's are the building blocks of the manufacturing process.

SOP's provide a step by step written account of a procedure, fully documented and detailed. SOP's ensure complete understanding of each activity that the operators have to implement without variations ensure the products' safety and effectiveness are not comprised in the manufacturing process. SOPs also serve as a training tool for the manufacturing operation and maintain the standards for productions, processing, monitoring and testing. (See Figure 6)

SOP's are dynamic documents, which require revisions and up-dates to ensure all changes within the procedures are accurately reflected in the SOP. Revisions to any SOP must require approval by a recognized group in the manufacturing institution. The approval process is usually the responsibility of the Quality Assurance Department.

Technical written procedures for LANAVET's manufacture of tetanus toxoid were originally developed in 1990 to transfer to LANAVET the technology and know-how by UNIDO technical consultants. However, no action has been taken to revise the original written procedures to record accurately revisions now incorporated into LANAVET's manufacturing process, as required for cGMP practices.

There are several acceptable formats and styles to produce SOPs. In general, the following elements should be included in developing SOP's:

- Written in the language used in the institution.
- Be specific and clear.
- Include:
  - description of the originator, approval and authorization
  - identification and date
  - purpose
  - scope
  - responsibilities
  - general GMP guidelines
  - detailed instructions
  - glossary of terms
  - exhibits (drawings, forms templates, etc)

A guideline for a standard SOP is presented in Annex 5.

7. REORGANIZATION OF THE QUALITY CONTROL UNIT

The quality control function in biological production is essential to ensure that products are safe, effective and conform to specifications of appearance, uniformity and stability and other characteristics specified for the product.

The quality control function is an integral part of a quality assurance system responsible to sample and test product specimens at the critical points throughout the manufacturing process. Quality control is involved in the testing of raw materials and components used in the manufacturing process.

Quality control is also responsible for the documentation and release procedures of final product, which ensures that all necessary and required test are carried out.

The quality control unit requires proper facilities, equipment, materials and accessories and skilled, qualified staff.

All the quality systems is required to be independent from the manufacturing units and should report directly to the executive offices.

The UNIDO technical consultants reviewed LANAVET's existing quality control department and determined that the existing quality control department had:

- Limited space and equipment
- Testing laboratories were not consolidated in one dedicated area
- Deficiencies in technical procedures and organizational structure

The technical consultants recommended an immediate reorganization.

With LANAVET senior management's approval, the UNIDO technical consultants developed a remedial plan to up-grade the facilities to minimum acceptable standards.

The remedial plan's recommendations included:

- Identification of and relocation to a suitable location
- Design of a suitable facility within the budgetary constrains of LANAVET.
- Conditioning of new location
- Furnishing with suitable equipment
- Initiate a plan for test standardization
- Training of the personnel in quality assurance and laboratory techniques.

After an assessment of the available physical space at LANAVET facilities, the area occupied by the maintenance department was identified and selected. This area was close to the existing quality control offices and allowed for easy expansion of the quality control facilities.

A laboratory lay-out was developed and discussed with LANAVET's senior technical and administrative personnel.

The new design of the quality control department incorporates suitable testing areas in accordance with cGMP guidelines. The new Quality Control unit's facilities include laboratory environment for:

- Bacterial testing
- Viral testing
- Chemical testing
- Moisture testing
- Sterility testing

Office space for the department head and a general area for the laboratory personnel is also included. The new lay-out of the quality control department is presented in Annex E.

An assessment of LANAVET's equipment, materials and accessories was conducted to meet the requirements for the new facility. Equipment was moved into position, installed and commissioned.

The physical facilities for the new quality control department were established and conditioned in 19 weeks.

During the same period as the relocation and restructuring of the Quality Control unit, the Quality Assurance training programme was conducted. Activities, such as the review and standardization of the testing procedures and the development of the SOP's for testing, were addressed at the training sessions with three laboratory tests (sterility, RP potency and moisture content) used as examples.

Sampling methods were reviewed and recommendations were given for final product container test, to ensure compliance with PANVAC recommendations. Other aspects such as personnel, equipment use, laboratory safety and technical procedures were reviewed with the technical laboratory personnel.

A programme was set-up for the review and standardization of the testing procedures and the development of the proper SOP's.

The animal testing facilities were not included in the reorganization, as the current space allocated and working environment of the animal facilities are sufficient for their purpose.

8. RECOMMENDATIONS

8.1 LANAVET Focus

LANAVET, in short term, will likely be required to adopt a new mission: To become a commercially viable, self sustaining institution which manufactures, markets, sells and distributes vaccine and other complementary products.

To rationalize its overhead and build on its strengths, it is recommended that LANAVET focus its attention on three core business areas:

- Tetanus toxoid production
- Rinderpest and CBPP production
- Training services in disease management (prevention, diagnostics and control of infectious diseases in domestic animals).

LANAVET's commercial viability will depend on its ability to achieve significant increases in export generated revenues. In order to be able to support expansion of its exports sales, LANAVET should concentrate its efforts to obtain:

- WHO certification as a tetanus toxoid producer and supplier.

- PANVAC certification recognizing LANAVET as a reference centre for rinderpest and CBPP.

- Cameroon government's mandate for LANAVET to implement national control laboratory for biological products.

- Technical leadership in rinderpest and CBPP in the following areas:

    - Epizootiological studies
    - Diagnostics and reference centre
    - Vaccine and diagnostics research and development
    - Training in disease management (prevention, diagnostic and control)

8.2 LANAVET Organizational Structure

LANAVET should re-structure its organization to fit a new mission to become a high quality, self sustainable, commercially viable institution dedicated to the manufacture, sale and distribution of vaccines and other complementary products.

The re-structuring should focus on separating those services provided at cost or no commercial gain and revenue generating activities such as vaccine manufacturing, sales and distribution. The simplified new organizational structure could be highly effective with fewer levels of hierarchy and less bureaucracy, encouraging effective

communication between senior administration and operative technical personnel.

8.3 General Facilities:

- Repair or replace all sections of the leaking roofs above tetanus production, virology, bacteriology and quality control.
- Construct and install fencing in the main cold storage room to physically separate different products as well as provide separation of final product inventory.
- Perform inventories of all equipment at LANAVET indicating serial number, age and point of use.
- Establish maintenance log books and/or records for all equipment and/or facilities maintenance activities.

8.4 Central Services (washing, sterilization and media preparation)

- Initiate mandatory record keeping of sterilization activities for equipment and materials, for both steam and dry heat sterilization.
- Initiate system of run number and expiry date labelling of each and every item sterilized.
- Establish Standard Operating Procedures (SOP's) for all activities in washing and sterilizing department.
- Initiate and keep records of maintenance of equipment in-use.
- Clean-up and remove daily unnecessary materials from all the working areas.
- Initiate validation program and keep records(log books) of all equipment used.

8.5 Human Resources Development

- Establish in-house training programmes for technical and support personnel. Programmes should deal with GMP, GLP and preparation of SOP's.
- Establish seminar activities on a monthly basis for senior scientific staff.
- Establish management training workshops for senior and key technical personnel with emphasis on planning, organizing, scheduling, control and logistics.

- Encourage attendance of senior technical personnel to conferences and up-date technical and management courses.

- Encourage and facilitate training abroad for senior professional and key technical personnel in the areas of tetanus manufacturing and quality control testing.

8.6 Quality Control

LANAVET should consider the establishment of the following testing sections:

- CHEMICAL TESTING SECTION :
  Incoming, raw materials analysis
  Production components analysis and testing
  In-process testing
  Final container testing

- BACTERIOLOGY :
  Sterility testing
    - in-process
    - bulk product
    - final product
  Environmental Monitoring
  Bacterial Vaccines potency testing

- VIROLOGY :
  Potency testing
    - virus harvests
    - final bulk
    - final container
  Identity testing / serum neutralization

- STABILITY STUDIES :
  Thermo stability
  Accelerated stability

- ANIMAL TESTING:
  General safety
  Immunogenicity
  Efficacy study

LANAVET Quality Control Department should:

- Develop and establish Standard Operating Procedures for all tests performed in the quality control department.

- Develop and establish standards and references.

- Introduce additional tests to ensure international compliance for veterinary products

- Implement stability programme for all vaccines produced at LANAVET.

- Implement mandatory receipt of manufacturer certificate of analysis for each batch of raw materials.

- Implement mandatory testing and release of all incoming raw materials upon receipt.

- Set up and enforce procedures for the staff and visitors of QC and the production units.

- Establish mandatory recording on regular basis of all temperature controlled equipment.

- Establish statistical analysis. Report mean and standard deviation for all in-house standards and references used for testing.

In order to provide immediate technical support to the newly reorganized quality control department, LANAVET should consider the cross-appointment of professional personnel currently available in the department of veterinary services (diagnostic and research). These cross-appointments would strengthen the technical capabilities by establishing in-house training programs for the existing senior and support personnel involved in the quality control activities. A well structured incentive programme for the personnel, which includes both financial and non-financial rewards, will also be necessary to ensure that personal goals correspond to the corporate goals of the institution.

8.7 Process Improvement

8.7.1 Tetanus toxoid production

- Remove all cleaning materials and accessories from production and processing areas.

- Prepare special cleaning accessories including sterile towels for cleaning and disinfecting of the working environments.

- Establish practical and effective cleaning and disinfection procedures for the manufacturing areas.

- Establish an environmental monitoring system.

- Re-organize working environment for concentration of toxoid in formulation room.

- Design and prepare necessary accessories to eliminate open processing procedures for pooling and collecting toxoid concentrate and effluent. Implement tank pooling system.

- Design and prepare a procedure for cleaning, washing and maintaining ultrafilter.

- Eliminate all wood surfaces and wood accessories from the production and processing working environments.

- Establish SOP's for ultrafiltration.

- Re-design production unit uniforms to include coveralls, shoe covers, large caps capable of covering all hair and beard.

8.7.2 Rinderpest vaccine production :

- Establish a new effective gowning procedures.

- Establish and enforce a 24 hour quarantine rule for entrance and working in different production environments.

- Establish Standard Operating Procedures for validation of all steps of the rinderpest vaccine manufacturing process.

- Repair and re-paint all wall surfaces with the Epoxy or oil based paint.

- Cover or eliminate all exposed wood surfaces in production working environments.

- Design and implement closed system procedures for all steps of manufacture, particularly for virus harvest, final bulk preparation and filling stages.

- Replace or repair all temperature recording devices of all refrigerators, freezers and incubators.

- Establish and enforce validation programme for all critical equipment.

- Establish environmental monitoring program with proper record keeping.

- Produce sufficient stocks (10-20 years) of the VERO cells at the master and working seed levels.

- Complete experimental work on the virus yield maximization.

- Continue and complete work on the development of the production procedures with use of roller bottles.

- Implement harvesting by freezing and towing as a replacement to the use of the glass bead system.

- Place filled containers immediately after filling into the freeze dryer. The shelves must be pre-cooled to -35C to -40 C.

- Re-design the freeze drying trays to allow direct contact of the vials with the freeze drying shelve.

- Design experimental work for the reduction of the freeze drying cycle from 72 to 48 hour or less.

8.7.3 CBPP vaccine production

- Establish, validate and implement Standard Operating Procedures for all steps of the CBPP and any other bacterial vaccine manufacturing.

- Modify and enforce gowning procedures.

- Establish and enforce the 24 hour quarantine rule.

- Remove all unused equipment from the fermenter or any other rooms within the bacterial production unit.

- Repair all wall surfaces and repaint wit epoxy or oil based paint.

- Eliminate or paint all exposed wood surfaces.

- Design and implement a close system procedure for all necessary steps of the production, final bulk preparation and filling operations.

- Implement routine temperature recording of all incubators, refrigerators and freezers on continuous basis.

- Establish and enforce validation programmes for all critical equipment.

- Establish Environmental monitoring programme on continuous basis.

- Establish in-house training programme for technical and support staff of the Bacterial vaccines with emphasis on GMP including preparation of SOP's.

8.8 Enhancement of Production and Commercialization

8.8.1 Tetanus toxoid

- Secure national market by formalizing government procurement of

LANAVET's tetanus toxoid production on a regular scheduled basis.

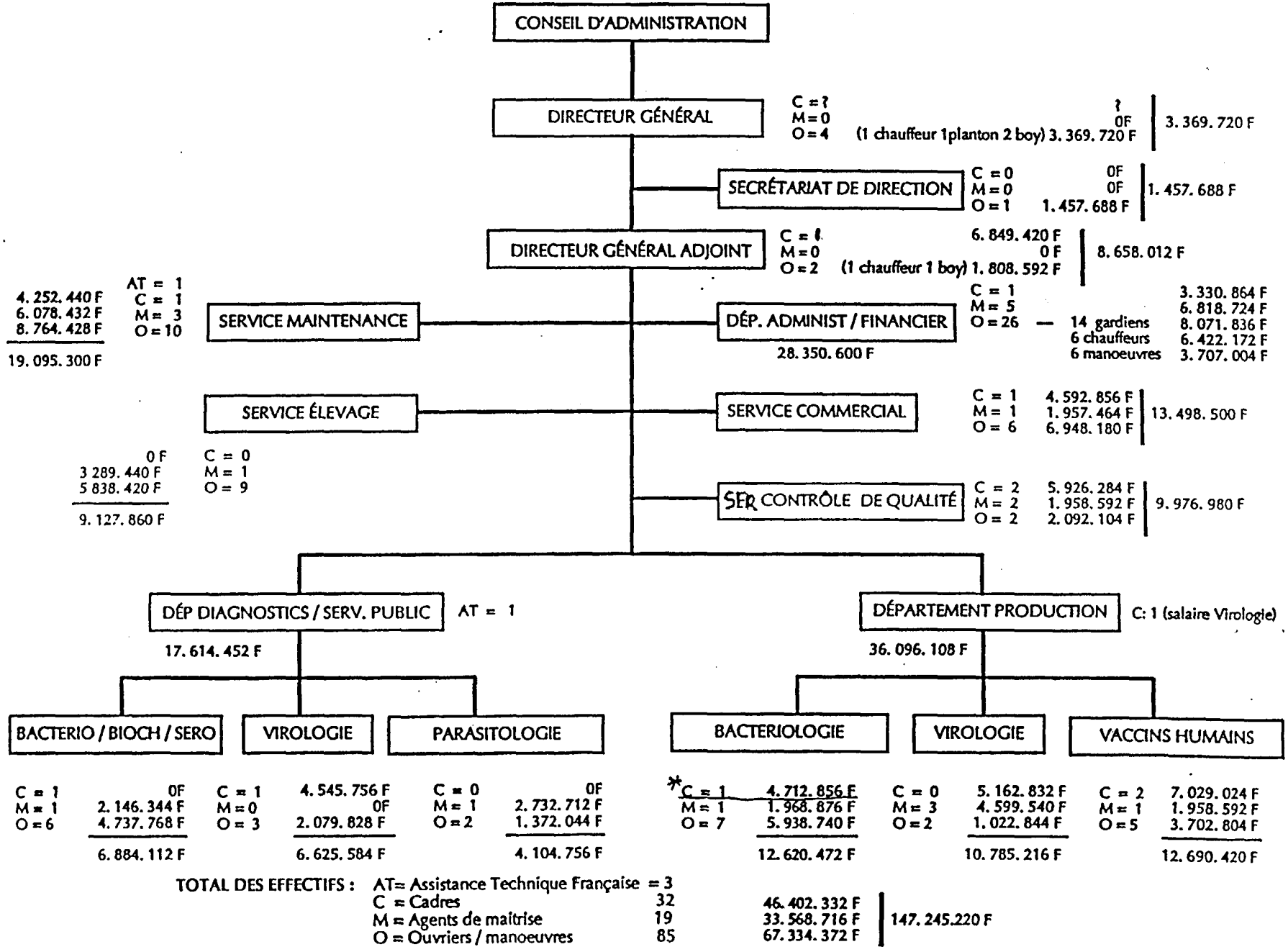
- Rationalize annual production activities by consolidating production time.
- Reduce in-process losses by incorporation of technical recommendations.
- Change product presentation to better suit end users' requirements, in particularly change product presentation from current 20 dose vials to single and five dose ampoules as soon as possible.
- Implement continuous stability and efficacy studies.
- Put in place programme to gain WHO certification.

8.8.2 Rinderpest and CBPP

- Consolidate current market base.
- Initiate market expansion programme, domestic and exports.
- Develop annual sales forecasting tools.
- Introduce technical recommendations to reduce work in-process losses.
- Rationalize annual production activities by consolidating production time.
- Optimize production output.
- Implement continuous stability and efficacy studies.
- Put in place programme to gain PANVAC certification.

