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ASSISTANCE IN THE PRODUCTION OF VETERINARY DRUGS IN SADCC COUNTRIES

DP/RAF/86/012

MOZAMBIQUE

Technical report: The supply of veterinary drugs and vaccines in Mozambique*

Prepared for the Government of the People's Republic of Mozambique
by the United Nations Industrial Development Organization,
acting as executing agency for the United Nations Development Programme

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INTRODUCTION

Mozambique is situated on the South East coast of Africa between parallels 10 degrees and 26 degrees south. Its land area is approximately 800,000sq.km. and it is bordered by Tanzania to the north, to the west Malawi, Zambia and Zimbabwe and with Swaziland and South Africa to the south. To the east is the Indian Ocean. The human population is estimated at 14million (January 1986) and is projected to grow at 2.6%p.a. reaching 20million in the year 2000. Agriculture, although occupying most of the labour force, provides only a small percent of the income and has been almost universally in rapid decline over the last 10 years; this fall is paralleled in the livestock sector.

1. LIVESTOCK POPULATION AND PRODUCTION TRENDS

The national cattle herd declined from an estimated 1.4million in 1980 to 750,000 in 1986 (-45%), national beef production (through official channels) has declined from 14,700 tons in 1973 to 3,200 tons in 1985. However there was a significant increase in private sector pork production in 1985 (1,000 tons). The decline in productivity has occurred in all three market sectors (state, private and traditional). The private cattle production in particular having reduced (from 3,000 tons in 1980 to 404 tons in 1985) and the state poultry production having declined from 5,900 tons in 1980 to 565 tons in 1985.

Animal Population Statistics 1986

Year	Cattle	Sheep/Goats	Pigs	Chickens
1986	750,000	600,000	150,000	300,000

The cattle are concentrated in the two southern provinces of Maputo and Gaza, the goats are mainly in Tete province. Commercial pig and poultry production is almost entirely near population centres for reasons of transport of food stuffs and accessibility to markets. Pork production has remained between 1 and 4 thousand tons per year, but fluctuating considerably from year to year. Poultry meat production reached a peak of 6,000 tons in 1980 but has now fallen to 0.6 thousand tons in 1985.

2. NATIONAL DISEASE CONTROL STRATEGIES

Animal Diseases

2.1 Trypanosomiasis

About 80% of the land surface of Mozambique is infested with tsetse fly, Inhabame province, central Gazu and parts of Maputo and Tete provinces being free. A mild form of trypanosomiasis affects cattle in Maputo province (about 30% of the total population).

Trypanosomiasis is the major constraint to livestock throughout most of the country, affecting all domestic species, being particularly severe in pigs.

The control of tsetse fly and trypanosomiasis has long been the object of official schemes, but for a variety of reasons the progress has been restricted, especially

since the Muabsa Centre for Training and Research in tsetse and trypanosomiasis ceased operations in 1982.

The current approach to the control of tsetse and trypanosomiasis is to collaborate with the scheme co-ordinated by Zimbabwe in Malawi, Zambia, Mozambique and Zimbabwe. This scheme is based initially on surveys (both tsetse flies and trypanosomiasis incidence) to be followed by hand and aerial spraying and the use of targets to reduce fly incidence and challenge, and subsequent phases based on strategic and therapeutic use of anti-trypanosomal drugs. In the meantime the strategy is to limit the economic effects of the disease by the use of drugs as availability permits, ideally 3 doses of Samorin and one dose of Berenyl per animal per annum.

2.2 Tick-borne Diseases

Second only to trypanosomiasis in importance are tick-borne diseases. Of a former 700 dip tanks, ony 420 are still in existence, 290 are working and 130 are in need of repair. Various species of tick occur notably rphipcephalus, boophilus and amblyomma. Amblyomma is particularly significant in the South.