LIST OF FIGURES

ORGANIGRAMME DU LANAVET ET CHARGES SALARIALES DU 01/07/93 AU 30/06/94

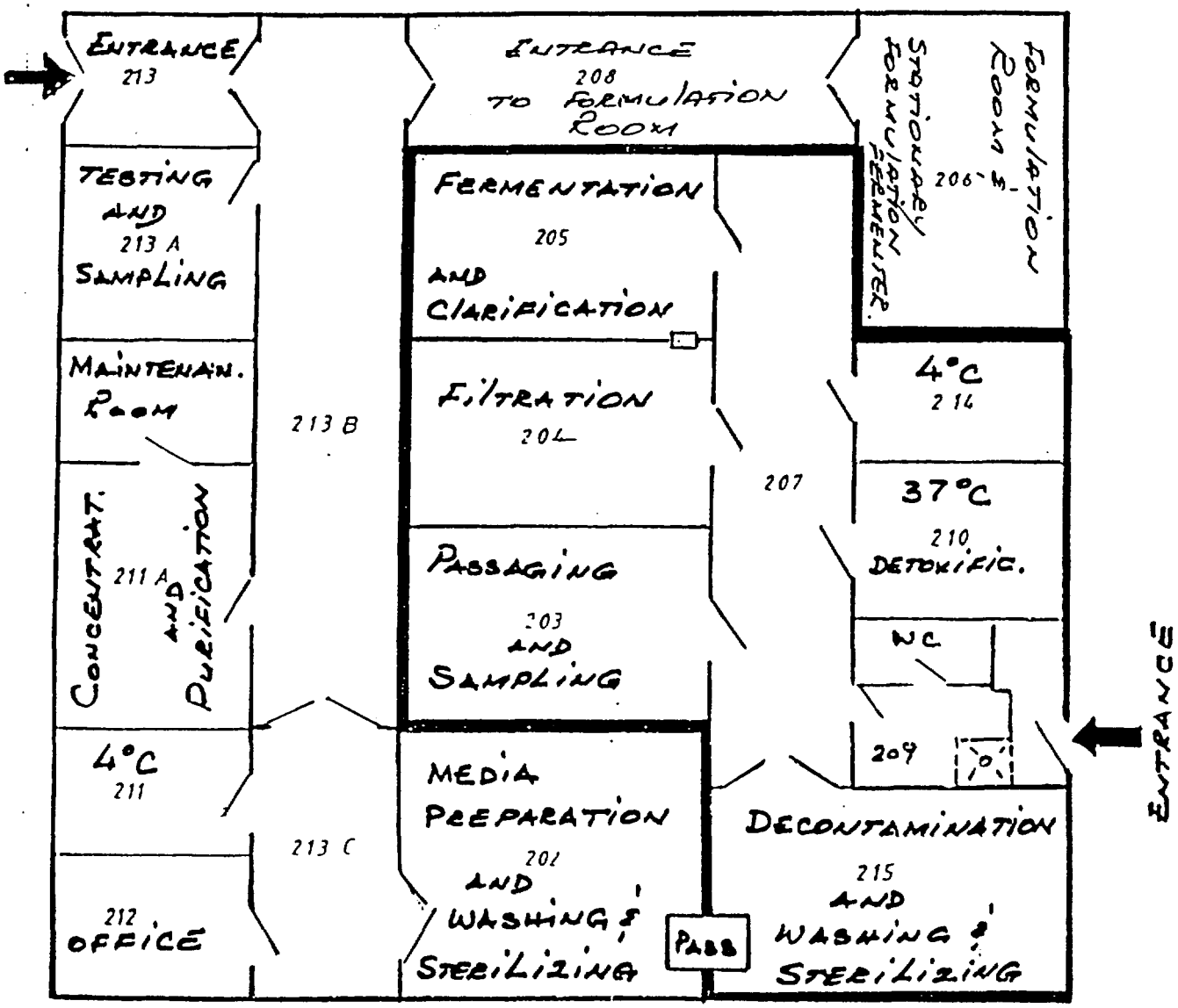


LANAVET Organizational Structure

Figure 1

Figure 2

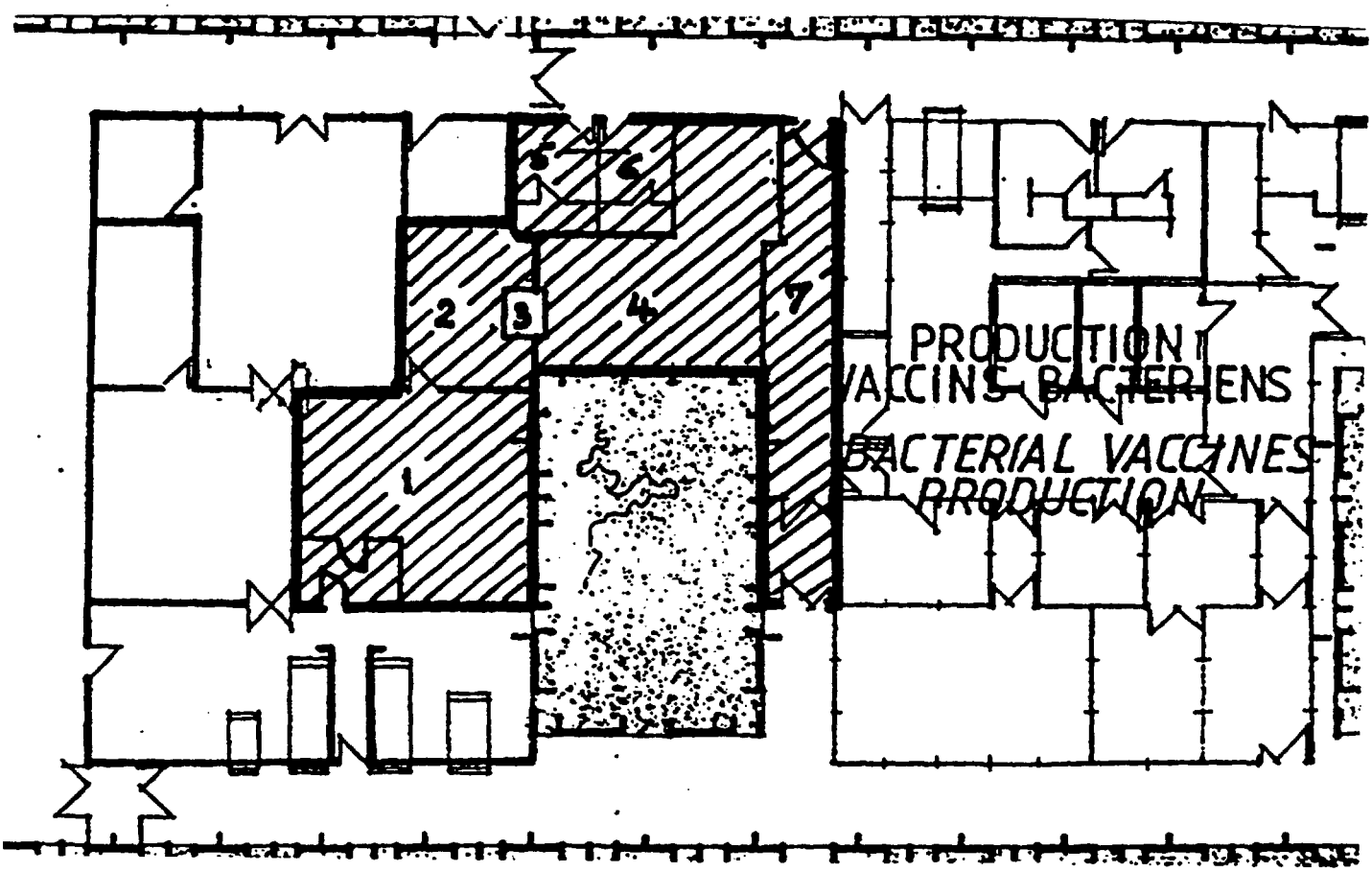
Tetanus Toxoid Production Facility Lay-out



Rooms No. 203, 204, 205, 206 and 207 are equipped with steril air.

Figure 3

Tetanus Toxoid Production Process



LEGEND

1 Equipment set-up
2 Vial washing room
3 Sterilizing oven
4 Filling room
5 Entrance for personnel
6 Material pass-through
7 Examining room

FLOW CHART OF TETANUS TOXOID PRODUCTION

Figure 4

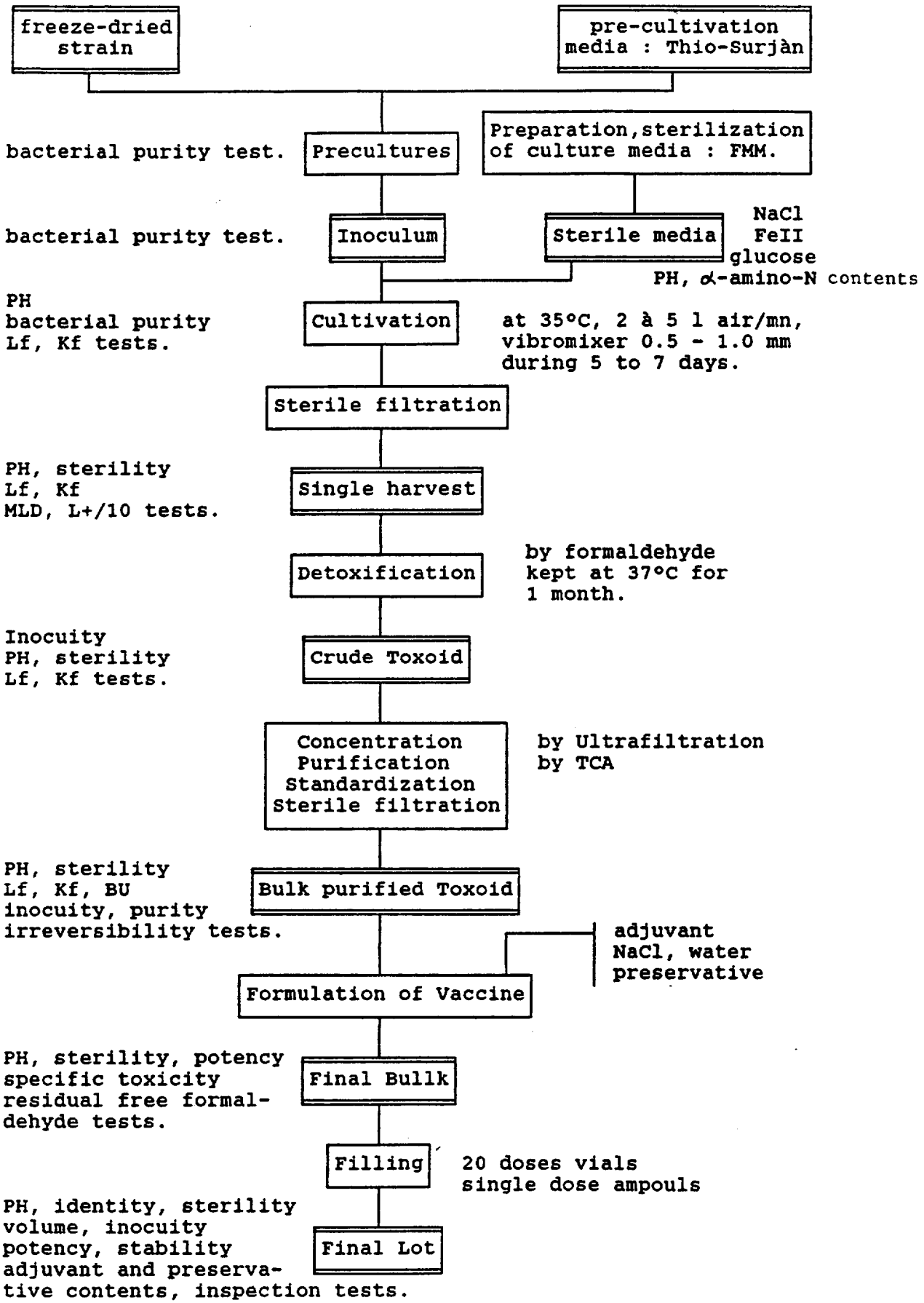


Figure 5

Chart of Complete freeze-Drying Cycle
(Edward High Vacuum Crawley)

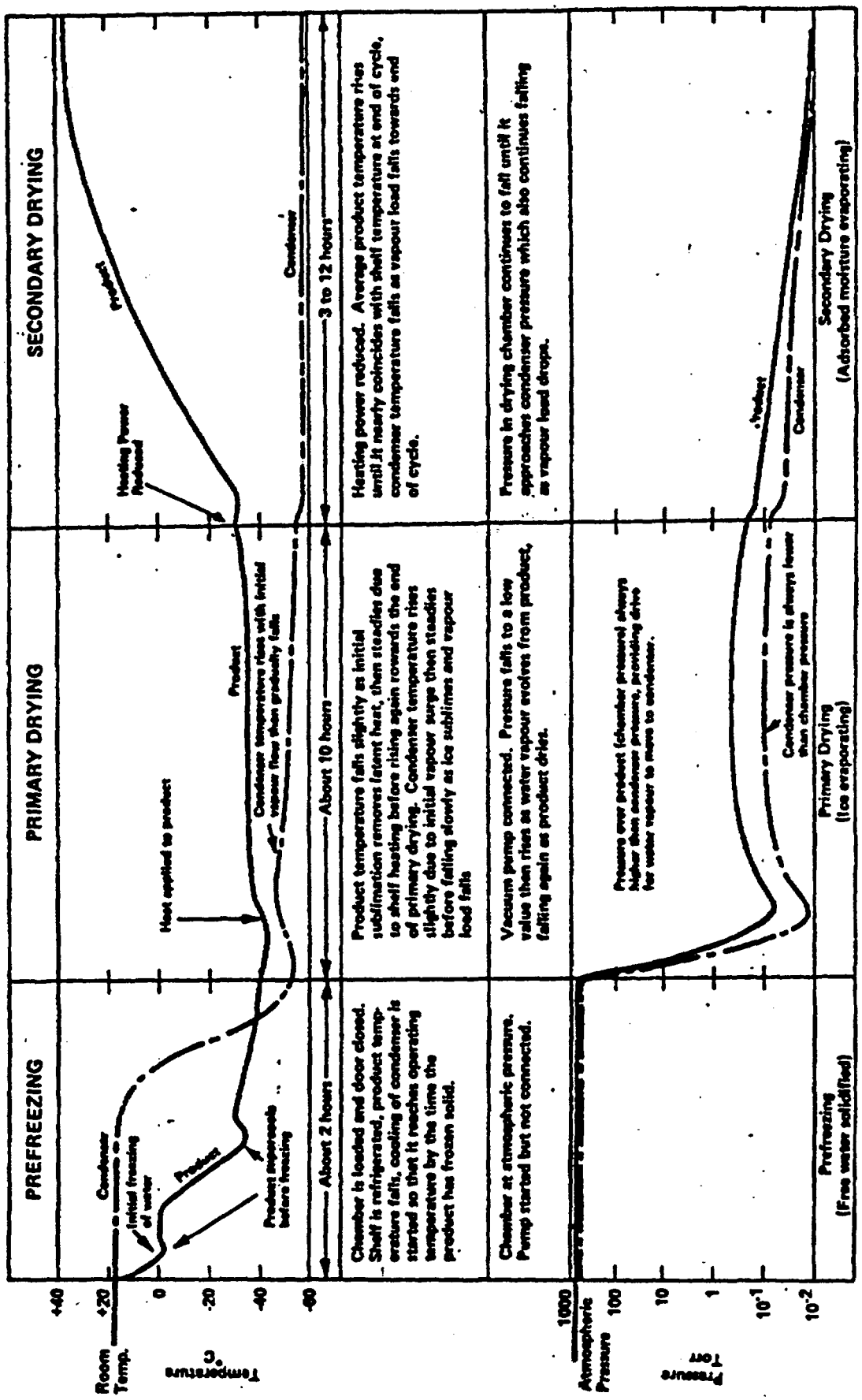
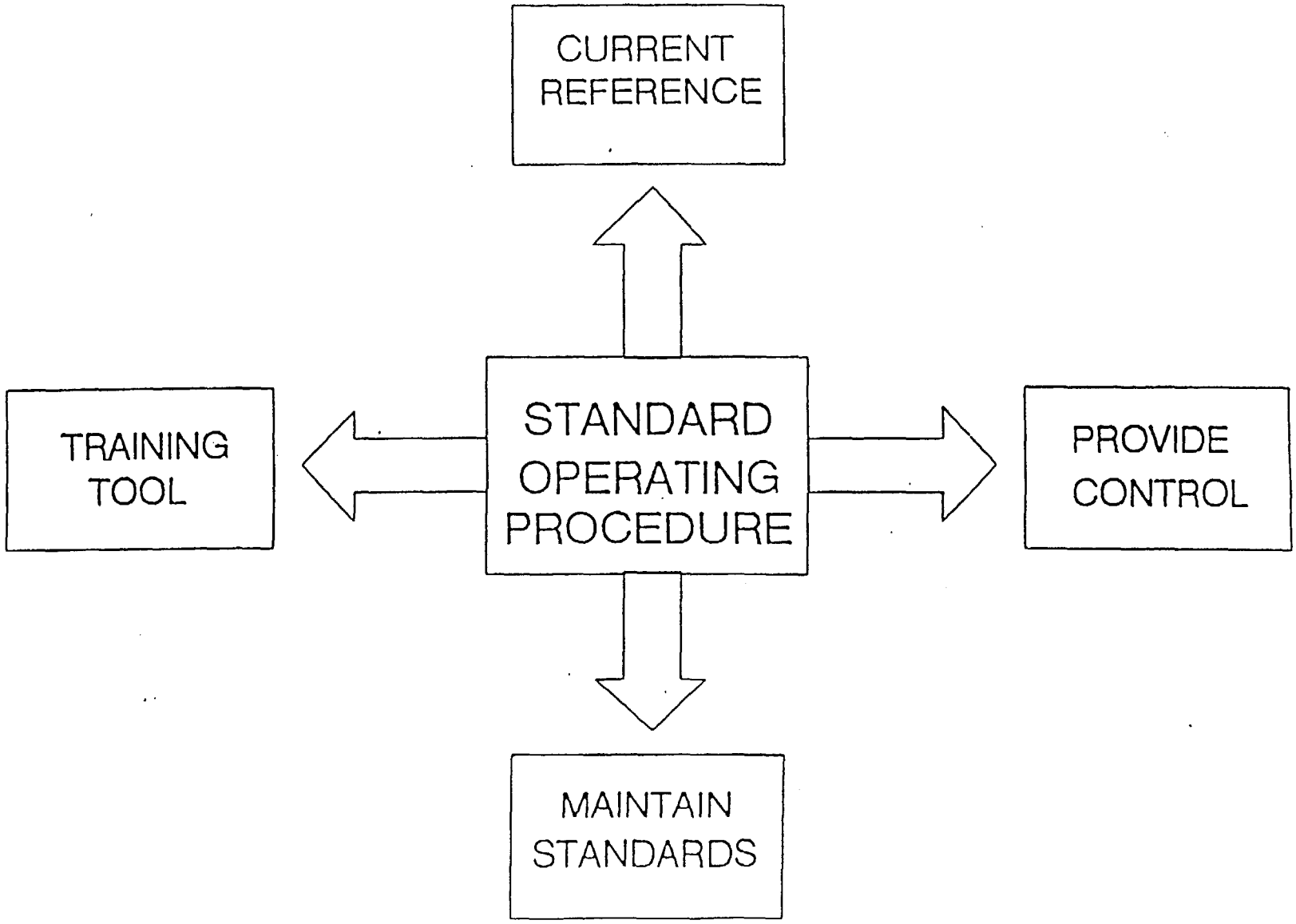


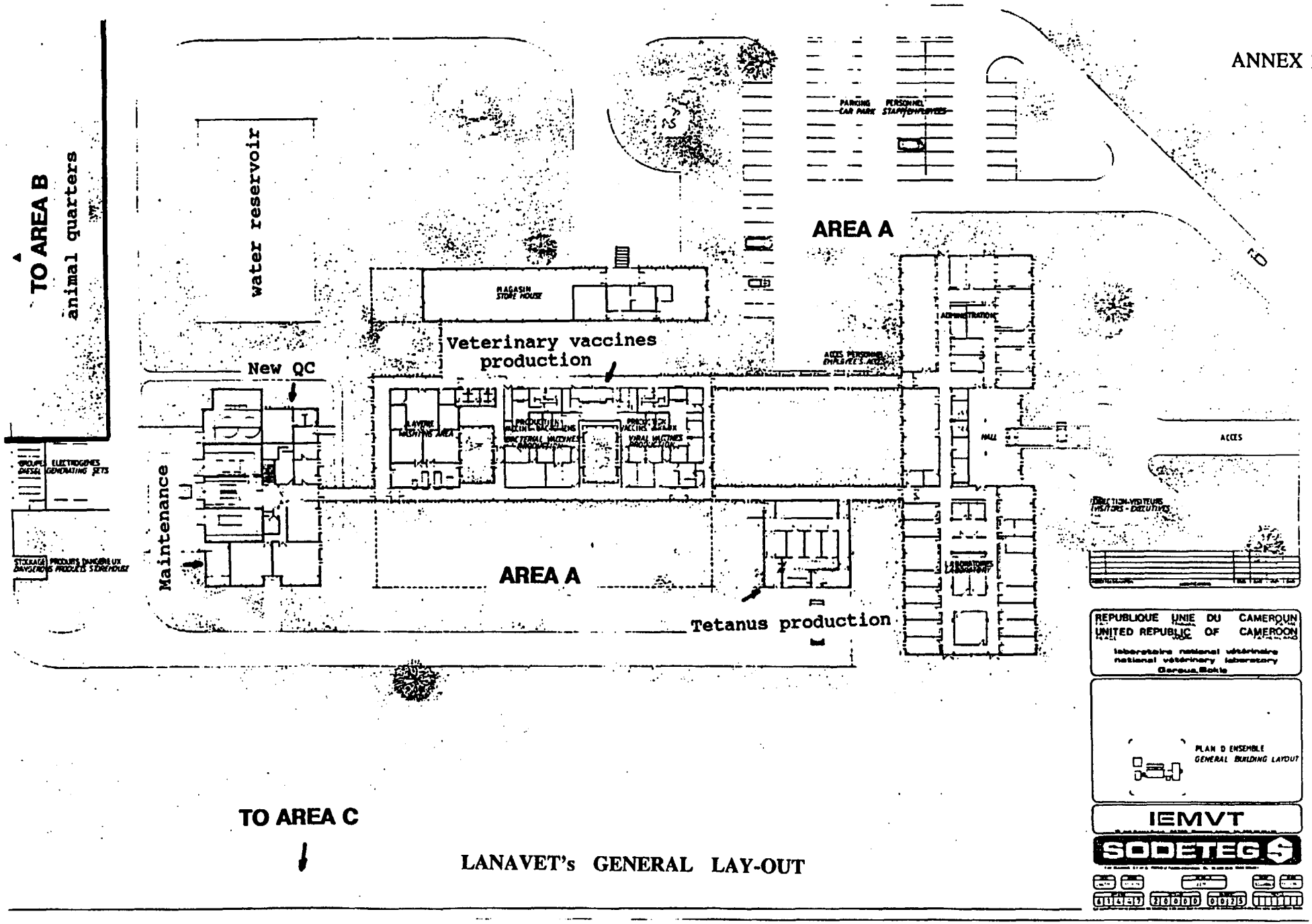
Figure 6

Standard Operating Procedures



LIST OF ANNEXES

ANNEX 1



LANAVET's GENERAL LAY-OUT

ANNEX 2

NATIONAL LABORATORY - BOKLE
GAROUA - CAMEROON

TETANUS TOXOID VACCINE ADSORBED

DESCRIPTION

Tetanus toxoid adsorbed is prepared by detoxification of the sterile filtrate of broth cultures of Clostridium tetani with formalin and heat. The toxoid is purified by chemical methods and is adsorbed on to aluminium phosphate or aluminium hydroxide as adjuvant, corresponding to not more than 1.25 mg aluminium per single human dose. 0.01% Methiolate is added as preservative. The vaccine has the appearance of a fine grayishwhite suspension and does not contain any horse serum protein. Therefore it does not induce sensitization to sera of equine origin.

POTENCY

The vaccine meets the requirements of WHO and EP when tested by the methods outlined in WHO, TRS (1979), 638, (1981), 658, (1982), 673, (1984), (1985), 700, (1985), 725 and in the European Pharmacopoeia. Each single dose contains 10 Lf Tetanus toxoid with not less than 40. I.U.

INDICATIONS

The vaccine is used for the prevention of tetanus in children and adults, especially those liable to be exposed to tetanus infection, particularly women of childbearing age and persons engaged in outdoor activities e.g. gardeners, farm workers and athletes.

APPLICATION AND DOSAGE

Vaccination is carried out with 2 doses of 0.5 ml each at 4-6 week intervals. To ensure long-lasting immunity a further 0.5 ml booster does is recommended 6 months to one year later. To maintain a high level of immunity further 0.5 ml booster doses are recommended every 5-10 years.

METHOD OF INOCULATION
BEFORE USE THE VACCINE SHOULD BE WELL SHAKEN

Only sterile syringes and needles should be used. The vaccine should be given intramuscularly into the gluteal muscle or the M. Deltoideus, according to the choice of the physician. Children younger than 2 years should be inoculated into the M.quadriceps femoris, between the upper and middle third, on the lateral side. Care should be taken not to inject into a blood vessel or the skin. Open vials should not be preserved for later use.

VACCINATION OF INJURED PERSONS

For those subjects who have proof of either completing their course of primary immunization containing tetanus toxoid or receiving a booster shot within the previous 5 years, no additional dose of tetanus toxoid is recommended. If more than 5 years have elapsed, and infection with tetanus because of injury of other cause is suspected, 0.5 ml of the adsorbed tetanus toxoid should be given immediately. Where the immunization

history is inadequate, 1500 IU (3000 old AU) tetanus antiserum and 0.5 ml toxoid should be injected, with separate syringes, to different body sites. [If available, 250 units of tetanus immune globulin (human origin) can be substituted for the tetanus antiserum]. A second 0.5 ml dose os toxoid is recommended after 2 weeks and a third dose after a further 1 month. (A note of caution: if horse origin tetanus antiserum is used in prophylaxis, the patient should be tested for sensitivity to horse serum protein prior to its administration. It is desirable to have 1 ml of Epinephrine Hydrochloride Solution (1:1000) immediately available and the normal precautions followed when injecting antitoxins).

REACTIONS

Reactions are generally mild and confined to the site of injection. Some inflammation may occur together with transient fever, malaise and irritability. Occasionally, a module may develop at the site of injection but this is rare. Infiltration can be polluted by putting on a cold compress.

CONTRADICTIONS AND WARNINGS

Individuals receiving corticosteroids, other immunosuppressive drugs or undergoing radio-therapy may not develop an optimal immune response. The vaccine should not be given in febrile states, acute infectious diseases, leukemia, severe anaemia and other severe diseases of the blood system, severe impairment of the renal function, decompensated heart diseases, or known allergies to vaccine components. Occasionally, an increased severity of reactions to vaccination is noted in subjects who have had many booster immunizations.

STORAGE OF THE VACCINE

The vaccine should be stored in a dry, dark place at a temperature between 2°C and 8°C. Transportation should also be at 2° - 8°C. DO NOT FREEZE. Once a vial has been opened, its contents should be used the same day.

SHELF LIFE

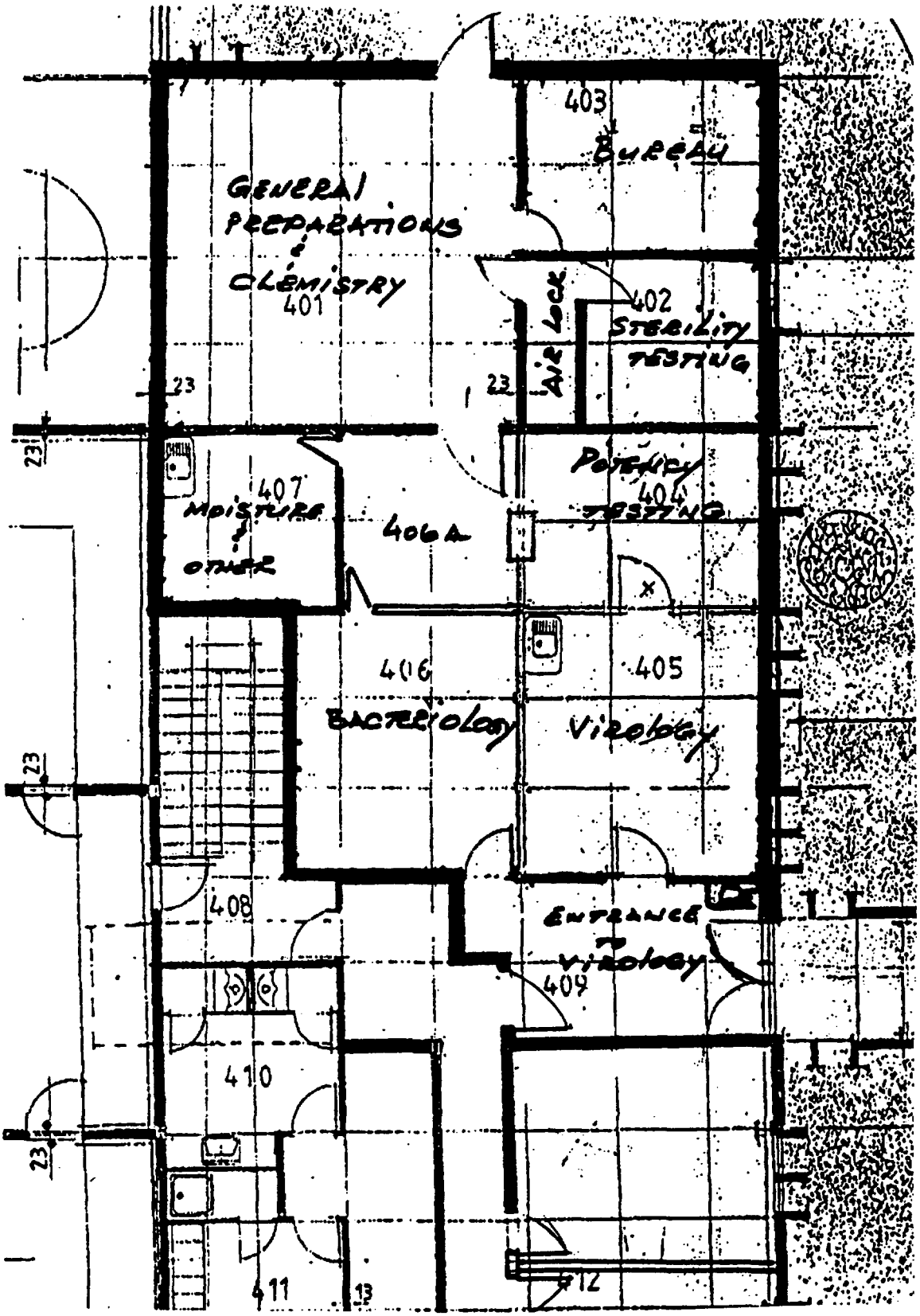
Thirty six months from the date of manufacture.

PRESENTATION

1 dose Ampoule of 0.5 ml
10 dose Vial of 0.5 ml
20 dose Vial of 10 ml
Manufactured by:
NATIONAL LABORATORY - BOKLE
GAROUA - CAMEROON

ANNEX 3

NEW QUALITY CONTROL UNIT LAY-OUT



ANNEX 4

STANDARD OPERATING PROCEDURES FOR N.Z. CASE PREPARATION

20% N.Z. CASE SOLUTION

1. INTRODUCTION

This SOP describes the procedure for the preparation of 20% N.Z. case solution for the preparation of tetanus culture media, for the production of tetanus toxin.

2. PERSONNEL

The procedure is performed by 2 qualified technicians.

Proper laboratory garments including safety glasses and gloves should be worn when handling and mixing components.

3. EQUIPMENT

3.1 Suitable stainless steal (SS) container vessel for the N.Z.case solution.

3.2 Final SS tank to receive final solution

3.3 Flasks, graduate cylinders and stirring roads.

3.4 SS container for charcoal treatment.

4. CHEMICALS AND REAGENTS

4.1	N.Z. case	210g/Litre
4.2	Potassium Phosphate Dibasic	7.5g/Litre
4.3	Calcium chloride Dihydrate	4.97g/Litre
4.4	Pyrogen-free distilled water	

5. PROCEDURES

5.1 Weigh the required amount of chemicals according to be volume to be prepared.

5.2 Measure the require amount of distilled water for the N.Z. case solution (5% more of the necessary amount is recommended).

5.3 Transfer the amount of N.Z. case to the container with distilled water.

5.4 Heat the water containing the N.Z. case to a boil and the N.Z. case is completely dissolved.

5.5 Dissolve the potassium phosphate dibasic in a flask and dissolve by adding distilled water (approximately 2ml of water per gram), and heat to dissolve.

5.6 Dissolve the calcium chloride in a flask and dissolved with distilled water (approximately 2 ml of water per gram) and mix to dissolve.

5.7 Transfer the potassium solution into the container with N.Z. case.

5.8 Transfer the calcium solution into the container with N.Z. case.

5.9 Mix all the components and adjust the required volume with distilled water.

5.10 Adjust the pH of the N.Z. case solution with 10 N NaOH to pH 9.5 ± 0.2.

5.11 Label the container with the description, lot number, and date.

5.12 Store the solution in a refrigerator at 2-8° C for a minimum of 24 hours and no more than 2 weeks, prior to use.

5.13 Prior to use filter the N.Z. case solution through a Ford-Carlson filter.

20% N.Z. CASE SOLUTION CHARCOAL TREATED

1. INTRODUCTION

This SOP describes the procedure for the preparation of charcoal treated 20% N.Z. case solution for the preparation of tetanus culture media, for the production of tetanus toxin.

2. PERSONNEL

The procedure is performed by 2 qualified technicians.

Proper laboratory garments including safety glasses and gloves should be worn when handling and mixing components.

3. EQUIPMENT

3.1 Suitable stainless steal (SS)container to dissolve the N.Z.case.

3.2 Final SS tank to receive final solution

3.3 flasks, graduate cylinders and stirring roads.

3.4 SS container for charcoal treatment.

4. CHEMICALS AND REAGENTS

4.1	N.Z. case	210g/Litre
4.2	Potassium Phosphate Dibasic	6.5g/Litre
4.3	Calcium chloride Dihydrate	4.97g/Litre
4.4	Darco G60 charcoal	50g/Kg of N.Z. case
4.4	Pyrogen-free distilled water	

5. PROCEDURES

5.1 Weigh the required amount of chemicals according to be volume to be prepared.

5.2 Measure the required amount of distilled water for the N.Z. case solution (5% more of the necessary amount is recommended).

5.3 Transfer the amount of N.Z. case to the container with distilled water.

5.4 Heat the water containing the N.Z. case to a boil and the N.Z. case is

completely dissolved.

5.5 Transfer the dissolved N.Z.case solution to a charcoal treatment container.

5.6 Add charcoal to the treatment container and mix for suspension.

5.7 Allow the suspension to stand for one hour.

5.8 Insert syphon into charcoal suspension and draw supernatant.

5.9 Filter suspension through a buchner funnel to remove charcoal, (see Figure 1).

5.10 Transfer filtered N.Z case to formulation vessel.

5.11 Dissolve the potassium phosphate dibasic in a flask and dissolved by adding distillate water (approximately 2ml of water per gram), and heat to dissolve.

5.12 Dissolve the calcium chloride in a flask and dissolved with distilled water (approximately 2 ml of water per gram) and mix to dissolve.

5.13 Transfer the potassium solution into the container with N.Z. case.

5.14 transfer the calcium solution into the container with N.Z. case.

5.15 Mix all the components and adjust the required volume with distilled water.

5.16 Adjust the pH of the N.Z. case solution with 10 N NaOH to pH 9.5 ± 0.2

5.17 Label the container with the description, lot number, and date.

5.18 Store the solution in a refrigerator at 2-8° C for a minimum of 24 hours and no more than 2 weeks, prior to be use.

5.19 Prior to use filter the N.Z. case solution through a Ford-Carlson filter.

SUGGESTED SOURCES OF KEY N.Z CASEIN FOR THE PRODUCTION OF TETANUS TOXOID

The list shown below represent some manufactures of caseine commonly used in the manufacture of tetanus toxoid.

a) **SHEFFIELD CHEMICAL**
2400 Mprris Avenue, Union,
New Jersey, 07003
USA.
Refer to: N-Z case TT.

b) **BIOMEDICAL RESOURCES**
21 North York Road,
P.O.Box 490
Hatboro, Pennsylvania, 19040
Phone: 215-672 7587
Fax: 215-672 7149
Contact: Mr. Scot Merves

Refer to: Tryptic Digest of casein for TT.
product # TD 0661,
Example Lot: BM68276

Product profile:

Total Nitrogen	13.68%
Amino Nitrogen	4.20%
Loss on drying	4.70%
Ash	5.00%
PH	7.0

c) **OXOID LTD.**
Wade Road,
Baingstoke, Hants
RG24 OPW
England
Refer to: Casein Hydrolysate (Acid)
Product code L41

Product profile:

Total Nitrogen	7.60%
Amino Nitrogen	4.90%
Sodium chloride	28.30%
Tryptophan	< 0.1%
PH (1% Sol)	7.0

d) **BIONOPSYS INC.**
Montreal, Quebec
H2H 1W9, Canada
Contact: Ms. Brigitte Lebreton
Phone: 514 525 8139
Fax: 514 524 8191
Refer to: Acid Hydrolysate of Casein

Product profile:

Total Nitroge	7.50%
Amino Nitrogen	5.40%
Amino Nitrogen/ total nitrogen ratio	0.72
Total carbohydrates	0.10%
Cholrides(NaCl)	40.00%
Calcium	0.20%
Iron	0.002%
Loss on drying	2.30%

e) **DIFCO LABORATORIES**
Detroit, Michigan, 48232,
USA
Refer to: Casein Digest Bacto
0116-17-0

F) **BENGAL IMMUNITY CO.**
Calcutta, India
Refer to: Casein Digest for TT

ANNEX 5

ศูนย์บริการเทคโนโลยีเภสัชอุตสาหกรรม
PHARMACEUTICAL TECHNOLOGY SERVICE CENTRE
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กทม. 10330 โทร. 2511871-7
FACULTY OF PHARMACEUTICAL SCIENCES CHULALONGKORN UNIVERSITY BANGKOK 10330 THAILAND

SOP # 65-0007

STANDARD OPERATING PROCEDURE

FOR

RAW MATERIAL INVENTORY CONTROL

INDEX

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL INVENTORY CONTROL	Effective Date D M Y ....
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1. PURPOSE

Establish a "FIFO" inventory control system which ensures the accountibility and traceability of inventory items in compliance with the GMP Regulations and Company Policy.

2. SCOPE

This procedure is applicable for all active and inactive materials used for the production of semi-finished or finished goods.

3. RESPONSIBILITY

The Production and the Quality Assurance Managers are be responsible that this procedure is being implemented.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE RAW MATERIAL INVENTORY CONTROL	SOP # .....65-0007..... Effective Date D M Y .... Page .....2..... of .....9.....

4. GENERAL GMP GUIDELINES

DO

- Maintain raw material storage area in neat, orderly and clean condition.
- Check carefully the accuracy of the different reference documents obtained from the Receiving and Q.A. departments.
- Identity clearly the content of each container.
- Alert the supervisor and Q.A. department about any discrepancy or error observed during the material handling operations.
- Record the justification for any variance of raw material as applicable for each lot number and advise QA and Supervisor.
- Process only one raw material at the time of the same lot number in order to avoid errors during the transaction operations.

DO NOT

- Accept or store in the warehouse dirty containers.
- Erase or use white ink to correct written errors on the documents but cross out and initial the correction !!!

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
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5. FLOW CHART

Activities	Responsibility
1. SET UP a Sequential Numerical Inventory Control system.	Material Storage
↓	
2. OBTAIN the reference documents for each lot of raw material.	Material Storage
↓	
3. RECORD the reference data on the Material Receipt Record.	Material Storage
↓	
4. TRANSFER the raw materials to the allocated storage area.	Material Storage
↓	
5. DISPENSE the raw materials on a FIFO basis.	Material Storage
↓	
6. MONITOR the inventory variances for each lot of raw material.	Material Storage
↓	
7. COORDINATE the resampling procedure of each lot of raw material.	Material Storage

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

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STANDARD OPERATING PROCEDURE

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6. DETAILED INSTRUCTIONS

6.1 SET UP a Sequential Numerical Control System.

- Set up a Standard Inventory Control System which summarizes all the required reference information regarding each raw material transaction to ensure the accountibility and traceability of each lot number.
- Complete the required reference information which must be recorded on the inventory record to comply with the GMP Regulations as illustrated in EXHIBIT # 6
- P.S. set up, if necessary, a separate sequential numerical filing system for the active and non active ingredients which is based upon the Product Code Number.

6.2 OBTAIN the reference documents for each lot of material.

- Obtain a copy of the Receiving Report (EXHIBIT #1) and the Q.A. Sampling Report (EXHIBIT # 3) which includes all the necessary reference information for each lot of raw material.
- Keep all the above documents "on file" to justify the accuracy of each inventory record.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

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6.3 RECORD the required reference information.

- Record all the required reference from the Receiving report (EXHIBIT # 1) and the Sampling Report (EXHIBIT # 3) on the Receipt of Material Record (EXHIBIT # 6) for each lot number.

- Indicate clearly the sequence in which each lot has been received on the Raw Material Record to facilitate the usage of raw materials on a FIFO basis or based upon the shortest expiry date (EXHIBIT # 1).

6.4 TRANSFER the Raw Materials to the allocated storage area.

- Proceed with the storage of the raw materials in accordance with the storage location system which has been established by the Company.

- Identify clearly each container and/or pallet regarding the "Q.A. Release Status" (e.g. Quarantine/Released) prior to storage and apply the appropriate sticker. (EXHIBIT # 4 and # 5)

- Segregate the active and non active ingredients within the storage area as deemed neccessary.

- Use a sequential numerical storage system to facilitate the location and retrieval of raw materials which is based upon the Product Code Number.

- Keep on file the most updated standard location layout for all raw materials.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
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6.5 DISPENSE the raw materials on a FIFO basis.

- Indicate on the "Material Usage Record" (EXHIBIT # 7) which specific lot number is being used for dispensing as illustrated on EXHIBIT # 7 (lot # 920017)
- Dispense the raw materials on a First in/ First out (FIFO) basis in order to comply with the GMP Regulations. Except, whenever a lot with the shortest expiry date is on hand.
- Record prior to start up of the weighing operations each lot number of the raw material which has been allocated for each Manufacturing order (EXHIBIT # 8). In the event that two different lot numbers are required clearly indicate on the Formula Sheet the "exact quantity" weighed for each lot.
- Indicate clearly the balance of the gross weight for each container partially filled. (EXHIBIT # 9)
- Attach the above record to the partially filled container.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

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Date _____

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6.6 MONITOR the inventory variances for lot of raw materials.

- Calculate the inventory variance upon depletion of each lot number of raw material. (EXHIBIT # 7 : Usage of Materials Record)
- Investigate the cause of the variance and clearly indicate the justification on the "Usage of Materials Record" (EXHIBIT # 7).
- Report any inventory variances to the supervisor and the inventory control department in order to adjust the inventory and accounting records.

6.7 COORDINATE the resampling procedure of each lot of raw material.

- Set up an effective monitoring system to ensure the timely retesting of raw materials which must be completed at least 4 months prior to the expiry date (SOP # 60-0015)
- Contact the Q.A. department to initiate the resampling procedure in accordance with the existing SOP #60-0007 for Sampling of Raw Materials.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

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7. GLOSSARY OF TERMS

QUARANTINE:
Effective restriction of the availability of material for use until released by a designated authority.

LOT:
A quantity of any drug in dosage form, a raw material, or a packaging material, homogeneous within specified limits, constituting all or part of a single batch and identified by a distinctive lot number (Receiving Control Number)

RECEIVING CONTROL NUMBER (LOT NUMBER):
Any combination of letters, figures, or both, by which any material can be traced prior, during or after the production cycle (e.g. Distribution).