Tick-borne diseases occur throughout the country but differ in their importance. Babesiosis and anaplasmosis are country-wide and are regarded as the most important. Heartwater (cowdria) is of major significance where the incidence of amblyomma is high. Theileriosis occurs widely but confirmed cases of East Coast Fever or Corridor Disease are limited. The other theileria species (mutans and velifera) are of flow pathogenicity. Generally speaking the indigenous cattle are highly resistant to ticks and tick-borne diseases, but those with a higher proportion of exotic blood are highly susceptible. (These are mainly in the north of the country).

A major cause of economic loss as a result of ectoparasites is the tick damage resulting from amblyomma infestation, predisposing to mastitis in cows and sterility in bulls, as a result of the prediliction for the perineal region.

The tick control strategy was originally based on weekly dipping of cattle. However, the actual immersions are estimated to be 10-15 per head p.a. for the traditional (family) sector in the south and an estimated 16 immersions per head (p.a.) in the north, but with very large differences between districts.

In the light of the need to keep a balance between innate or acquired resistance (to both ticks and tick-borne disease) and a measure of tick control through the use of acaricides, the objective is to achieve a cost-effective balance through dipping, varying the frequency of immersions regionally (North and South) and according to tick burden, disease incidence, climate, etc. In these conditions, a national average of immersions per annum per animal would probably not exceed 25, weekly immersions being given in the wet season (4 months) and once fortnightly in the dry season.

Arsenic is no longer used, toxaphene is little used and organophosphorous compounds and synthetic pyrethroides are preferred. There is considerable interest in Bayer's pour-on (Flumethrin), in view of the lack of functioning dip tanks and the relative unimportance of the control of tick-borne diseases as an objective.

2.3 Reproductive Disease

Reproductive diseases generally are regarded as the third most serious threat to livestock in Mozambique. The calving index is estimated at only 0.4% and calf mortality is at least 10-15%. Of the predisposing causes, nutrition and management are ranked first, followed by internal parasites. Then come bacterial infections (including brucellosis), specific causes of abortion such as ECF and FMD, tick

damage causing sterility in bulls etc. The brucellosis control policy is to vaccinate female calves at 4-8 months of age.

2.4 Endoparasites
Insidious losses from helminths and fasciola are widespread and largely untreated. Fascioliasis varies greatly in incidence.

2.5 Miscellaneous Bacterial Disease
These too are widespread and, mostly, untreated.

2.6 Foot and Mouth Disease
FMD occurs sporadically south of the Limpopo river where it is believed to spread from the Kruger National Park. Occasional outbreaks of type O disease in the Zambesi Basin would suggest that a low enzootic situation probably exists. The strategy is to apply prophylactic vaccination twice a year, the great majority in the south of the country, some 20,000 animals being vaccinated in the Zambezi province also. This prophylactic use of vaccine is combined with other measures such as stand-still, quarantine and additional ring vaccination in the event of an outbreak.

The FMD control strategy is part of a regional project funded by ADP/ADF.

2.7 Rabies
Rabies is widespread in urban dog populations and the reported incidence in humans is increasing (over 100 cases a year). The control strategy is to vaccinate dogs annually and to destroy strays. In fact, resource limitations mean that insufficient animals are vaccinated (flury vaccine).

2.8 African Swine Fever
This is epidemic in Angona. Movement restrictions are in force. There is no treatment.

2.9 Newcastle Disease
Newcastle is epidemic throughout the country and causes serious losses. Vaccination with the Kamorav strain is practised.

2.10 Anthrax
There is little evidence of anthrax in Mozambique but vaccination is practised.

2.11 Blackquarter
Blackquoter is sporadic and believed to be localised.

2.12 Tuberculosis
Surveys would suggest that TB is widespread. Bluetongue, Lumpyskin - sporadic but infrequent.

3. ORGANISATION OF VETERINARY SERVICES

Veterinary activities and animal production are divided into three: INVI, research, vaccine production, quality control and diagnosis. DINAP Field Services, nutrition production and administration. IREMA Animal Production.

A good infrastructure exists in principle in the extension services but shortage of trained personnel, transport, repairs to dip tanks and lack of medicaments, compounded by the security situation have led to its virtual collapse.

Worst of all, the dipping programme, on which most animal health strategies are hinged, is largely inoperable.