SCOPE:
Range of action

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

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8. EXHIBITS

Exhibit # 1	Receiving Report
Exhibit # 3	Sampling Report
Exhibit # 4	Quarantine Label
Exhibit # 5	Released Label
Exhibit # 6	Material Receipt Record
Exhibit # 7	Material Usage Record
Exhibit # 8	Master Formula Sheet
Exhibit # 9	Container Record

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

ANNEX 6

QUALITY ASSURANCE AND GOOD MANUFACTURING PRACTICES IN VACCINE PRODUCTION TRAINING PROGRAM

Prepared by:

Dr. Manuel M. Carpio

Prepared for:

The National Laboratory Veterinary Bokle
(LANAVET)

October-November, 1995
Garoua, Cameroon

OBJECTIVES

The training programme has three primary objectives:

a) To enable LANAVET technical personnel to update technical knowledge and basic skills needed To establish an effective core quality assurance programme for the manufacture of human and veterinary vaccines.

b) To enable LANAVET technical personnel responsible for the quality control of vaccines to perform comprehensive quality control testing of vaccines manufacture by LANAVET in accordance with internationaly recognized standards and to assure the quality of the production processes.

c) To assist LANAVET in the reorganization of the quality control department as a primary step to meet international standards of quality for biological products.

TRAINING PROGRAMME METHODOLOGY

1. Customized training programme directed towards LANAVET professional and technical personnel involved in the manufacture, quality control, maintenance and diagnostic services.

2. "Hands-on" training programme implemented on site at LANAVET facilities in Garoua, Cameroon.

TRAINING PROGRAMME DESIGN

The training programme is designed to familiarize the trainees with the following aspects:

- Quality Assurance
- Good Manufacturing Practices for vaccine manufacturing and testing
- International regulatory bodies and regulations
- Laboratory safety

The programme is composed of the following units:

1. The Quality Assurance Process

   1.1 Introduction
   1.2 Objectives
   1.3 Tools
   1.4 Method of Implementation

2. The Working Environment

   2.1 The facility
   2.2 The personnel
   2.3 The equipment and accessories
   2.4 The raw materials and production components
   2.5 Laboratory safety

3. The Manufacturing Process

   3.1 Processes
   3.1 Scheduling work
   3.3 Master Plan

4. The Quality and Documentation

   4.1 Test requisitions
   4.2 Records
   4.3 Forms
   4.4 Standard Operating Procedures

5. Implementing a Quality Assurance Programme

   5.1 Set-up
   5.2 Monitoring
   5.3 Evaluations

6. Introduction to ISO 9000

7. Working Groups exercises

QUALITY ASSURANCE IN QC TESTING WORKING GROUP EXERCISES

GUIDELINES :

Material provided by QC :

List of all Quality Control Tests
List of all Tests for Rinderpest Virus Production
Demonstration of the selected procedures
Provide base technical information (reference for the selected tests)

OBJECTIVE :

To develop a set of Standard Operating Procedures (SOP),for the selected tests, used for testing of the Rinderpest Virus Vaccine.

These developed SOP's are to serve as reference for the eventual development of Standard Operating Procedures for all production and testing at LANAVET.

KNOWLEDGE :

The participants will be instructed, and are expected to have:

- Knowledge of all activities necessary for the development of SOP, incorporating all of the basic guidelines of GMP.
- Knowledge of the organization of the Quality Control unit.
- Knowledge of all tests and testing activities for Rinderpest vaccine production.
- Knowledge of all guidelines for testing, including the guidelines for GMP, GLP and QA.

The facilitators will present and assist in the following:

- The SOP concept.
- The standard SOP guidelines.
- Implementation of the codification for QC testing.
- Assistance and progress monitoring of each of the three working groups.
- Draft a sample SOP and/or present the elements and guidelines for sample collection, identification and distribution of samples:

    - o preparation
    - o labelling
    - o storage
    - o flow
    - o test request form
    - o documentation
    - o test results
    - o retention
    - o disposal

When the SOP's are completed, they can be used for the following:

- Compliance with cGMP for certification
- Establishment of the capacity for each test.
- Establishment of the cost for each test.
- Establishment of overall QC capacity.
- Establishment of guidelines for the space and personnel requirements.

An internal audit team is to be appointed and trained for this purpose.

IMPLEMENTATION

The training program is to be implemented over a one month period with an average of 2.5 hours per week of classroom sessions and an additional 6-8 hours of laboratory demonstrations and experiments.

WORKING GROUPS ORGANIZATION

A. BACTERIOLOGY TESTING
Sterility test SOP.

Mme. Yaya
Mr. M. Bouba
Mr.Zourmba
Mr.Fokou
Mr.Ngangnou

B. VIROLOGY TESTING
Potency test SOP

Mr. Lamna
Mr. Lenes
Dr. Zoyem
Mle.Tamon
Dr. Guerre
Mr. Ndamkou

C. CHEMICAL TEST
Moisture test SOP

Mme. Abdoulaye
Mr. Daouda
M. Meh
Mme. M. Aboubakar
Mr. Goneth
Dr. Yaya
Mr.Haman

ISO-9000

INTERNATIONAL ORGANIZATION FOR STANDARDIZATION (ISO), Geneva, Switzerland).

Addresses the relationships between suppliers and manufacturers and customers.

Provides both general guidelines and contractual agreements used to meet quality requirements.

- **ISO-9000** — **QUALITY MANAGEMENT AND QUALITY ASSURANCE (1987)**
- **ISO-9001** — **QUALITY SYSTEMS MODEL FOR QUALITY ASSURANCE IN DESIGN DEVELOPMENT/PRODUCTION, INSTALLATION AND SERVICING**
- **ISO-9002** — **QUALITY SYSTEMS MODEL FOR QUALITY ASSURANCE IN PRODUCTION AND INSTALLATION**
- **ISO-9003** — **QUALITY SYSTEMS MODEL FOR QUALITY ASSURANCE IN FINAL INSPECTION AND TEST**
- **ISO-9004** — **QUALITY MANAGEMENT AND QUALITY SYSTEMS-GUIDELINES**

TERMINOLOGY IN ISO-9000

SUPPLIER → MANUFACTURER → CUSTOMER

Iso-context

SUB-CONTRACTOR → SUPPLIER → PURCHASER

TYPES OF EVALUATIONS

- **FIRST PARTY (SELF-AUDIT)**
- **SECOND PARTY (PURCHASER AUDITS SUPPLIER)**
- **THIRD PARTY (INDEPENDENT)**

ISO-9000 REGISTRATION PROCESS

- **APPLICATION**
- **QUALITY MANUAL**
- **PRELIMINARY EVALUATION**
- **ON-SITE AUDIT**
- **REGISTRATION**
- **SURVEILLANCE**

ELEMENTS OF ISO 9001

- Management responsibilities
  - . Quality policy
  - . Organization
  - . Management review
- Quality systems
  - . Documentation
  - . Effective implementation
- Contract review
  - . Define & documented
  - . Capability assessment
- Design control
  - . Procedure, control and verify
- Document control
  - . General
  - . Development planning
  - . Activity assignment
  - . Organizational and technical coordination
  - . Design input documentation
  - . Design output(requirements, calculations & analysis).
  - . Design verification
  - . Design changes
- Purchasing
  - . Product conformation to specified requirements
  - . Assessment of sub-contractors
  - . Purchasing data
  - . Verification of purchased product
- Purchaser supplied product
  - . Inspection of specification and storage
  - . Report to purchaser of losses, damages & unsuitable material
- Product identification & traceability all stages

- Process control
  - . Work instructions
  - . Monitoring and control
  - . Approval and qualification process
  - . Workmanship criteria
  - . Special processes
- Inspection & testing
  - . Receiving inspection and testing
  - . In-process inspection and testing
  - . Final inspection and testing
  - . Inspection and test records
- Inspection measuring & test equipment
  - . Calibrations
  - . Records and documentation
- Control of non-conforming product
  - . marked(identification)
  - . segregated
  - . Recorded
  - . Dispositioned
  - . Responsibilities and procedures
- Corrective action
  - . Determine cause
  - . Identified lasting solution
  - . Detection and prevention
- Handling storage packing & delivery
- Quality records
- Internal quality audits
- Training
- Servicing
- Statistical techniques

SCOPE OF ISO-9002

(MODEL FOR QUALITY ASSURANCE IN PRODUCTION AND INSTALLATION)

SUPPLIERS

INCOMING MATERIALS
SUPPLIER MANAGEMENT

PRODUCTS AND PROCESS DESIGN

PRODUCTION

FINAL INSPECTION AND TESTING

DISTRIBUTION

CUSTOMER SERVICE

CUSTOMER

SCOPE OF ISO-9003

(MODEL FOR QUALITY ASSURANCE IN FINAL INSPECTION AND TESTING)

SUPPLIERS

INCOMING MATERIALS
SUPPLIER MANAGEMENT

PRODUCTS AND PROCESS DESIGN

PRODUCTION

FINAL INSPECTION AND TESTING

DISTRIBUTION

CUSTOMER SERVICE

CUSTOMER

THE 20 ELEMENTS OF ISO-9001

- MANAGEMENT RESPONSIBILITY
- QUALITY SYSTEM
- CONTRACT REVIEW
- DESIGN CONTROL
- DOCUMENT CONTROL
- PURCHASING
- PURCHASER SUPPLIED PRODUCT
- PRODUCT IDENTIFICATION & TRACEABILITY
- PROCESS CONTROL
- INSPECTION & TESTING
- INSPECTION MEASURING & TEST EQUIPMENT
- INSPECTION & TEST STATUS
- CORRECTIVE ACTION
- HANDLING, STORAGE, PACKAGING & DELIVERY
- QUALITY RECORDS
- INTERNAL QUALITY AUDITS
- TRAINING
- SERVICING
- STATISTICAL TECHNIQUES

ISO-9004 QUALITY MANAGEMENT AND QUALITY SYSTEM ELEMENTS-GUIDELINES

Provides guidance for a supplier to use in developing and implementing a quality system and in determining the extent to which each quality system element is applicable. ISO 9004 examines each of the quality system elements(cross-referenced in the other ISO-9000 standards) in grater detail and can be used for internal and external auditing purposes.

ANNEX 7

DEVELOPMENT OF THE VACCINE PRODUCTION IN AFRICA
A CASE STUDY
LABORATOIRE NATIONAL VETERINAIRE DE BOKLE
(LANAVET)
Garoua, Cameroon

Prepared by:
Manuel M. Carpio

FEBRUARY 1996

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EXECUTIVE SUMMARY

The objective of this case study, funded by UNIDO, is to analyze the viability of LANAVET as a commercially sustainable institution for the manufacture of human and veterinary vaccines and as a regional centre for excellence for vaccine manufacturing technology in Africa. This initiative resulted from the "UN system-wide initiative on Africa" which focused on relaunching Africa's economic and social development by implementing effective initiatives to coordinate and rationalize efforts for more effective development programs in Africa.

The study of LANAVET operations and commercial activities was based on a review of technical, commercial and financial evaluations conducted by several experts under the auspices of UNIDO during 1995. The financial analysis included comparative evaluations using the Computer Model for Feasibility Analysis and Reporting, COMFAR III Expert.

The development and maintenance of cost-effective indigenous manufacture of veterinary vaccines at LANAVET are essential for Cameroon and neighbouring countries to establish a sustainable livestock industry. Among the incentives are: (i) availability of quality product at all times including emergencies; (ii) minimization of foreign exchange expenditures; (iii) creation and maintenance of local economic activity ; and (iv) development of a high technology industry in Cameroon and technological spin-offs for the region.

LANAVET has the required physical infrastructure, technology, know-how and the necessary human resources to manufacture and commercialize human and veterinary vaccines in Cameroon and other African countries. However, in recent years decreasing budget allocations from the government and a limited marketing and sales organization have reduced LANAVET's annual revenues, resulting in reductions of vaccine production. LANAVET is aware that the institution's long term viability will require increasing reliance on income generated directly by LANAVET's marketing and sales efforts.

In order to achieve suatainability LANAVET's overall strategy has to incorporate changes in administration, manufacturing, marketing and sales of vaccine products. These changes could be either adapted into LANAVET's existing structure or the organization could be restructured.

Based on the analysis of technical information generated by UNIDO studies on LANAVET's status and capabilities the following options could be available to LANAVET to achieve sustainability:

I The maintenance of the "Status Quo" (SQ)

II The maintenance of the "Status Quo" plus the reduction of 50 % of the current LANAVET's labour force. (SQ-50)

III The Privatization Option (PO)

IV A combination of II and III (CO)

The four principal options identified are outlined in the interest of achieving financial sustainability with the minimization of cost to LANAVET and/or the Government of Cameroon. The options considered are not intended to be examined on an "either/or basis".

On the basis of the economic analysis it appears that all options are viable for LANAVET to continue its operations in a 4-5 year horizon (1996-1999) provided that the institution meets the level of sales forecasted for the period 1996-1999. The difference among the options is the capital required to establish the initial inventory and to sustain operations and the time required for the achievement of a break-even point for LANAVET's operations.

It is evident that of the four options under consideration, option I, is the less desirable, due to the perpetuation of institutional conditions which more likely will constitute a limiting factor for sustainable development.

However, it is essential that the restructuring approach, to which LANAVET commits, must balance the viability of the change process within the organization's structure and the long-term objective of achieving financial sustainability.

To restructure LANAVET's operations effectively, as required in options II to IV, long term strategic planning will be required. It is recommended that UNIDO continue to provide technical assistance to LANAVET for the development of a strategic plan to ensure the sustainability of vaccine production in Cameroon.

LANAVET vaccine manufacturing operation has considerable potential to be economically viable and to earn substantial revenues for its economic sustainability. LANAVET could become a Centre of Excellence for vaccine production in Africa with a role to promote the concept of self-reliance in vaccine requirements in the region as an integral part of the livestock development in Africa.

NOTICE TO THE READER

UNIDO is pleased to present this report entitled "A Case Study of the National Laboratory Veterinary Bokle (LANAVET) in Garoua, Cameroon". This report provides an opportunity to explore and analyse the evolving status of LANAVET, a successful African Institution dedicated to the manufacture and commercialization of vaccines. It also examines the current demands on LANAVET's organizational structure to adapt its management practices and operations to maintain its position in the market place.

This report is not intended to be an official statement of UNIDO policy, nor does it offer the definitive word on LANAVET's future opportunities. Rather, the report is designed to stimulate debate, to suggest possible approaches to LANAVET's economic stabilization and sustainable growth.

The case study incorporates the analysis of three UNIDO technical reports which were developed in three technical missions to LANAVET; a Marketing Study of LANAVET's Vaccine Products prepared by C. Ndamkou, published in French, November 1995; an Evaluation of LANAVET's Commercial and Financial Activities published in French by P. Bouchez, December 1995; and a Technical Evaluation of LANAVET's Infrastructure and Technology to Manufacture Vaccines published in English by M. Carpio and N.Cucakovich, January, 1996. These technical reports provide the data framework of the case study and are utilized for the analysis and discussion.

The case study focuses on the capabilities and complexities of LANAVET's current situation. Some alternatives open to LANAVET are identified and described. Priorities for LANAVET's future direction are identified.

Many of the challenges being faced by LANAVET reflect the developments within the national economy and public policy changes in the Cameroon. Cameroon shares common features with several other African countries located in the Sub-Saharan region. Similarities include a high level dependence on external conditions, common social patterns of income inequities and market structure. The issues addressed in this case study are specific to LANAVET, but may provide some parallels to challenges faced by organizations in other Sub-Saharan countries.

This report is the result of UNIDO's on-going efforts to contribute to the development of vaccine production in Africa and UNIDO's strong commitment to assist this sector's growth which will be key for sustainable development of African industry.

ABBREVIATIONS

ASU	Administration support unit
C°	Degrees celsius
CBPP	Contagious bovine pleuropneumonia
CBR	Crude birth rate
CDR	Crude death rate
cGMP	Current Good Manufacturing Practices
CO	Combination Option
COMFAR	Computer Model for Feasibility Analysis and Reporting
CU	Commercialization unit
DPT	Diphtheria pertussis and tetanus
EEC	European Economic Union
EPI	Expanding program for Immunization
FAO	Food and Agriculture Organization
FMD	Foot and mouth disease
GDP	Gross domestic product
GNP	Gross national product
GREP	Global Rinderpest Eradication Program
IMR	Infant mortality rate

LANAVET	Laboratoire National Veterinaire Bokle
LC	LANAVET commercialization
LVS	LANAVET veterinary services
MU	Manufacturing unit
OAU	Organization of African Unity
OIE	International Office of Epizootics
PANVAC	Pan African Veterinary Vaccine Centre
PARC	Pan African Rinderpest Campaign
PO	Privatization Option
RAFR	FAO Regional Office for Africa
RNEA	FAO Near East Region Office
Sq Km	Square Kilometre (0.3861 square mile)
SQ	Status Quo
SQ-50	Status Quo-50
UNICEF	United Nations Children's Fund
UNIDO	United Nations Industrial Organization
U.S.$	United States dollars
VSU	Veterinary service unit

1. PROJECT BACKGROUND

The mission's objective was to prepare a case study on LANAVET, based on all available technical and marketing reports on LANAVET's vaccine manufacturing activities.

LANAVET, is recognized as an important organization in Cameroon which provides technical support to the national veterinary services and the private sector dedicated to the development of livestock.

In the last five years developing countries have been trying to transfer some of the economic activity from the public to the private sector. The government of Cameroon, also is committed to privatization expecting that these public sector transfers will activate the private sector.

UNIDO commissioned this case study to review LANAVET's current situation to demonstrate some of the elements which need to be considered for the achievement of sustainability.

2. CAMEROON COUNTRY PROFILE

2.1 Geographic profile

Cameroon, facing the Gulf of Guinea in the Atlantic Ocean, borders with Nigeria, Gabon, Equatorial Guinea, Chad, The Central African Republic and Congo.

With a land area of 467,900 square kilometres, Cameroon is richly endowed with coastal fisheries, fertile agricultural land, tropical forests and mineral resources including petroleum and natural gas.

2.2 Economic profile

From 1960, when the country achieved independence, until 1985, Cameroon's real economic growth averaged 7% a year. From the late 1970s until 1986, the country's economic growth was in large part based on royalties and investments generated from oil

production. This production decline and the 1986 reduction of international oil prices, imposed serious restraints on Cameroon's economy.

The eight year oil boom, 1979-1986, had allowed the Cameroon government to undertake significant infrastructure investments and expand public sector enterprises. By 1986, Cameroon had developed substantially its infrastructure, expanded its civil service and public enterprise sector. However, the economic crisis, 1986-1993, strained the government's ability to sustain these investments and developments.

Over the 1986-1989 period, Cameroon's real GDP fell by an average of 3.4 % annually and per capita income dropped over 35%. From 1989 to 1993, the recession continued to deepen, so that by 1993 the Cameroon economy had declined by about 30%.

Prior to the oil boom, agriculture had been Cameroon's major source of economic growth and foreign exchange. However in the 1989-1993 period, rural incomes fell by 50% and agricultural production by 25%.

In January 1994, the CFA franc was devalued 100% against the French franc. Concurrently, the government of Cameroon introduced new economic policies based on three key objectives:

- To reduce and strengthen the public and parapublic sectors
- Improve incentives framework for productive and production supporting sectors
- To increase effectiveness of poverty reduction programs.

2.3 Demographic profile

In mid-1992, the population was estimated at just over 12 million, with over 46% below the age of 15. The population growth rate is estimated between 3.5 - 4.0% per year.

Population density is approximately 24 people per square kilometre. The ratio of urban to rural population is nearly 50:50. The labour force is just over 4.5 million, and is estimated to be increasing by 3.0% annually.

More than 200 ethnic groups are present in the Cameroon population. The Fang, Bamilike, and Bamun are the major ethnic groups. Cameroon's official languages are English and French. In addition, a variety of local languages are also spoken.

2.4 Health profile

UNICEF has estimated that currently 70% of the population has access to health services. EPI estimates a vaccination coverage for 1-year old children against tuberculosis of 46%, and a 31% coverage against DPT, polio and measles. Coverage for pregnant woman tetanus is estimated at 9%.

In 1994, the crude birth rate (CBR) is estimated at 4%, with an average of 5.8 births per woman. Life expectancy is 57 years.

3. SITUATION ANALYSIS

3.1 Livestock resources and vaccines:

- Livestock resources are vital for the sustainable development of most African nations.
- Rinderpest and Contagious Bovine Pleuropneumonia (CBPP) are two of the serious infectious diseases in cattle and small ruminants in the African continent.
- International organizations, such as FAO Regional Office for Africa (RAFR), are actively engaged in livestock development programs to implement animal disease control and monitor animal health in the region.

- The establishment of revolving funds for livestock development in Africa by international organizations significantly improved the efficiency of veterinary services by facilitating purchase of vaccine and drugs and the initiation of small scale disease control projects in different African countries.

- About 90 million head of cattle are vaccinated annually in Africa under the Pan African Rinderpest Campaign (PARC).