4. VETERINARY DRUG AND VACCINE MARKET (1985/86) AND ESTIMATED FUTURE REQUIREMENTS (1990 and 2000)

4.1 The Mozambique Veterinary Market had been estimated as follows:

	Value US$			
Year	Veterinary Drugs	Veterinary Vaccines	Ectopara-siticides	Total
1981	1,580,000	121,229	2,200,000	3,901,229
1982	1.210,000	185,123	250,000	1,645,123
1983	1,800,000	68,351	275,000	2,143,352
1984	2,000,000	87,267	750,000*	2,837,267
1985	200,000	67,084	170,000	437,084
1986	50,000	37,845	-	87,854

* Most lost in a fire.

The approximate breakdown of Veterinary Drugs is:

Trypanocides	25%
Anthelmintics	15%
Antibiotics	10%
Feed Supplements	25%
Biologicals (FMDV)	15%

All purchases are made by government tender of generics, placed by MEDIMOC, the para-statal drug importing agency.

However, since 1973 no funds have been allocated by the Government for drug purchase and only a donation in 1984 allowed any purchases to be made in that year and subsequently. Local production of toxaphene is at a halt for lack of drums. There is hope of aid donation for 1986 (from Italy).

4.2 Estimated Requirement for Drugs

These are shown in the upper half of Annex 1. Given foreign exchange and a solution to the security problem the maximum off-take would be no higher than the 1981 level (see 4.1) in view of the disastrous drop in the cattle population.

4.3 Current Use and Estimated Optimal Requirements for Vaccines

These are shown in lower half of Annex 1. With the exception of regional strategies for FMD, tsetse, and tick and tick-borne disease control, no increased drug usage over the 1981 level can be envisaged.

4.4 Marketing and Distribution

All drugs imported by MEDIMOC are supplied to the Veterinary Department who control their distribution and use.

4.5 Approved Drug List

Recently a list of approved drugs has been drawn up which will be the code for drug purchases in the future.

5. CONSTRAINTS ON DRUG AND VACCINE USAGE

Even given foreign exchange for drug and vaccine purchase, there are overwhelming constraints on drug usage, notably:

5.1 The security situation.

5.2 Veterinary infrastructure and extension services.

5.3 Trained personnel.

5.4 Transport.

5.5 Communications.

5.6 Equipment.

5.7 Functioning dip tanks.

5.8 Diagnostic services.

6. PRE-REQUISITES FOR INCREASED DRUG AND VACCINE USAGE

(See 5 above)

7. CONSIDERATIONS FOR LOCAL MANUFACTURE

7.1 Pharmaceuticals

Mozambique-Maputo-Pesticides

Visit to Boror Industrial Machava - Maputo

The company has a very well laid out plant for producing pesticides. Safety has however been neglected and the products produced, including Toxaphene which is solvent based, are produced in an area which has no flame-proof electrics and which has no fire precautions of any kind. The solvent store and the finished goods store are of brick construction and do not conform to regulations for storage of imflammable materials. There are no fire precautions in the storage areas.

Production is in 2000 litre batches with a capacity of 800,000 litres per annum.

Production in figures:

1985 - 300,000 litres (various formats
1986 - 100,000 litres of pesticides)

No Toxaphene based dips had been produced in 1985/86 due to drum problems for storage of finished goods.

There is no analysis of raw materials, original certificates from suppliers are accepted. Samples are retained for 2 years. Final analysis is carried out at the plant in a control laboratory. Copy certificates are issued. Plant - 2000 litre Stainless Steel tank with propellor stirrer. Centrifugal pump for circulation through pipework bulk fill into drums on scale principle.

7.2 Biologicals

Vaccine Institute - Maputo

The Institute and support building are on the outskirts of Maputo on a piece of land 120,000sq.mtrs. The land has adequate storm drainage and sewage drainage and is supplied with water from the local authority supply and from an artesian well supply. There are two storage tanks of approximately 25,000 litres each; one to store water from the local supply, the other to store water from the well supply. Electricity supplies from the local authority are adequate and seem to be reliable. A standby generator of capacity 108 KVA has been installed. There is adequate security at the site which is bordered by a perimeter fence of concrete posts topped by barbed wire. The infill of the fence is of the chain link pattern. The site is flat and apparently is not susceptible to flooding. There is no fire-hydrant system.