- In some African countries, such as Egypt, successful control and monitoring of rinderpest has resulted in eradication of the disease, resulting in complete withdrawal of rinderpest vaccination activities.

- PARC's current program is to eradicate rinderpest in the next 15-20 years. Success of PARC's program will result in the elimination of current rinderpest vaccination programs by 2010-2015.

3.2 Tetanus Toxoid Vaccine

- WHO, in 1989, committed to eliminate neonatal tetanus worldwide. Since 1990, a significant reduction in neonatal tetanus has been reported.

- In Africa, reports of tetanus toxoid cases has declined by over 50% since 1990.

- The vaccination coverage for tetanus toxoid for pregnant women in Cameroon in 1994 was estimated at 9%.

- In the Expanded Program for Immunization (EPI) managed by UNICEF tetanus toxoid is delivered to children as a combination with diphtheria and pertussis vaccine as DPT.

- In 1996 the UNICEF purchase price for tetanus toxoid, 10 dose vial, ranges from U.S. $ 0.40 to $ 0.65 per vial and for 20 dose vial U.S.$ 0.49 to $ 1.04 per vial.

- Tetanus toxoid for the prevention of neonatal tetanus in pregnant women is presented in multi-dose 10 and/or 20 doses for campaigns and single dose for the private market.

- In 1996, there are 8 suppliers of tetanus toxoid for UNICEF.

3.3 LANAVET's situation

- LANAVET is an important organization in Cameroon funded by the Cameroon government and revenues generated by the sale of vaccines.

- LANAVET has the necessary physical infrastructure and human resources for the manufacture of tetanus toxoid for pregnant women, rinderpest and CBPP vaccines.

- In Cameroon, sales and distribution of rinderpest and CBPP vaccines are conducted by the Veterinary Services under the Ministry of Livestock, Fisheries and Animal Industries.

- LANAVET rinderpest and CBPP vaccines are currently exported to countries in Africa.

- Currently, the government of Cameroon is the only client for LANAVET tetanus toxoid vaccine.

- LANAVET would require WHO certification to be able to supply tetanus toxoid to international agencies.

- LANAVET receives financial and technical assistance from international organizations such as French Cooperation, UNIDO and the European Community.

- LANAVET's current financial position is not strong and the institute's ability to sustain operations is in jeopardy.

- It has been recommended to the Government of Cameroon, that LANAVET be privatized to ensure the institute's long-term sustainability.

3.4 The African environment for LANAVET's vaccines

- In African countries most of the livestock is comprised of cattle and small ruminants such as sheep and goats.

- Veterinary services have traditionally been controlled by the government in most African countries.

- Veterinary Services have not been able to provide the technical support services required for the fast growing animal industry in many African countries. This situation has prompted to most African governments to explore different plans and programs to the rehabilitate these services.

- In May 1994, during the celebrations of the 70th anniversary of the Office International des Epizooties (O.I.E)in Paris, France. Delegates of 103 countries recognized the global problem of infectious diseases as one of the most important factors that curtail the development of the animal industry. Among the most important infectious diseases are rinderpest, foot and mouth disease (FMD) and diseases associated with mycoplasma infections such as CBPP.

- In order to control these diseases in the African continent, international organizations have established regional institutions such as Pan African Rinderpest Campaign (PARC), which involves most African countries. PARC mandate is to coordinate a continental effort for the control and eradication of these infectious diseases.

- In the control and eradication of infectious diseases there are two important tools: surveillance of the disease and prevention by means of vaccination. Based in these tools, PARC aims to protect livestock against rinderpest by vaccination of 100% of the population at risk and active monitoring of the disease in the African continent.

- The objectives of PARC provide a demand for low-cost high quality, safe and effective rinderpest and CBPP vaccines. This demand opens an opportunity for LANAVET to be one of the key suppliers of vaccine.

- PARC estimates that eradication of rinderpest will be accomplished in the next 10-15 years thus eliminating the requirement for vaccine campaigns with current live attenuated vaccines by 2020.

- The overall international market for rinderpest and CBPP vaccines in Africa includes 35 countries and is estimated to be 170 million doses annually. countries.

- The market for rinderpest and CBPP can be divided into two groups: a) the international agents market, composed mainly of organizations such as Pan African Rinderpest Campaign (PARC), FAO and UNICEF; b) African private market.

4. LANAVET's CURRENT SITUATION

4.1 Background

The National Veterinary Laboratory Bokle (LANAVET) was created by government decree N° 83/479 issued by the President of the Republic of Cameroon October 8, 1983. LANAVET was established as a parapublic institution under the Ministry of Livestock, Fisheries and Animal Industry to promote veterinary services and to manufacture veterinary vaccines to support the development of the livestock industry in the country.

LANAVET is located at Bokle, 4 km south of the city of Garoua, capital of the Department of Benoue, North Province. LANAVET's property covers approximately 1200 hectares of land on which 1.2 hectares is occupied by buildings. LANAVET's infrastructure is a complex of installations which brings together activities such as biological manufacturing and quality control, diagnostic services and research, animals husbandry, workshops and staff living accommodations.

LANAVET's mandate, as described in the 1983 decree, is:

- To produce biological products such as vaccines, sera and other antigens.
- To analyze specimens of animal origin for diagnostic purposes.
- To conduct research and epizootiological surveillance.
- To train technical personnel in laboratory activities applied to animals science.

4.2 Organizational Structure

The administration of LANAVET is the responsibility of the Director General who reports to a Board of seven directors. The Board has representatives from the Ministries of Finance, Public Health, Commercial and Industrial Development, and Superior Education Informatics and Scientific Research, the Director of Veterinary Services, the Director of the Bureau of Veterinary Pharmaceuticals and one representative designated by the President of Cameroon.

The executive management team is composed of the Executive Director, appointed by the Board of Directors, and six Department Heads.

LANAVET's functions are managed in six departments or services:

- Administration and Finance
- Maintenance
- Quality control
- Veterinary services
- Production
- Commercial services

4.3 Human Resources

LANAVET currently employs a total of 109 people from which only 29 (24%) are involved in activities related to vaccine production and their quality control.

4.4 Finances

LANAVET is owned and financed by the Government of Cameroon. In addition, LANAVET'S obtains revenues generated by the sales of vaccines. Also, LANAVET receives some contributions from International Organizations such as French Cooperation Program, The European Community, UNIDO and World Bank loans.

At present LANAVET's financial position is limited. Its annual administrative cost is approximately 466 million FCFA (US $ 1 million). From the total operation cost 65% are administrative cost from which 60.2% are salaries, and 35% production cost.

In the last five years some of LANAVET's original activities and services, such as the animals colony and agricultural support activities, have been reduced or stopped due to the shortage of funds for operations.

4.5 Operations

The commercial capabilities of LANAVET could be divided into products and services.

Products refer to the current available veterinary and human vaccines.

Services refer to the provision of veterinary services such as diagnostic and research and development in animal diseases.

LANAVET's vaccine product line is composed of one human vaccine tetanus toxoid for pregnant women and nineteen veterinary vaccines of which 9 are for poultry and 10 for livestock (Table 1). The major vaccines produced by LANAVET are rinderpest and contagious bovine pleuropneumonia (CBPP). In addition, LANAVET produces small quantities of clostridium bacterin and various poultry vaccines.

LANAVET's installed capacity for freeze dried veterinary vaccines (rinderpest and/or CBPP) is 172-345 million per year. In addition, LANAVET has capacity to manufacture over 1.5 million doses annually of Pasteurella, Clostridium and Anthrax vaccines for livestock. Currently, LANAVET's manufacturing capability for veterinary vaccines is greatly under utilized.

In 1993, with the assistance of UNIDO, a Technical Cooperation Project (TCP) was implemented to manufacture tetanus toxoid for human use to prevent tetanus neonatal in pregnant women. LANAVET's capacity for production of tetanus toxoid is approximately 6-7 million doses per year. This quantity is sufficient to fulfil the current and futures requirements for tetanus toxoid for pregnant women in Cameroon for the next 5-10 years with and additional product available for neighbouring countries.

4.6 Marketing and Sales

LANAVET's main revenue generating activity to date has been the manufacture and sale of veterinary vaccines for cattle and poultry in the domestic market and exports. Primarily to other African countries such as Benin, Central African Republic, Gabon and Burkina Faso. (See Figure 1).

In the last 10 years LANAVET has produced 123.4 million of poultry vaccines. Unit sales totalled 90.9 million, 73.7% of the total output.

The total revenues generated by poultry vaccine sales were U.S. $ 27,600.

In the same 10 year period, LANAVET has produced 122.9 million doses of vaccines for livestock. Sales of livestock vaccines total 107.5 million, 87.4%, generating U.S. $ 4.25 million.

LANAVET's revenues for the sales of vaccines in the last 10 years totalled U.S. $ 4.28 million. Sales of five products based on rinderpest and CBPP combinations account for 73% of the total sales.

LANAVET's current international sales infrastructure is not sophisticated. However, their international markets for veterinary vaccines include Benin, Burkina Faso, Ivory Coast, Guinea, Burundi and Togo.

5. THE FUTURE OF LANAVET

5.1 The Opportunity

- LANAVET is an institution with tremendous challenges, limited access to new capital, ambiguous enterprise objectives and unfamiliarity with competitive markets.

- LANAVET has the necessary infrastructure to develop new improved rinderpest and CBPP vaccines.

- Successful marketing, sale and distribution of vaccines is key for the future development of LANAVET.

- LANAVET is recognized in Africa as an important supplier of veterinary vaccines specialized mainly in rinderpest and CBPP vaccine.

- LANAVET's major African competitors for veterinary vaccines are Botswana, Ethiopia and Mali. However, other countries such Kenya, Sudan, Nigeria, Somalia, Senegal, Zaire and Chad also have infrastructure for veterinary vaccine production.

- LANAVET is an important centre in the Central Africa Region for research and diagnosis of infectious diseases in domestic animal species and collaborates closely with other African centres.

- LANAVET's tetanus toxoid for human use primary market is the government of Cameroon.

- The international regional markets for tetanus toxoid are Gabon, Equatorial Guinea, Chad, The Central African Republic and Congo.

- The development of a sustainable livestock is vital for the economies of African countries. Currently, the cattle population in Africa is approximately 189 million and sheep and 374 million goats.

- In Africa, infectious diseases such as rinderpest, CBPP and foot and mouth disease (FMD) are associated with the production of serious losses in the livestock.

- In May, 1994, during the celebrations of the 70th anniversary of the International Office of Epizootics (OIE) in Paris, France, delegates of 103 countries recognized the global problem of infectious diseases as one of the most important factors that curtails the development of animal industry in most developing countries.

- The Organization of African Unity and Pan African Rinderpest Campaign (OAU/PARC), Nairobi, Kenya, is responsible for the epidemiological surveillance, control and eradication of rinderpest.

- PANVAC's primary priority is to ensure the quality of the vaccines.

- In the control and/or eradication of infectious diseases the surveillance of the disease and the prevention by means of vaccination are the most important tools.

- FAO with their Regional Office for Africa (RAFR) in Accra, Ghana, the East Region (RNEA) Cairo, Egypt, and OIE, Paris, France, also participate in livestock development programs which also include monitoring and control of diseases.

- PARC has developed objectives to protect livestock against rinderpest by vaccination of 100% of the population at risk and the active monitoring of the disease in the African continent.

- The Global Rinderpest Eradication Programme (GREP) has been established by FAO and is responsible for the coordination and technical advise to control the disease in the affected regions.

- The privatization of Veterinary Services in some African countries will expand the private market for veterinary products including vaccines.

5.2 The Alternatives

Since its establishment in 1983, LANAVET has successfully developed technical skills to produce a variety of animal vaccines; provided technical training and laboratory support services to the livestock industry; and introduced technology and production capability for tetanus toxoid vaccine for humans.

However, the national economic situation has changed significantly since LANAVET was established and the cost of funding a para-public agency is currently under review. Privatization of LANAVET is being considered.

The public and private sectors have strengths and weaknesses intrinsic to each sector's organizational structure and mission. The public sector typically is the only vehicle to deliver services which provide a public good, manage policy, monitor or enforce regulations, generate little or no profit, and require stability over long periods of time. The private sector, based on the need for profit generation, typically is the most effective vehicle to deliver services which require on-going innovation, risk taking, customer responsiveness, and promotion of self-sufficiency.

Considering LANAVET's current operations, there are a number of issues which must be considered when evaluating the potential and benefits of successful privatization.

Among the many issues to be evaluated, the following are suggested as key:

- Of LANAVET's products and/or services: Which products and/or services are best provided by private sector or public sector? Which are appropriate to transfer to the private sector? Which products and/or services are likely to be viable in a new financial environment of profit and loss responsibility? Which products and/or services currently provided by LANAVET are not likely to achieve minimum cost recovery and will decrease the private organization's overall ability to maximize efficiencies and profit and minimize costs?

- What type of private sector ownership and organizational structure would best facilitate LANAVET's continued success?

- What institutional changes will be required within LANAVET to launch the institution successfully into the private sector?

LANAVET currently manufactures a variety of vaccines, many of which are not produced on a cost recovery basis. In particular, the poultry vaccines are not efficiently produced or effectively marketed to compete successfully with available imported products.

Rinderpest and CBPP are the two notable exceptions. Both rinderpest and CBPP are key products of LANAVET and have in the past generated the majority of LANAVET's revenues. As well, both LANAVET's rinderpest and CBPP have already established export markets, which substantially expands the total market currently open for these products.

Tetanus toxoid vaccine for human use is a relatively new product for LANAVET. Preliminary analysis indicates that LANAVET can decrease production costs for tetanus toxoid vaccine; improve overall production efficiencies; improve product quality to achieve international standards. The opportunity to become a national and/or regional supplier of this vaccine appears achievable.

The market demand for this product within the Cameroon is mainly the government immunization campaign requirements and a limited private market for tetanus toxoid for pregnant women vaccinations. Both the pregnant women market and government program demand are currently being served primarily from imported products. LANAVET does have the opportunity to enhance its market position within Cameroon by ensuring government uptake of LANAVET supply.

The training, research and development, and technical cooperation services can potentially be provided by a private sector LANAVET. To be competitive, it is likely that LANAVET would be required after privatization to focus these services on a niche area such as rinderpest and CBPP, to gain economies of scale and recognized expertise.

Training, research and development, and technical cooperation services which require policy management, enforcement of regulations, or general public good not recoverable by a user fee, may not appropriate services to be incorporated into a privatized institution. Examples of such services would be training to enhance Cameroon laboratory skills or enforcement of vaccination regulations ensuring total compliance. These services are not likely to be purchased by private sector firms or individuals if offered at a market price. If government subsidies are not available to support these activities, a privatized LANAVET could not continue to provide these services.

Services which are for general public good can, in theory, be contracted out by the government to a privatized institution on a cost recovery plus basis. From a government perspective, the key issues to consider in these areas are the nature of the demand, the level of competition among potential suppliers, and cost savings which the government could achieve by contracting such services to the private sector.

The strategy for the short-term viability of a privatized LANAVET should focus the institution's expertise in the manufacture of vaccines. The achievement of excellence in the manufacture of veterinary vaccines, such as rinderpest and CBPP, and tetanus toxoid will be essential for the long-term viability of LANAVET.

Type of Ownership

The new strategy needs to include consideration of the form of privatization which would benefit most the institution and preserve its integrity. Among the privatization alternatives are:

- Transfer of ownership to an existing private company or consortium
- Transfer of ownership to LANAVET's management and staff
- Establish a joint venture with ownership shared by government and private sector and/or LANAVET's management and staff.

Mechanisms which may be required to ensure the financial viability in the short-term of the newly privatized institution may include:

- Government backed loan guarantees
- Government commitment to a long-term contract to procure services and/or products from new LANAVET private company
- International cooperation to provide either financing support or to commit to contract to procure specified services and/or products from LANAVET.

Type of Structure

LANAVET could potentially be re-organized into three (3) distinct operational units in order to maintain segregation and functional integrity between the services and products offered.

- Veterinary Service Unit (VSU)
- Manufacturing Unit (MU)
- Commercialization Unit (CU)

The overall executive direction and administration of LANAVET would be assumed by the executive offices.

Veterinary Service Unit (VSU) could be established on a cost recovery basis. Training and laboratory support services for infectious diseases would be the major services offered. These services should be focused initially on rinderpest and CBPP expertise resident within LANAVET.

VSU would be responsible for research and development, diagnostic services, and other activities related to animal health issues. Specific services could include:

- Research in rinderpest and CBPP
- Reference Centre for diagnosis of infectious diseases with particular focus on rinderpest and CBPP
- Research immunological aspects of rinderpest and CBPP
- Development of new bio-technology products for control and prevention of rinderpest and CBPP such as vaccines and/or immunostimulants
- Veterinary research services for clinical trials and efficacy studies for pharmaceutical and/or biological veterinary companies
- Training in different areas of animal health
- Technical Laboratory services with specific focus on rinderpest and CBPP disease management and control
- Product development research and process optimization development activities.

VSU's revenues could be generated by entering into contracts with Cameroon government, international cooperative projects, international agencies and organizations dedicated to support of technical cooperation projects and research and development. As well, LANAVET could market these services to customers within the private sector who require clinical trials, diagnostic and laboratory services.

Research and development and training services undertaken internally within LANAVET could be structured with an internal fee charge which would allow cost recovery for VSU and rationalization of overall overhead costs for the institution.

Manufacturing Unit (MU) would be the production unit for vaccines and other complementary services. This unit would consolidate all current production groups at LANAVET, including veterinary bacterial and viral vaccines and tetanus toxoid vaccine for human use.

MU would continue to manufacture the existing product line. As well, if commercially viable, MU could introduce new complementary products either developed in-house or licensed from other firms.

Optimization of current manufacturing capabilities will be essential to ensure cost effective production capability and to build resources and capacity to meet the changing demands of the marketplace.

MU would also include the operations of quality control services. However, it would be essential that the reporting structure of the quality control services continued to be the overall responsibility of the administration.

MU's revenues would come directly from the sales of its products and services in the market, which would be sold by the Commercialization Unit.

Commercialization Unit (CU) could consolidate all elements necessary for marketing, sales, distribution, and after sales service of LANAVET's products and services.

CU's marketing responsibilities would also include market research and strategic initiatives to identify new product opportunities, alliances in export markets, alliances in product development and commercialization. In other words, CU's mandate would include responsibility to direct and manage LANAVET's focus and new initiatives as determined by the institution's capabilities and the market demands.

CU would evaluate the sale of ready-to-use vaccine products as well as bulk vaccine products.

In addition to its core responsibility to market and sell VSU and MU products and services, CU would also need to assume responsibility to obtain: product licenses, long term purchase commitments from Cameroon's Ministry of Health for tetanus toxoid, and international certification, endorsement, and approval required to position LANAVET's products and services effectively in the market.

CU's marketing plan should pay particular attention to streamlining the regulatory process in strategic target markets.

CU's market research should put in place a process to evaluate competitors operations, products and pricing strategies; and to monitor competitors' activities on an on-going basis. Market research must also include evaluation of the long term demands of the market for LANAVET's core products and services, identifying trends, developments, and changes in demand.

VSU and MU could on an annual basis develop an internal price based on cost of delivery, overhead, research & development requirements, and contribution. This internal price would be the cost to CU to obtain delivery of products and services sold. CU would establish selling prices based on this internal cost plus CU's cost of its market research, business development and sales activities, overhead, and contribution. CU's revenues would be obtained from sales of VSU's and MU's products and services.

The Executive Offices would assume responsibility for development and management of the institute's overall financial, operational, human resource, quality performance and strategic focus.

6.0 LANAVET OPTIONS

In the interest of achieving the most rapid possible development while, simultaneously, paying realistic attention to the minimization of LANAVET's cost for operations, four options should be analyzed (Figure 2).

The options are as follows:

Option I	The maintenance of the "Status Quo" (SQ)
Option II	The maintenance of the "Status Quo" plus the reduction of nearly 50 % of current LANAVET's labour force. (SQ-50)
Option III	The Privatization Option (PO)
Option IV	Combination of II and III (CO)

Option I: The maintenance of the "Status Quo".

This option is the easiest to implement but has several drawbacks. It is obvious that the Government of Cameroon has limited financial resources for the fulfilment of LANAVET's financial obligations. In the last few years LANAVET has undergone budget cuts from the Government of Cameroon which has impacted most areas of the institution. Delays in salary payments and procurement of supplies have been a common occurrence at LANAVET and has adversely effected production schedules. As a result, annual production of vaccine products has been declined.

LANAVET is significantly over-staffed and current productivity is poor. The existing organizational structure does not contribute to the effective operation of LANAVET's core activities - manufacture, quality control, and commercialization of vaccines.

Training, an essential activity to maintain quality product and qualified staff, is a key success factor. Currently LANAVET's does not have training programs focused on the needs of the institution.

It is recognize that the continuation with the "status quo" will curtail LANAVET's ability to grow.

Option II: The maintenance of the "Status Quo" plus the reduction of 50 % of the current LANAVET's labour force. (SQ-50)

This option focuses on the reduction of approximately 50% of the current LANAVET administration and service staff from 85 to 40 people. These staff reductions would reduce the operating cost by approximately 20% and increase productivity. (See Appendix 2). This option would allow for the increase of LANAVET's salaries to levels matching the salaries levels of Cameroon's private sector.

Ownership would continue to be within public sector.

Wide ranging structural changes to staff roles and responsibilities would be required to re-focus the remaining staff and to revise or, potentially, eliminate, some components of LANAVET's current operational mandate.

Option III: The Privatization Option (PO)

This option is based on the ability to attract local and/or foreign capital for participation in the project.

Privatization of LANAVET would require the institute to develop a new mandate and mission. The original 1983 mandate was to provide services to meet an identified national government policy to enhance and support the country's livestock industry. A private company mandate for LANAVET would require at minimum the financial sustainability of the organization based on its ability to generate sufficient revenues to cover all operating costs and to invest in future product and service development through internal research and development programs.

To achieve successful sustainability in the private sector, LANAVET would require that its functional departments and staff be involved in the profit drivers to establish the institution's competitive marketing culture.

The above issues and the implementation of appropriate strategies will impact various functional groups within LANAVET in a variety of ways. The impact of key operational elements in the overall institution performance is shown in Table 1.

To create a profit-driven culture within a privatized LANAVET there are at minimum three initiatives required:

1. To develop a new vision and mission for the institute
2. To develop an actionable strategic plan which addresses LANAVET's short-term (Year 1-3) and long term objectives (Year 5)
3 To create multi-functional teams within LANAVET to integrate the new vision into the organization and to execute the strategic plan.

Strong and effective leadership will be required to develop and implement a compelling new vision to guide the organization. LANAVET's vision for the year 2001 would need to be supported by specific, quantifiable goals. These goals could include:

- Achieve SUFFICIENT consolidated revenue from sales of vaccines and services to achieve the break-even point in no more than a 2-3 years.
- Achieve WHO recognition as Tetanus Toxoid producer and supplier.
- Achieve PANVAC recognition as reference centre for rinderpest and CBPP in Central Africa.
- Achieve economical and organizational independence from the Government of Cameroon.
- Achieve product registration and licenses in priority target country markets.

Strong and effective management will be required to undertake the necessary financial and operational restructuring. Organizational restructuring will need to establish profit centres and management profit and loss responsibilities.

Ownership in this option could be assumed either by LANAVET's management and staff or by a local or foreign firm.

Option IV: Combination of II and III (CO)

This option allows for the opportunity to incorporate some of the benefits of option II and III. This option could be staged in different phases and could be supplemented with the participation of foreign aid agencies, both private and government sponsored, to provide some of the capital assistance and/or co-financing.

Ownership in this option could be jointly held by government and existing private sector firm and/or LANAVET's management and staff.

7.0 GENERAL CONSIDERATIONS

Privatization of LANAVET would require the institute to develop a new mandate and mission. The original 1983 mandate was to provide services to meet an identified national government policy to enhance and support the country's livestock industry. A private company mandate for LANAVET would require, at minimum, the financial sustainability of the organization based on its ability to generate sufficient revenues to cover all operating costs and to invest in future.

The execution of a successful strategy to privatize LANAVET and ensure its sustainability, will require the executive office at minimum develops:

- Strong and effective leadership to develop and implement a compelling new vision
- Strong and effective management to undertake necessary financial and operational restructuring.
- A coherent plan for management interventions to address all major categories of activity including financing, human resources, marketing, cost cutting, quality control and production improvements.

Strategic issues

To meet a new mandate, significant changes in the organization and within each function would be required. LANAVET would be required to change its focus from being a provider of services to government, to being a market driven firm providing quality products and services to customers in a competitive environment.

A profit-driven LANAVET would be required to develop strategies to address a number of issues. Some of these issues would be:

- Market Share:
  - Add customer value
  - Differentiate product/services in competitive market
  - Improve customer relations
  - Expand and improve marketing and sales functions

- Market Size:
  - Expand in existing markets
  - Provide national and international quality products
  - Enter new geographic markets
  - Enter new segment within existing markets
  - Expand and improve marketing and sales functions

- Unit Sales:
  - Increase product usage rate
  - Add customer value
  - Provide national and international quality products
  - Differentiate product/services in competitive market
  - Improve sales function

- Price:
  - Add customer value
  - Differentiate product
  - Decrease customer price sensitivity
  - Meet Quality expectations

- Variable Costs:
  - Reduce variable costs
  - Increase production run lengths
  - Reduce waste and rejects

- Unit Margin:
  - Increase unit price relative to variable costs - OR
  - Reduce variable costs relative to unit price.

- Fixed Cost:
  - Improve productivity
  - Increase production output
  - Reduce production down time
  - Reduce staff costs
  - Reduce inventory costs
  - Reduce overhead costs

- Investment:
  - Reduce inventories
  - Increase production output
  - Improve productivity & Quality
  - Increase revenues

Institutional Changes

The new LANAVET will have to achieve the following:

- Improve employee relations including compensation policies
- Improve human resource deployment
- Improve overall quality
- Reduce cost of quality control and assurance
- Improve accounting processes, including cost control and profit allocations
- Reduce overhead costs
- Reduce operational costs
- Reduce production and testing errors
- Increase production reliability and on-time delivery
- Improve product lead time
- Improve productivity
- Reduce inventory turnover and inventory losses, improve inventory management
- Improve marketing and sales skills
- Improve market share
- Expand geographic markets

- Ensure financial and skill resources available for new product development
- Improve profitability
- Improve institutional capacity to maintain sustainable growth.

Quality Assurance

The implementation of quality assurance programs requires an integrated approach, based on committed leadership, restructuring of traditional management practices, and full participation of employees to achieve clearly stated corporate goals.

Quality Management

Quality management could be a key tool for strategy execution. Achieving high levels of quality has become an important factor in competitive success. The traditional methods to maintain quality with final inspection of processed product is no longer considered sufficient to achieve cGMP compliance. Internationally recognized quality procedures and cGMP compliance are increasingly based on integration of quality assurance programs and total quality management practices throughout the organization.

Generally, companies which adopted quality management practices have experienced an overall improvement in corporate performance, including increased productivity, increased market share, and increased profitability.

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Figure 1

LANAVET FUTURE ALTERNATIVES

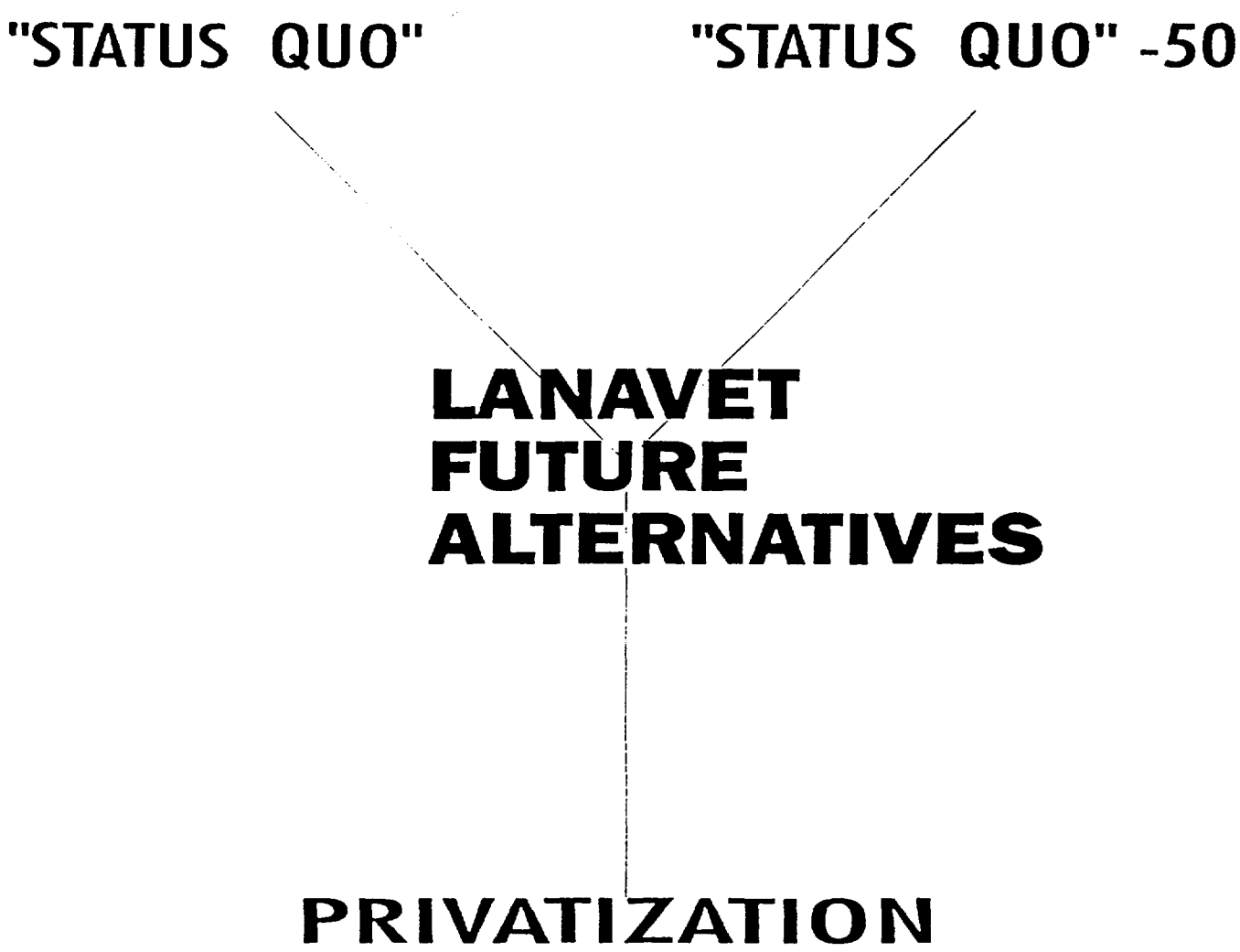

Figure 2

LANAVET VACCINE MARKET ALTERNATIVES

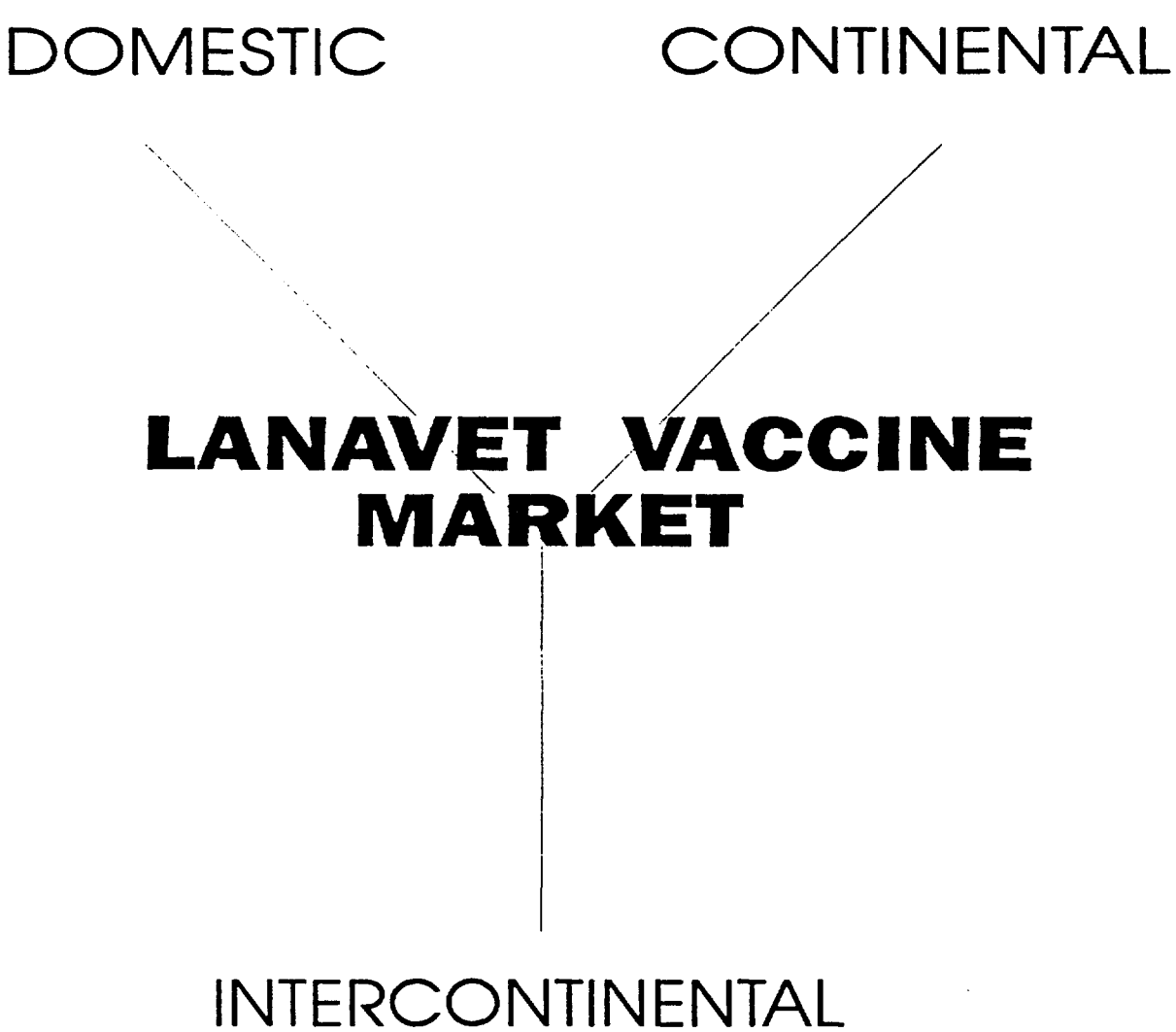

Table 1

LANAVET PRODUCT LINE

PRODUCT NAME	DISEASE TARGET
HUMAN PRODUCTS:	
Tetanus toxoid	Neonatal tetanus
VETERINARY PRODUCTS:	
Bovipestovax	Rinderpest
Avipestovax	Newcastle disease
Variovax	Fowl pox
Sotavax	Newcastle disease
Gumbovax	Gumboro disease
Avibronchovax	Avian infectious bronchitis
Clavovax	Sheep pox
Perivax	Contagious bovine pleuropneumonia
Mycovax	Contagious bovine pleuropneumonia
Pastovax	Bovine pasteurellosis
Symptovax	Black leg
Anthravax	Anthrax
Cholevax	Fowl cholera
Typhovax	Fowl typhoid
Biavivax	Fowl cholera & typhoid
Bivax	Rinderpest & contagious bovine pleuropneumonia
Thermovax	Thermostable rinderpest
Multivax	Newcastle,fowl cholera & typhoid

Table 2

INTERACTION OF OPERATIONAL ELEMENTS ON KEY PERFORMANCE VARIABLES

	MARKET SHARE	MARKET SIZE	UNIT SALES	PRICE	VARIABLE COST	UNIT MARGIN	FIXED COST	INVE
ACCNT					X		X	
FINAC					X	X		X
H.RES							X	X
MANUF					X	X	X	X
MARKT	X	X	X	X				
PURCH					X	X	X	X
R&D	X	X	X	X				
QA/QC	X	X	X	X				X
SALES	X	X	X	X				

ACCNT= ACCOUNTING
MARKT= MARKETING
R&D = RESEARCH & DEVELOPMENT
FINAC= FINANCE
PURCH= PURCHASING
QA/QC= QUALITY ASSURANCE QUALITY CONTROL
H.RES = HUMAN RESOURCES

ANNEX 8

LANAVET BUSINESS PLAN

DEVELOPMENT OF THE VACCINE PRODUCTION IN AFRICA

A CASE STUDY

NATIONAL VETERINARY LABORATORY, BOKLE (LANAVET)

GAROUA, CAMEROON

PREPARED BY

Messrs. Z. Csizer and M. Carpio

JUNE 1996

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EXECUTIVE SUMMARY

The business plan was prepared at the request of UNIDO to serve as a framework for LANAVET's future development activities as a privatized commercial operation dedicated to manufacture and sale of vaccine products. The plan incorporate information obtained from UNIDO technical reports on LANAVET conducted during 1995.

The business development plan outlined in this document is based on the sales forecast resulted from the expansion of LANAVET sales of current products to the domestic, Sub-Saharan, Middle East and Asian markets.

The proposed business plan assumes a significant sales increase in available markets resulted from transformation of LANAVET into a more market focused operation. These could be achieved by the establishment of a Marketing and Sales Group within a privatized LANAVET.

The business development plan identifies short and long term goals, marketing and sales group mandate and activities, financial forecast and funds required for the achievement of the proposed business objectives.

The proposed business plan demonstrate the feasibility of LANAVET restructure from a production driven operation into a successfully marketing driven, commercially viable operations under a privatized structure.

Successful implementation of the proposed business plan would have LANAVET achieve a gross profit of FCFA 362,144 in the year 2000, have 50% annual average increase in sales revenue, and maintain fixed costs to less than a 25% increase in the 1996-2000 period. The estimated initial funding required for the startup of the proposed business plan is U.S. $ 350,000.

LANAVET provides a reasonable investment opportunity with limited risk to private sector investors interested in participating in the development of vaccine industry in Africa.

UNIDO should continues to support LANAVET to become a private commercial operation for vaccine production in Africa and to contribute to the livestock development in the African continent.

1. INTRODUCTION

- LANAVET currently operates as a pari-state agency of the government of Cameroon and does not have profit and loss responsibilities.

- LANAVET's current operations are not profitable, and are forecast to experience approximately FCFA 9 million loss if status quo in operations, production, and sales are maintained in 1996.

- Earlier UNIDO reports on LANAVET's operations and finances determined that privatization is a viable option if changes to LANAVET's current operational structure and budget are undertaken.

- Following is a business development plan which could be used as a framework to establish a strategic direction for successful privatization to become a sustainable commercial privatized organization to manufacture and sell vaccines.

2. CURRENT SITUATION

2.1 Current Manufacturing Capability

- LANAVET's current manufacturing include capabilities to produce:
  - Poultry Vaccines
  - Livestock Vaccines
  - Tetanus Toxoid for Humans Vaccine.

- Production of livestock vaccines products have in the last three years been LANAVET's major manufacturing activity.

- LANAVET has the technical capabilities to provide the livestock industry with over 20 million doses of high quality veterinary vaccines products annually.

- LANAVET's annual total manufacturing output has ranged between 8 to 15 million doses of livestock vaccine. Individual product annual output has varied substantially. LANAVET does not have in place a coordinated production schedule which allows for maximization of equipment and optimization of current production processes.

2.2 Current Market Situation

2.2.1 Domestic Market

- Most of LANAVET's livestock vaccines products currently have significant shares of the domestic market. However, LANAVET has only achieved a majority domestic market share with sales of rinderpest vaccines.

DOMESTIC MARKET SHARE IN PERCENTAGE OF LIVESTOCK VACCINES
(market estimated at 2.8 million doses)

Product	Anthrax	Clostridium	CBPP	Pasteurella	Rinderpest
Market share %	4	36	27	25	52

- LANAVET has the production capability to grow its domestic market share.

- LANAVET does not have formal distribution channels into the domestic market. As a result, customer base in the private market for veterinary vaccines has not been developed.

- LANAVET has in the past 3 years become increasingly more reliant on domestic sales as export sales have decreased as percentage of total sales.

2.2.2 Sub-Sahara African Market

- LANAVET's exports of livestock vaccines products have been primarily to Sub-Saharan African countries, mainly Central African Republic, Benin, Burkina Faso, Cote d'Ivoire, Guinea.

- LANAVET's share of the Sub-Saharan market remains very low, under 1% share for each livestock vaccine. LANAVET's rinderpest vaccine product has gained the largest market share. However, LANAVET rinderpest products have only reached 0.05% market share.