7.2.1 Buildings on site are as follows:-

1 - Three-story multi-purpose production/diagnosis/control building.
1 - Similar building which is part of the University Veterinary Medicine Scheme.
2 - Animal houses for Guinea-pigs and rabbits.
1 - Mouse breeding unit.
1 - Chemical store.
1 - Glassware store.
1 - Packing material store.
4 - Cold stores for storage of bulk vaccine before and after test.
1 - Serology building.
1 - Laundry building.
1 - Set of garages.
1 - Offices and meeting rooms, miscellaneous.
1 - Auditorium under construction.
1 - Gatehouse

7.2.2 General Conditions

Most of the buildings are 20 years old and considering this they are in reasonable condition. The main building for production/diagnosis and control requires repairs to floor coverings, some painting and general refurbishing on finishes. Sadly this building has no central air conditioning system which could segregate different departments for air flow and thus prevent cross contamination. There is also no filtration system between the various departments which is essential for safe working. The lighting level in this building is low for the type of work involved. There is no control over effluent leaving the building which is essential considering the range of viruses being worked in the building. It is clear that the building is not compatible with the different types of work involved. There are only four fire extinguishers in the building which is inadequate. To summarise, the building does not conform to modern requirement but could be refurbished and modified to cope with a rationalised production/diagnosis programme.

The animal houses are of a minimum design and quite inadequate. Effluent is neither monitored or treated and the lack of ventilation and filtration emphasise the bad conditions. It would be more economic to build new accommodation than to try to adapt the existing to modern requirements.

Stores in general are adequate in size but could be organised differently to try to relieve the logistics problems. Office accommodation and meetings room, etc. appear to be adequate.

Central stores are new, are functioning and appear to be able to cope with the work load. Their location however is poor and it is necessary that the filling unit for vaccines be moved to a closer proximity to the cold stores. The cold stores are

connected to the emergency generator which is started automatically immediately following a cut in power.

7.2.3 Plant

This is mainly of Portuguese, British and some local origin, varying from quite new to 20 years old. One of the main failings is the lack of temperature recorders on both cold stores and hot rooms for determination of temperatures within the rooms on a permanent basis. Without these, temperatures during silent hours are unknown. A fair proportion of plant is broken awaiting spare parts. As an indication, of eleven autoclaves only seven are operational, of the five freeze drying units only two are functional. Of the two boilers only one is functional. As the processes are not plant orientated the list of plant is small and is as follows:-

7.2.4 Boiler House

1 - Vaporax Boiler 1600kg per hour from and at 100 degrees Celsious - Functional.
1 - Farra Boiler 600Kgs per hour - Functional.
1 - Mascarini 150L. per hour still for distilled water - Non-functional
1 - Rotterman Deioniser for Boiler Feed Water Tank - Functional.
1 - Rotterman Still 15L per hour electrically operated - Functional.
1 - Storage tank for boiler feed water - Functional.
1 - Oil-fuel storage tank - Functional.

7.2.5 Preparation Area

11 - Autoclaves Portuguese origin - Seven functional.
2 - Bottle Washing Troughs - Functional.
1 - Deep freeze - Functional.
1 - Incubator - Functional.

7.2.6 Laboratories Various

1 - Roller bottle apparatus - Functional.
12 - Microscopes
3 - Fume cupboards - Functinal.
18 - Deep freeze - Functional.
6 - Refridgerators - Functional.
1 - 9000 Egg cap incubator - Functional.
26 - Laboratory incubators.
1 - Bottle shaker filling machine - Functional.
3 - Capping machine - Functional.
2 - Lab. test ovens - Functional.
2 - Lamina flow hoods vertical - Functional.
6 - Lab. centrifuges - Functional.
5 - Freeze driers - Two functional.

7.2.7 Maintenance Staff

Comprises of 2 electricians who have to service all equipment but who occasionaly sub-contract out to near-by companies. A mechanical fitter should be recruited to carry out mechanical repairs.

7.2.8 Staffing, training, administration

	Cult bed	Production Bacter- iology	Viro- logy	Diagnostic work Bacter- iology	Viro- logy
Professional					
Local	-	1	1	-	1
Expatriated	-	1	-	-	-
Assistant					
High Level	-	-	1	1	1
Medium Level	1	2	1	1	1
Basic Level	7	3	4	1	2
Cleaner	-	1*	1+	1*	1+

Cleaners marked with * and + are working for diagnostic and production departments.

Training: in 1985 training course was held for laboratory workers, the teachers were the professionals and high level assistants of the Institute. Ten students finishing 6th class of primary school were taught during one year, and were qualified as assistants of basic level, 12 students finishing 9th class of primary school after 3 years attendance became assistants of medium level. No course started in 1986.

7.2.9 Communication and Distribution. On the base of the request of the provinces targets of production are given to the producers via the Director of the Institute as several times this procedure caused delays and the requisition and reception of materials needed for production is a slow process, the producers themselves used to make their own plan based on the statistic of the past years, in or excluding doses not included into official target received later.

7.2.10 Distribution is made in the same manner as mentioned before but despatch is made on written request of provinces. Packing material: cardboard boxes of different size with cardboard separators, strapped. Transport used: by car (for provinces at neighbourhood of laboratory if conditions of safety permits it), by air for other provinces. The distinctive labels indicating biologicals/fragile material are unobserved by transporters, damage/delay occurs frequently.

7.2.11 Production of biologicals

For products and specification see Annex 2. All of the standards (protocols of production Annexes 3-5) of producing viral vaccines are based on embryonated hens' eggs, are considered out of date, and only one of the bacterial biologicals (tuberculin, Annex 6) meets the recently introduced production technology using stationary cultivation methods on solid or liquid culture media. The cultivation of Brucella S19 (Annex 9) is carried out in a horizontal shaking machine, described by Van Drimmelen about 20 years ago.

General standards of master seed, seed and production cultures and batches are established in the right manner for identification, purity, freedom of abnormal toxicity, safety, potency and labelling (Annexes 3-12).

Discussion

It is clear from production figures 1984, 85 and 86 that during 1985 production activities declined and in 1986 little or nothing was produced. The prime reason is lack of foreign exchange, but there has also been a serious decline in all laboratory activities as well.

8. RECOMMENDATIONS

8.1 The strategy must be to try to maintain such expertise in biological production and control that still exists in the field of bacterial vaccines, concentrating on the following:

8.1.1 Anthrax	5×10^6)	MAXIMUM
8.1.2 Blackquarter	2×10^6)	CAPACITY
8.1.3 Brucella	0.5×10^6)	PER
8.1.4 Brucella Antigens	2×10^6)	ANNUM
8.1.5 Tuberculin	2×10^6)	

The production of egg origin viral vaccines should cease.

8.2 A smaller purpose built bacterial vaccine plant based on classical methods consistent with the international standards should be constructed on the site adjacent to the present building when local conditions permit.

8.3 Some suitable plant, equipment and essential services can be transferred from the present building.

8.4 New animal facilities for breeding, maintaining and for test purposes must be provided.

8.5 Quality control facilities to meet European Pharmacopoein requirements must be established in the existing building.

8.6 Outside expert assistance will be required in the design, construction and commissioning phases.

Further outside technical assistance will be needed to assist in on-site training and to ensure continued reliable production.

8.7 Budget figure for proposed new project, including laboratories, animal facilities and refurbished control laboratory - US $ 3.5million.

8.8 Project Time
It is estimated that the project will take not less than two years from time of approval.

8.9 Emergency Plan
The INVI are preparing an emergency plan to enable the laboratory to maintain production in the existing building.

It is strongly recommended that a plan be implemented so as to retain such expertise and discipline that does exist pending the construction and commissioning of the new facilities and this will depend on factors entirely outside the Veterinary Department control.