SUB-SAHARAN MARKET IN PERCENTAGE OF LIVESTOCK VACCINES
(market estimated at 86.4 million doses)

Product	Anthrax	Clostridium	CBPP	Pasteurella	Rinderpest
Market share %	.001	.006	.020	.004	.050

- LANAVET has the production capability to grow its market share in the Sub-Saharan market by increasing sales to international agencies involved in regional livestock disease control, government agencies, and private sector end-users throughout the region.

- Currently LANAVET does not have proper distribution channels in the Sub-Saharan regional market as LANAVET only sells directly to international agencies and a few government agencies. LANAVET has not established effective distributor channels to sell directly to private sector wholesaler and end-user markets in the region.

2.2.3 Other International Markets

- LANAVET has, to date, limited export experience outside of the Sub-Saharan regional market.

2.2.4 Competitive Environment

- In LANAVET's primary markets, the domestic Cameroon and the Sub-Saharan African market, there are African-based and European-based manufacturers competing in the market.

- Of the African-based manufacturers, there are at least 8 major vaccine manufacturers, most of which are government or government related institutions. It appears that of all the African-based vaccine manufacturers only one is private sector owned.

- The veterinary vaccine market in Africa is very price competitive.

2.3 Current Revenue and Cost Situation

- LANAVET's 1996 projected budget has an operational deficit where operating costs exceed revenues by approximately FCFA 9 million:

	FCFA	
° Revenues	473,650	
° Variable Costs	166,877	(35.2% of Revenues)
° Gross Margin	308,773	(65.2% of Revenues)
° Fixed Costs	315,624	(66.6% of Revenues)
° Gross Profits	(8,851)	

- In 1996 LANAVET's variable and fixed costs are projected to exceed revenues by 1.8%. Fixed costs alone claim 66.6% of total revenues generated.

- On a product specific analysis, LANAVET's fixed costs are very high, and for some products per unit fixed cost exceeds the price of the product.

- Contributions or gross profits per unit are low. Only Bivax, the combination CBPP-rinderpest product, provides a reasonable (17.68%) contribution to LANAVET.

- Variable costs are high in the case of the clostridium and pasteurella vaccines products, with both exceeding 50% of total product price.

3. FINANCIAL FORECASTS - TWO SCENARIOS

3.1 Assumptions

- Two forecast scenarios are presented for the 1996-2000 period.

- Pricing in each scenario is based on 1996 prices as in UNIDO report on marketing analysis for LANAVET; Ndamkou, 1995.

- Fixed cost are based on UNIDO report on financial analysis of LANAVET; Bouchez, 1995: privatization option.

- All costs and prices are calculated in Cameroon's local currency FCFA.

- **Scenario I** is based on unit sales forecast presented on the marketing analysis for LANAVET's by Ndamkou, 1995.

- **Scenario I** assumed prices increases for two products in the 1996-2000 period.

- **Scenario II** assumes higher unit sales reflecting impact of marketing and sales group's activities.

- **Scenario II** is based on the consultant's best estimates of the domestic and international markets available for LANAVET's veterinary vaccines. The potential available markets have been estimated at 40% of the cattle population of the geographical market described.

- **Scenario II** assumes the establishment of a marketing and sales group. The marketing group's mandate would be to grow LANAVET's market share and to direct LANAVET'S business development strategy.

- **Scenario II** forecast sales include an annual increment expected as a result of the implementation of an effective marketing and sales group to LANAVET's operations.

- Detailed data on Scenarios **I** and **II** is presented in the Appendices to this document.

3.2 Comparative Summary

- The analysis demonstrates that both scenarios give LANAVET the opportunity to expand their current veterinary vaccines sales.

- **Scenario I** overall gross margin decreases after the second year of operations 1998-1999, indicating a risk to LANAVET's long term viability.

- **Scenario II** provides attainable market growth targets and recognizes the need to invest during 1997-2000 an average of 5% of the gross revenues into marketing and sales activity.

- **Scenario II** is the base for the development of the proposed business development plan.

4. PROPOSED BUSINESS DEVELOPMENT PLAN (Scenario II)

4.1 Goals

4.1.1 Short-Term Goals

1. To meet the 1996 budget projections
2. To re-invest 45% of the profits into the business annually in 1996-2000 period.
3. To minimize capital expenditures until 2000
4. To reduce fixed cost by at least 20% by the year 2001
5. To repay the debt by 2000
6. To reduce production cost of bacterins (symptovax, anthravax and pastovax) by 50% by year 2000
7. To increase the domestic sales of vaccines by a minimum of 10% per year in the period 1996-2000
8. To increase export market sales by at least 20% over 1996 by year 2000

4.1.2 Long-Term Goals

1. To provide high quality veterinary vaccine products, recognized by international agencies to the domestic and international markets.
2. To earn an annual net profit equivalent to 20% of the gross revenues.
3. To ensure an average annual 30% gross profit margin in each vaccine products
4. To become one of the top 3 veterinary vaccine suppliers in Africa as ranked by the sales of vaccine products by 2010.

4.2 Product Offering

- An analysis of current and future market demands should be undertaken to identify and confirm which products are to be manufactured and sold by the LANAVET.

- For this working model it has been anticipated that LANAVET's current livestock vaccines will be the core of the business.

  Continue manufacture of:
  - Rinderpest Vaccines - Bovipestovax and Thermovax
  - CBPP standard - Perivax
  - Rinderpest and CBPP combination vaccine - Bivax
  - Anthrax Bacterin - Anthravax

- Clostridium Bacterin - Symptovax
- Pasteurella Bacterin - Pastovax.

Limit manufacturing of poultry vaccines:
- Combination, newcastle, fowl cholera and typhoid - Multivax

4.3 Organizational Structure

NOTE: As the final management structure to be adopted will be determined by the corporate culture of the new ownership, It is difficult to elaborate in detail the future organizational structure and style of operations for the new LANAVET. However, in order to develop a working model, we have utilized the estimated costs which have been defined in the privatization scenario recommended by Bouchez in the UNIDO Report on Financial Evaluation of LANAVET, 1995.

4.3.1 Operational Restructuring

- It is recommended that the new LANAVET should be re-organized into three major groups:
  - Operations:
    Manufacturing
    Quality (quality control and quality assurance)
    Physical plant (maintenance)

  - Administration:
    Finance
    Human Resources
    Managing information systems

  - Marketing and Sales:
    Marketing
    Sales

- It is recommended that LANAVET reduce its overall work force. Previous studies have recommended that the total work force be reduced to 51 people, including management and labour. However, the final number of people required by a re-structured LANAVET will depend on the organizational structure of the new owners and operations.

4.3.2 Marketing and Sales Structure

- The establishment of an effective marketing and sales group at LANAVET is an essential element for the implementation of the proposed strategic plan 1996-2000.

- A fully functionally marketing and sales group would likely have staffing requirements of:
  - 1 Manager (Team Leader)
  - 1 Responsible for product management
  - 1 Responsible for regulatory affairs
  - 1 Sales Representative for the domestic market
  - 1 Sales Representative for international markets

- The marketing and sales group should be functioning prior to privatization and startup should be no later than the fourth quarter of 1996.

- LANAVET's new marketing group will be responsible to put in place the necessary elements to secure the sales of veterinary vaccines including product registration and licensing, sales, distribution and after sales service of all LANAVET's vaccine products.

- The marketing group will also be responsible to develop and monitor:
  - Marketing Strategic Plan
  - Product Registration and Licensing Plan

- Marketing Strategic Plan to be developed, with a 5 year horizon, which includes:
  - Domestic Market Environment and Opportunity Identification
  - International Market Environment and Opportunity Identification
  - Determination of Market Potential
  - Competitive Environment and Key Competitor Profiles and analysis
  - Pricing Strategy
  - Marketing Support Programs Plan including promotional literature, activities, advertising, etc.
  - Key Target Client Identification and Tactical Plan
  - Determination of Client Preferences.

- Product Registration and Licensing Plan to be developed which incudes:
  - Evaluation of regulatory environments in key international markets
  - Product registration and trade mark applications programs in target markets
  - Government/Regulatory Authorities Contact Plan

- Strategic alliances:
  - Initiate program to establish strategic alliances with distributors and/or complementary product manufacturers in foreign markets to expand LANAVET's sales potential and potentially introduce strategic alliance's products into LANAVET's domestic market.

- Distribution:
  - Establish and maintain sales accounts in domestic market
  - Establish and manage distributors network in key international markets

- In addition to selling, on-going activities of the marketing and sales group which include:
  - Regular marketing and promotional programs
  - Effective monitoring of competitors' activities and sales with particular attention to pricing, product presentation and delivery.
  - After-sales services and follow-up.
  - Annual planning and forecasting activities.
  - Co-ordination of forecasted requirement with production schedule.

- It is expected that the marketing group will have significant inputs and work with manufacturing group in the production planning, production scheduling and inventory control of LANAVET's veterinary vaccines so that production and marketing are coordinated.

- Marketing group should work with the manufacturing group to review best practices for:
  - Product delivery logistics for international markets
  - Product presentation
  - After-sales services

- Establish a proper budget allocation for marketing and sales group and activities. It is recommended that 5% of total revenues be allocated to marketing and sales, which would have the marketing and sales group having a Year 1 budget of KCFA 10,000 for 1996 and average of 5% on the gross revenue for 1998-2000.

4.4 STRATEGIC APPROACH

- To implement successfully LANAVET's business development strategy the new organization should have two approaches:
  - Concentrate in markets currently serve by LANAVET's existing products
  - Expand to other prospective geographical areas that could be served with LANAVET's existing products and expand product line.

4.4.1 Concentrate in markets currently serve by LANAVET's existing products:

i. Domestic market

- Total domestic market has been estimated at 2.8 million doses annually.
- Expand domestic market share in each of LANAVET's products by 10% annually in the 1996-2000 period:
  - Develop a comprehensive marketing strategy which include: product promotion, distribution and pricing.
  - Determine priority for marketing activities in accordance to market segments, and products.
  - Introduce innovative approaches to increase government sales by the end of 1997.
  - Establish and/or expand sales to Cameroon's private sector clients by end 1997.
  - Generate 20% of total domestic revenues from private sector clients by 1998.
- LANAVET should set a strategic priority to expand current domestic market share by at least 10% annually over the next 5 year period, achieving a minimum domestic market share for each product of 35% by the year 2000.
- In order to achieve the domestic market expansion LANAVET will have to establish effective distribution channels in the key regions of Cameroon to reach directly to the private sector end users.
- Pricing policy should be reviewed to evaluate opportunities to revise price schedule either to increase market share or increase unit revenue.

ii. **Sub-Saharan Market**

- Sub-Saharan market has been estimated at 86.4 million doses annually (40% of the estimated cattle population)

- In order to achieve the Sub-Saharan market expansion LANAVET will have to:
  - Establish effective distribution channels in the key markets of the Sub-Saharan region to expand market reach.
  - Obtain certification of quality from recognized international agencies for livestock vaccines in particular rinderpest and CBPP.
  - Product registration and licensing plan
  - Establishment of strategic alliances for product distribution.
  - Review pricing policy for potential distributors and/or direct sales.
  - Monitor competition, pricing, product presentation and delivery.
  - Review product logistics to reduce cost.
  - Review product presentation.
  - Develop value added products such as the inclusion of diluents for freeze dried vaccines.
  - Produce technical data for vaccine products such as potency, stability, comparative efficacy studies versus competitive products.
  - Establish promotional plan including participation in scientific events, advertisement in regional and international magazines, etc.

iii. **Middle East and Asian Market**

- Middle East and Asian markets have been estimated to be 139.2 million doses annually (40% of estimated cattle population). The markets potentially open to LANAVET are, into Middle East, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, U.A.E., Yemen,Turkey, Iran, and Iraq and, in Asia, Malaysia, Mongolia, Myanmar, Nepal, Pakistan, Thailand, and Viet Nam.

- In order to enter into the Middle East and Asian market LANAVET will have to:
  - Establish effective distribution channels in the key markets of the Middle East and Asian region to reach private sector.
  - Register and license product.
  - Review pricing policy for potential distributors.
  - Review product logistics to minimize shipping cost.
  - Review product presentation.

- Develop of value added products such as the inclusion of diluents for freeze dried vaccines.
- Produce technical data for vaccine products such as potency, stability, comparative efficacy studies versus competitive products.
- Establish a marketing support plan for distributors.

4.4.2 New products

- Introduce value added products for existing vaccine product line such as diluent and/or accessories such as disposable syringes, markers, etc.
- Develop combinations of current vaccines.
- Identify other products to expand current product line either imported bulk for final processing, distribution and sale; Or import of ready-to-use products which LANAVET could market, sell and distribute in domestic market.

4.5 Financial Performance (Forecast)

- Continuous increase in unit sales in 1996-2000 period.

- Marketing cost to increases from a 3% of gross revenue in 1996 to an average 5% of the gross revenues in the period 1997-2000.

- Gross margin to increase annually 18% for 1996, 30% for 1997, 32% for 1998, 33% for 1999 and 37% for 2000.

- Expected gross profits to increase five-fold s (557%) in the period 1996-2000.

- No capital investment required in the period 1996-2000.

- The financial summary is presented below:

SCENARIO II

ESTIMATED INCOME STATEMENT 1996-2000
(FCFA '000s)

	1996	1997	1998	1999	2000
SALES REVENUES	**359,767**	**464,372**	**648,119**	**751,104**	**989,351**
DIRECT COST	89,698	96,740	189,341	231,165	325,239
FIX COST	194,697	206,337	220,449	235,983	252,501
MARKETING COST	10,000	23,219	29,000	37,555	49,467
TOTAL COST	**294,395**	**326,269**	**438,790**	**504,703**	**627,207**
GROSS PROFIT	**65,372**	**138,103**	**209,329**	**246,401**	**362,144**
MARGIN %	18.2	30.0	32.3	32.8	36.6

4.6 Funds Required

- An initial investment of approximately U.S. $ 350,000 will be required to finance the development of the initial six month inventory, to provide sufficient working capital for a six month period and to establish the required marketing and sales group. The money could be acquired as a loan to be pay in five years (1996-2000) at the going market interest.

- No funds will be required for capital expenses as LANAVET's existing facilities have the necessary infrastructure to meet all projected production targets.

- The financial summary demonstrate that LANAVET's could become a profitable and sustainable operation based on the manufacture and sales of veterinary vaccines for the period 1996-2000.

5. GENERAL CONSIDERATIONS

- Any additional reductions of either the variable or fixed cost will impact positively in additional profits for the operations.

- Attention should be given to the development of new products in order to reduce the dependency in the existing product line. The incorporation of additional products can potentially enhance further the profitability of the operation.

- LANAVET has the opportunity to expand its product range and revenue base by establishing strategic alliances with other vaccine manufacturers in the region, either to establish co-marketing and sale programs and/or market and sell other manufacturers products in the Cameroon market.

- To maintain LANAVET's customer base for poultry vaccines, it is recommended that LANAVET identify potential suppliers of ready-to-use product and enter into distributor agreements with the best available supplier whereby LANAVET markets, sells, distributes their products in the domestic market.

- Enhanced and expanded marketing and sales capabilities would enable LANAVET to capitalize on its position of strength in the domestic market - as Cameroon's only manufacturer of quality livestock vaccines.

- It is expected that the that the implementation of the new operational plan will be market driven and will result in a sustained revenue growth based on increases unit sales to a widening client base.

- Enhanced and expanded marketing and sales capabilities would enable LANAVET to gain greater control of its long term viability and refocus LANAVET from a production driven to a competitive market-driven organization.

APPENDICES

Appendix 1

LANAVET'S LIVESTOCK VACCINE PRODUCTION 1992-1995
(doses)

PRODUCT	1992-93	1993-94	1994-95
ANTHRAX	344,000	487,000	0
CLOSTRIDIUM	1,936,000	1,823,000	842,000
CBPP	3,587,000	1,999,000	2,239,000
PASTEURELLA	1,322,000	630,000	1,079,000
RINDERPEST	2,238,000	3,247,000	11,170,000
TOTAL	**9,427,000**	**8,186,000**	**15,330,000**

Appendix 2

LIVESTOCK VACCINE SALES
DOMESTIC AND EXPORT
PERCENTAGE OF TOTAL SALES

	1992-93	1992-93	1994-95	1994-95	1995-96	1995-96
	D (%)	E (%)	D (%)	E (%)	D (%)	E (%)
Anthrax	28.5	71.5	58.7	41.3	52.9	47.0
Clostridium	51.2	48.8	79.1	20.9	65.4	34.6
CBPP	3.8	96.2	32.8	67.2	82.3	17.7
Pasteurella	39.8	60.2	62.7	37.3	100.0	0
Rinderpest	5.3	94.7	26.8	83.2	25.3	74.7

D=domestic market E= export market

Appendix 3

LANAVET'S PRODUCT PRICE ANALYSIS
(FCFA)

	Price/dose	Fixed Cost	Variable Cost	Total Cost	Gross Profit
Anthrax	n/a	n/a	n/a	n/a	n/a
Clostridium	26.0	11.7	14.9	26.0	0
CBPP	26.39	17.3	2.16	19.56	6.89
Pasteurella	24.0	11.9	14.79	26.69	-11.2
Rinderpest	19.09	15.6	2.29	17.9	1.19
Rinderpest thermostable	33.0	36.1	2.41	38.51	-5.51
Combination Rinderpest/CBPP	35.29	15.9	1.71	17.61	17.68
Poultry combination	29.86	20.7	11.35	20.7	-7.33

Appendix 4

SCENARIO I
ESTIMATED PER UNIT COST AND PRICE
LANAVET'S VACCINES
(FCFA)

	1996	1997	1998	1999	2000
Anthravax (cost)	13.4	13.4*	13.4*	13.4*	13.4*
(price)	23.0	23.0	3.0	23.0	23.0
Bivax (cost)	1.71	1.71	1.71	1.71	1.71
(price)	35.29	35.16	35.0	35.0	35.0
Bovipestovax					
(cost)	2.29	2.29	2.29	2.29	2.29
(price)	19.10	19.10	19.10	19.10	19.10
Thermovax (cost)	2.41	2.41	2.41	2.41	2.41
(price)	33.0	33.0	33.0	33.0	33.0
Perivax (cost)	2.51	2.51	2.51	2.51	2.51
(price)	26.39	26.39	26.39	26.39	26.39
Pastovax (cost)	14.79	14.79	14.79	14.79	14.79
(price)	24.0	24.0	24.0	24.0	24.0
Symptovax (cost)	14.29	14.29	14.29	14.29	14.29
(price)	26.0	26.0	26.0	26.0	26.0
Multivax (cost)	11.35	11.35	11.35	11.35	11.35
(price)	29.86	30.06	30.16	30.16	30.16

* estimated cost

Appendix 5

SCENARIO I
FORECAST LIVESTOCK VACCINES SALES FOR DOMESTIC AND INTERNATIONAL MARKETS
(doses)

	1996	1997	1998	1999	2000
ANTHRAVAX	0	0	0	0	FNA
BIVAX	3,500,000	3,700,000	4,000,000	4,477,000	FNA
BOVIPESTOVAX	3,300,000	3,300,000	3,300,000	3,465,000	FNA
THERMOVAX	1,500,000	1,500,000	1,500,000	1,575,000	FNA
PERIVAX	3,100,000	3,100,000	3,100,000	3,255,000	FNA
PASTOVAX	1,890,000	2,000,000	2,120,000	2,226,000	FNA
SYMPTOVAX	2,240,000	2,460,000	2,730,000	2,886,500	FNA
MULTIVAX	1,750,000	2,550,000	3,350,000	3,517,500	FNA
TOTAL	**17,280,000**	**18,610,000**	**20,100,000**	**19,717,000**	**21,105,000**

Appendix 6

SCENARIO I

FORECAST REVENUES FROM SALES OF LIVESTOCK VACCINES 1996-2000
(FCFA '000s)

	1996	1997	1998	1999	2000
ANTHRAVAX	0	0	0	0	FNA
BIVAX	123,515	130,092	140,000	147,000	FNA
BOVIPESTOVAX	62,997	62,997	62,997	66,147	FNA
THERMOVAX	49,500	49,500	49,500	51,975	FNA
PERIVAX	81,809	81,809	81,809	85,899	FNA
PASTOVAX	45,360	48,000	50,880	57,876	FNA
SYMPTOVAX	58,240	63,960	70,980	74,529	FNA
MULTIVAX	52,255	76,653	101,036	106,087	FNA
TOTAL	**467,676**	**513,011**	**557,202**	**589,513**	**FNA**

FNA = Forecast not available

Appendix 7

SCENARIO I
LANAVET ESTIMATED DIRECT COST/VARIABLE COST FOR LIVESTOCK VACCINES 1996-2000
(FCFA '000s)