ANNEX 1

VETERINARY DRUGS AND VACCINES USED (1986) AND ESTIMATED OPTIMAL REQUIREMENTS (1990 and 2000)

DRUG/BIOLOGICAL	YEAR 1986 UNITS	1986 VALUE US$000's	1990 UNITS	1990 VALUE US$000's	2000 UNITS	2000 VALUE US$000's
Ectoparasiticides			500,000	261	500,000	712
Anthelmintics		10		50		100
Antibiotics		15		50		100
Antiprotozoons		15		400		600
Feed Additives		10		50		50
SUB-TOTAL		50		811		1562
Biologicals						
FMD	30,000	30	900,000	300	900,000	300
Rinderpest						
Rabies	20,000	2	100,000	20	200,000	40
Poultry vaccines						
Other viral vacc. (Rift Valley Fever African Horse Sickness etc)	100,000	5	1,000,000	20	2,000,000	40
Blackquarter	0	0	500,000	50	500,000	50
Anthrax	0	0	300,000	30	300,000	30
Brucella	0	0	20,000	5	30,000	75
Pastuerella	0	-	-	-	-	-
Botulism						
Others	10,000	1	20,000	2	30,000	3
SUB-TOTAL		38		427		470.5
TOTAL		88		1238		2032.5

These figures are highly speculative as they depend on stability in the country and re-establishment of the veterinary services and disease control campaigns.

ANNEX 2

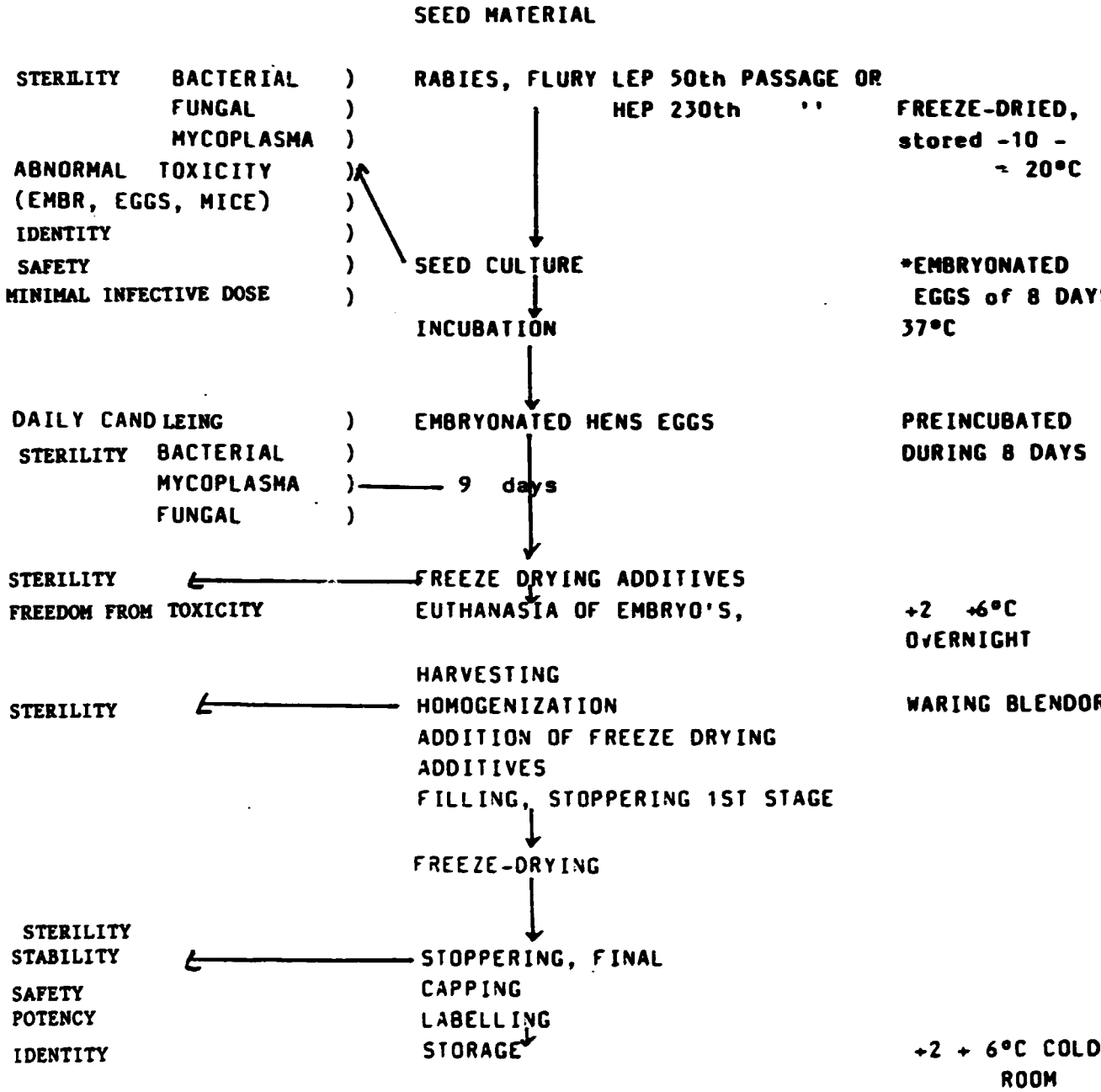
Products and specifications

	NAME	STRAIN USED	CULTURE MEDIUM/TIME
Bacterial vaccine	Anthrax (Living Spores, saponin adjuvant)	Prod*: 34F2(STERNE) Chall**: 17JB(Pasteur)	Brewer Agar 4-5days
	B 19 (Freeze Dried)	Brucella abortus	Yeast Extr, liquid
	Black Quoter (Anaculture, Alum adjuvant)	Prod: Locally isolated 3 strains (Nos 2,16,18) Chall: Locally isolated 1 strain(No 9)	Liver Broth with glucose 5 days Hiblers Medium
	Pulpy Kidney	Prod: Obtained from VRI Onderste-poort	Meat Broth with Dextrin
Bacterial Antigen	Tuberculin, mammalian and avian, PPD	AN5 D4	Dorset-Henley 12 weeks 8 weeks
	Brucella antigen for tube agglutination	Brucella abortus 1119-3	Potato agar 3 days
	Fowl typhoid antigen	Salm. Gallinarum/. Pullorum	Nutrient agar 3 days
Viral Vaccine	Rabies (Freeze Dried, living)	Flury LEP. HEP egg	Embryonated eggs
	Fowl pox (Freeze Dried, living)	Beaudette	" "
	Newcastle disease (Freeze Dried, living)	La Sota, Kamarov	" "

* Production
** Challenge

ANNEX 3

RABIES, VACCINE



NB*=MDV (Minimal Disease Free) eggs are used

FOWL POX VACCINE

SEED MATERIAL

BEAUDETTE VIRUS STRAIN — FREEZE DRIED, STORED AT -10 - -20°C

↓

MASTER SEED CULTURE — *EMBRYONATED HENS EGGS

INCUBATION — 37°C

6 days

SEED CULTURE — *EMBRYONATED HENS EGGS

36°C

CANDLEING)
STERILITY BACTERIAL)
MYCOPLASMAS)
FUNGAL)
SALMONELLA)
ABSENCE OF ABNORMAL)
TOXICITY)
EMBR, EGGS)
CHICKEN, 1 DAY OLD)
IC. INCULATION)
IM. ")

INCUBATION
5 days

MINIMAL INFECTIVE DOSE ON EMBR. HENS EGGS

PRODUCTION INOCULATION — EMBRYONATED HENS EGGS 11 DAYS OLD

DAILY CANDLEING

INCUBATION — 36°C

6 days

EUTHANASIA — +2 +6°C

HARVESTING — NEGATIVE PRESSURE

HOMOGENIZATION — WARING BLENDOR 3 MIN

FILTRATION

ADDITION OF ANTIBIOTICS + FREEZE DRYING ADDITIVES — STREPTOMYCINE, PENICILLI KANAMYCINE, PEPTONE & LACTOSE SOL.