	1996	1997	1998	1999	2000
ANTHRAVAX	0	0	0	0	FNA
BIVAX	5,985	6,327	6,840	7,182	FNA
BOVIPESTOVAX	7,557	7,557	7,557	7,983	FNA
THERMOVAX	3,615	3,615	3,615	3,796	FNA
PERIVAX	7,781	7,781	7,781	8,190	FNA
PATOVAX	27,953	29,580	31,355	32,992	FNA
SYMPTOVAX	32,010	39,297	41,084	42,870	FNA
MULTIVAX	19,862	28,942	38,022	39,918	FNA
TOTAL	**104,763**	**118,955**	**134,182**	**141,119**	**FNA**

Appendix 8

SCENARIO II
ESTIMATED PER UNIT COST AND PRICE
LANAVET'S VACCINES
(FCFA)

	1996	1997	1998	1999	2000
Anthrax (cost)	13.4*	13.4*	13.4*	13.4*	13.4*
(price)	23.0	23.0	23.0	23.0	23.0
Rinderpest					
(cost)	2.13	2.13	2.13	2.13	2.13
(price)	19.10	19.10	19.10	19.10	19.10
CBPPP (cost)	2.51	2.51	2.51	2.51	2.51
(price)	26.39	26.39	26.39	26.39	26.39
Pasteurella (cost)	14.79	14.79	14.79	14.79	14.79
(price)	24.0	24.0	24.0	24.0	24.0
Clostridium (cost)	14.29	14.29	14.29	14.29	14.29
(price)	26.0	26.0	26.0	26.0	26.0
Multivax (cost)	11.35	11.35	11.35	11.35	11.35
(price)	29.86	29.86	29.86	29.86	29.86

* estimated cost

Appendix 9

SCENARIO II
FORECAST VETERINARY VACCINES SALES FOR DOMESTIC MARKET
(doses)

	1996	1997	1998	1999	2000
ANTHRAX	168,000	280,000	560,000	840,000	1,120,000
CLOSTRIDIUM	1,120,000	1,400,000	1,680,000	1,960,000	2,240,000
CBPP	840,000	980,000	1,260,000	1,540,000	1,960,000
PASTEURELLA	840,000	1,120,000	1,260,000	1,400,000	1,680,000
RINDERPEST	1,540,000	1,680,000	1,960,000	2,240,000	2,520,000
POULTRY	1,750,000	2,550,000	3,350,000	3,517,000	4,000,000
TOTAL	**6,258,000**	**8,010,000**	**10,070,000**	**11,497,000**	**13,520,000**

Appendix 10

SCENARIO II
FORECAST VETERINARY VACCINES SALES FOR SUB-SAHARAN MARKET
(doses)

	1996	1997	1998	1999	2000
ANTHRAX	60,000	432,000	648,000	864,000	1,300,000
CLOSTRIDIUM	432,000	648,000	1,000,000	1,300,000	2,600,000
CBPP	1,600,000	2,160,000	2,600,000	3,034,000	3,460,000
PASTEURELLA	432,000	648,000	1,000,000	1,300,000	1,680,000
RINDERPEST	7,000,000	9,100,000	9,450,000	9,800,000	4,320,000
POULTRY	130,000	250,000	500,000	1,000,000	2,000,000
TOTAL	**9,654,000**	**14,848,000**	**16,948,000**	**20,840,000**	**16,280,000**

Appendix 11

SCENARIO II
SALES FORECAST FOR MIDDLE EAST AND ASIAN MARKETS
(doses)

	1996	1997	1998	1999	2000
ANTHRAX	NIL	NIL	500,000	695,000	1,390,000
CLOSTRIDIUM	NIL	NIL	500,000	695,000	1,390,000
CBPP	NIL	NIL	700,000	1,000,000	1,500,000
PASTEURELLA	NIL	NIL	500,000	695,000	1,390,000
RINDERPEST	NIL	NIL	700,000	1,000,000	1,500,000
POULTRY	NIL	NIL	NIL	NIL	NIL
TOTAL	**NIL**	**NIL**	**2,900,000**	**4,085,000**	**7,170,000**

Appendix 12

SCENARIO II
TOTAL SALES FORECAST FOR LANAVET's POTENTIAL MARKETS
(DOSES '000s)

	1996	1997	1998	1999	2000
ANTHRAX	228	712	1708	2399	3810
CLOSTRIDIUM	1552	2048	3180	3955	6230
CBPP	2440	3140	4560	5574	6920
PASTEURELLA	1272	1768	2760	3395	4750
RINDERPEST	4132	4704	6116	7120	8340
POULTRY	1880	2800	3850	4517	6000
TOTAL	**11504**	**15172**	**22174**	**26960**	**36050**

Appendix 13

SCENARIO II
TOTAL VARIABLE COST FOR LANAVET's VACCINES 1996-2000
(FCFA 000's)

	1996	1997	1998	1999	2000
ANTHRAX	3,055	9,541	22,887	32,147	51,054
CLOSTRIDIUM	22,178	29,266	45,442	56,517	89,027
CBPP	6,124	7,881	11,446	13,991	17,369
PASTEURELLA	18,813	26,149	40,820	50,212	70,252
RINDERPEST	18,190	20,725	25,049	27,030	29,437
POULTRY	21,338	31,780	43,697	51,268	68,100
TOTAL	**89,698**	**164,853**	**189,341**	**231,165**	**325,239**

Appendix 14

SCENARIO II
ESTIMATED REVENUES FROM THE VACCINE SALES 1996-2000
(FCFA '000s)

	1996	1997	1998	1999	2000
ANTHRAX	5,244	16,376	39,284	55,177	87,630
CLOSTRIDIUM	40,352	53,248	82,680	102,830	161,980
CBPP	64,392	82,865	120,338	147,098	182,619
PASTEURELLA	30,528	42,432	66,240	81,480	114,000
RINDERPEST	163,114	185,843	224,616	242,379	263,962
POULTRY	56,137	83,608	114,961	122,140	179,160
TOTAL	**359,767**	**464,372**	**648,119**	**751,104**	**989,351**

Appendix 15

SCENARIO I

ESTIMATED INCOME STATEMENT 1996-2000
(FCFA '000s)

	1996	1997	1998	1999	2000
SALES REVENUES	**467,676**	**513,011**	**557,202**	**589,513**	**NA**
DIRECT COST	104,763	118,955	134,182	141,119	NA
FIX COST	194,697	206,337	220,449	235,983	NA
MARKETING COST	10,000	10,000	10,000	0	NA
TOTAL COST	**309,460**	**335,292**	**364.631**	**375,572**	**NA**
GROSS PROFIT	158,216	177,719	192,571	213,941	NA
MARGIN %	33.7	34.6	34.5	29.6	NA

NA = Not available

ANNEX 9

THE ESTABLISHMENT OF GMP VIRAL VACCINE PRODUCTION in DEVELOPING COUNTRIES

"The use of the Multi-surface Cell Propagator (MSCP) as a viable alternative for large-scale cell culture production"

In many developing countries, establishing and maintaining cost effective and safe production of efficacious viral vaccines for human and veterinary use is often limited by the vaccine manufacturer's capacity to grow and maintain sufficient cell substrate within cGMP standards.

Most viral vaccine production operations in developing countries utilize conventional stationary disposable systems which are readily available from a number of U.S. and European manufacturers. These stationary disposable systems are not closed systems, as a result control during production can become a major issue due to inability to achieve the standardization of the yields from batch to batch.

Moreover, these systems require ready-to-use plastic disposable containers manufactured in U.S. and Europe. The disposal of these plastic culture vessels generates a waste which requires special handling, treatment and disposal, introducing additional costs.

Micro-carriers and large-scale fermenters, are the most technically sophisticated cell-growth equipment available for commercial vaccine manufacturers. Generally these systems require dedicated infrastructure to support micro-carrier or fermenter operations and maintenance under GMP conditions. These systems are usually expensive, complex and require special maintenance procedures not readily available in some developing countries.

A cost effective and efficient alternative to these systems is the Multi-Surface Cell Propagator (MSCP) which can be readily introduced to grow cell substrate from pilot to large-scale production. (See Figures 1 and 2).

The MSCP consists of rows of glass discs, mounted closely on a shaft inside a transparent glass cylinder, which allows for easy monitoring of cell attachment, growth on the discs and changes to pH. The cylinder ends are closed with steel plates which also support the inside shaft. At

the front of the cylinder, the shaft is extended to allow connection to a rotary drive. Ports at the front permit continuous exchange during the gaseous phase. Ports at the back of the cylinder are easily reached and provide access for addition of cells and medium exchange. All the ports can be adapted to allow for automatic monitoring and adjustments of the critical parameters. By varying the lengths of the glass cylinder, shaft and tie rods, MSCP vessels can provide growth areas from 7,500 to 25,000 cm2.

The MSCP offers many advantages to viral vaccine producers, particulary those production institutes located in the developing world. MSCP can provide larger cell growth capacity than the conventional systems at a substantially lower price. Operational costs are low, there is no on-going consumable requirements of imported material and the resulting plastic waste disposal needs are eliminated. Maintenance of MSCP is not complex. The equipment has a small footprint, thus freeing up laboratory space. Finally MSCP allows for cell substrate growth in a controlled closed system environment, thereby enhancing overall operational safety and facilitating cGMP implementation and compliance.

MSCP systems is used to grow primary and continuous cell substrates from mammalian, avian and fish origin for the production of human and veterinary vaccines.

Several features make the new MSCP an attractive choice for the production of a wide range of human and veterinary viral vaccines. These include:

- Low capital cost
- Low operating costs
- Small footprint, requiring minimal space
- No dedicated infrastructure requirements
- System production capacity very flexible, can be quickly adapted from pilot plant to scaled up commercial production capacities
- Efficient, safe, consistent production in a closed system
- Improved and safer control of environmental conditions
- Material and labour requirements reduced
- Easy to clean, sterilize, and maintain
- Limited generation of waste, thus decreasing plastic bottle waste disposal requirements.

In conclusion, there are many features of the MSCP system which provide significant benefits to vaccine manufacturing operations, particularly those in the developing world. The MSCP system provides biotechnology institutions the means to reduce expenditures, which often in developing countries require foreign exchange that has controlled or limited availability. The ease of monitoring and in-process adjustments in the MSCP system can increase productivity of cell substrate growth.

The MSCP's controlled, closed system improve standardization of production methods, thereby improving overall GMP compliance in viral vaccine manufacturing.

MSCP

FIGURE 1

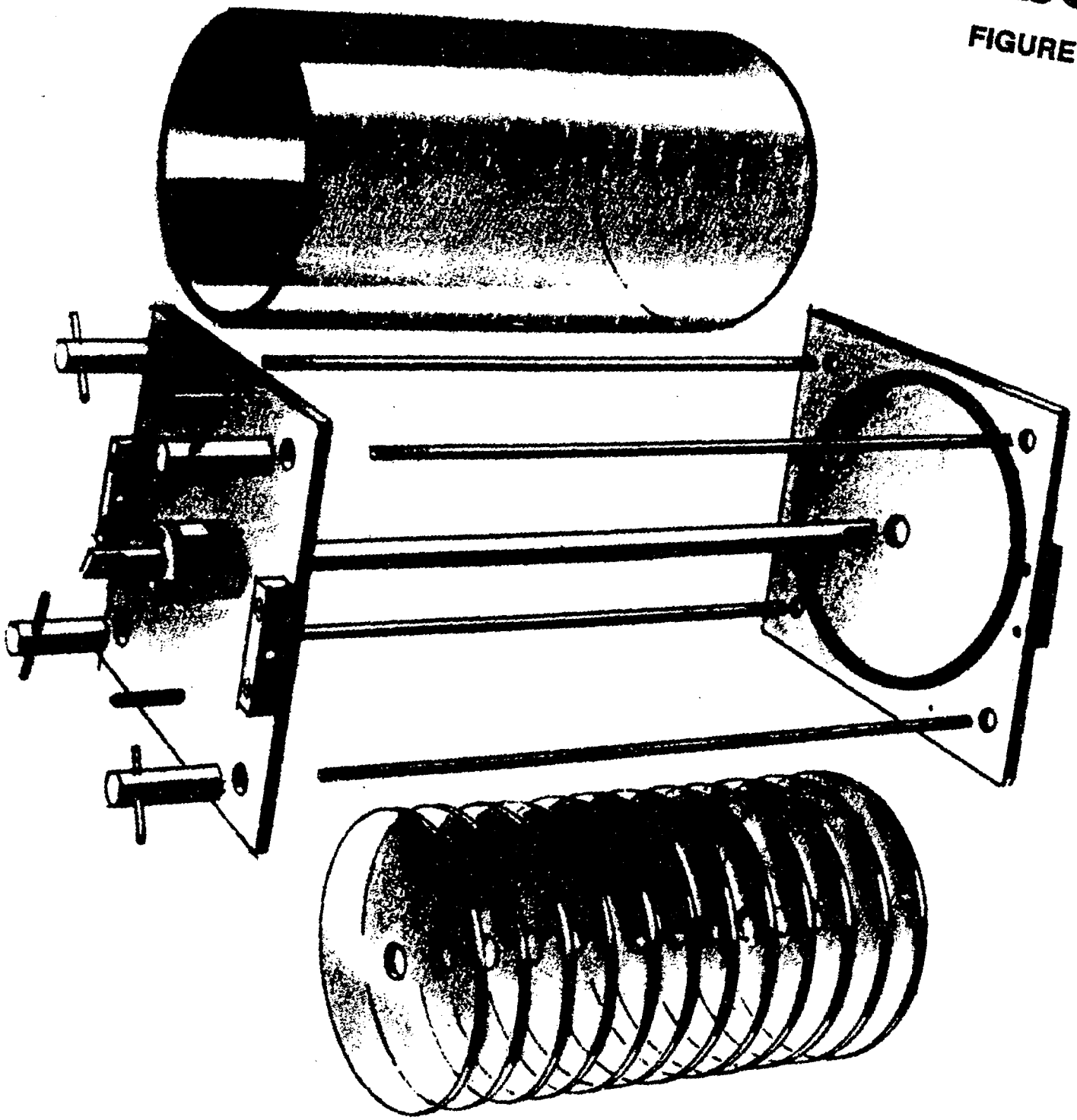
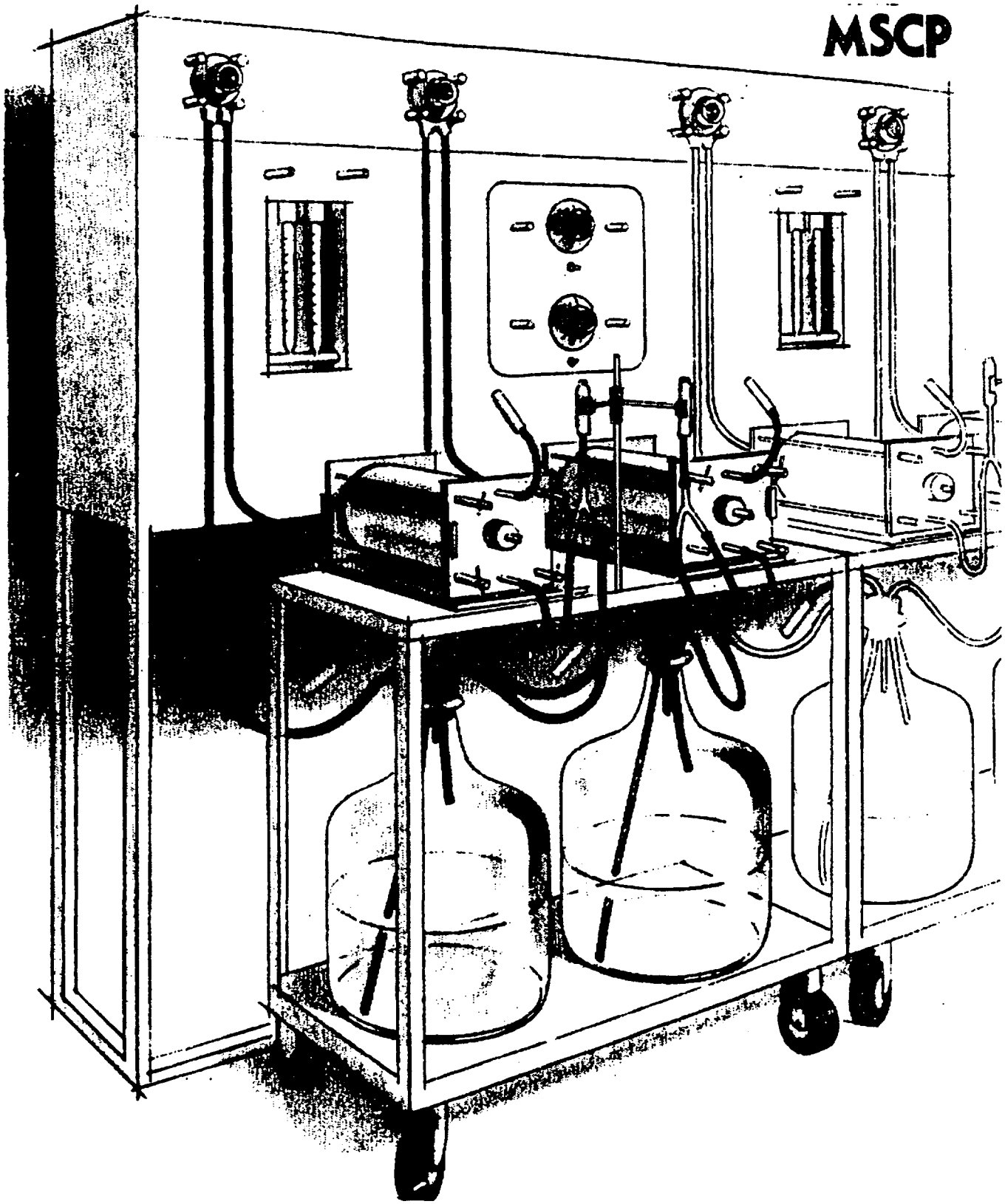


FIGURE 2

MSCP



ANNEX 10

PROJECT MANAGER'S COMMENTS TO THE REPORT

The technical cooperation programme of UNIDO in vaccine production in Cameroon started in late 1970s and aimed at the rehabilitation and upgrading of the facilities of Institut Pasteur. Since that project had not been found technically feasible, the programme was provided with a new initiative by the Presidential Decree to achieve self-sufficiency by domestic vaccine production in Cameroon. In 1983, Dr. Charles Merieux, President of the Fondation Marcel Merieux, offered technology transfer for the country during the Second Consultation on the Pharmaceutical Industry of UNIDO held in Budapest, Hungary. His advice was taken and the Laboratory National Veterinaire (LANAVET) was identified as the site of the new project. The actual work was hampered by conflicting interests of the shareholders in the selection of manufacturing equipment, but with the strong recommendation of the UNIDO Advisory Panel on Preventive Medicine further delays could be avoided. The appropriate technology of tetanus vaccine for human use was selected from the Institute HUMAN (currently HUMAN Ltd., Gödöllö, Hungary). The project was successfully implemented and the new facilities were inaugurated in 1991 by Dr. Lajos Aradi, Director of Institute HUMAN and Dr. Charles Merieux in the presence of high level officials of the Government of the Republic of Cameroon, UNIDO and WHO, Geneva.

The current project aimed at addressing the most pressing needs of the country and the regions and attempted to strengthen LANAVET to become a Centre of Excellence in vaccine production in Africa. The priority has been given to veterinary vaccine manufacture for which a business plan was proposed. The production of tetanus vaccine for human use was upgraded taking into consideration all of the citations made by a French team of auditors who visited LANAVET recently.

The strategy, which UNIDO is promoting, includes the establishment of a strong marketing unit at LANAVET, since without this capability, the sustainability of the laboratory cannot be assured. The mission of LANAVET is to become a Centre of Excellence with the objectives to have significant share of the market in Africa and to expand to Near and Middle East (globalization). These objectives can realistically be achieved if the Government of Cameroon supports LANAVET. The support can be ranged from creating an independent profit centre for vaccine manufacturing at LANAVET to privatization by a strategic partner.

UNIDO is ready and willing to share its experience and provide, if requested, its services for LANAVET. To demonstrate this willingness, UNIDO sponsored the participation of a senior level official of the Government of Cameroon in the UNIDO/International Vaccine Institute (IVI) Training Course on Effective Management of Vaccine Manufacturing at the National Vaccine and Serum Institute, Beijing, 8-13 September 1996.