STOPPERING 1st phase

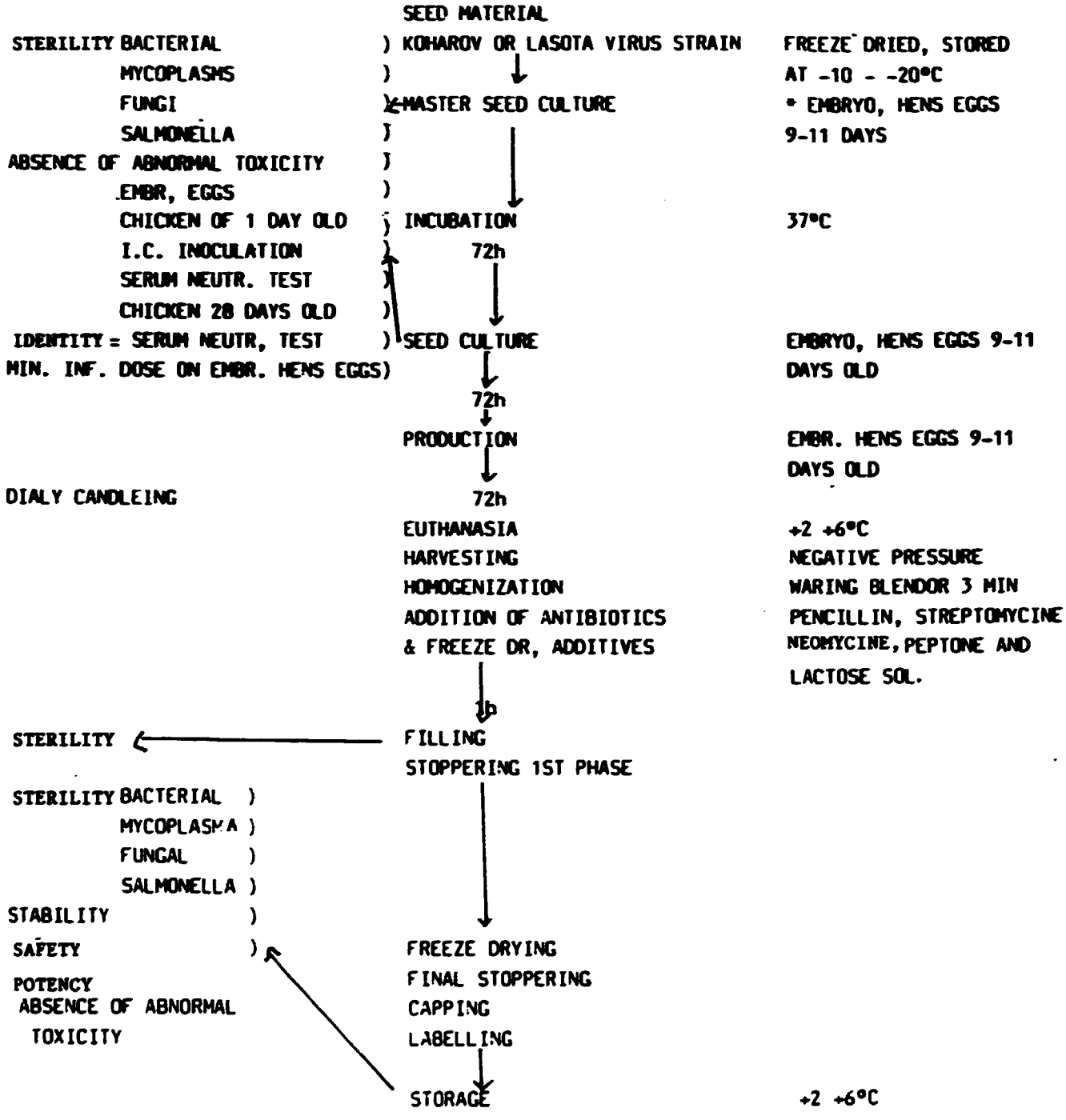
STERILITY BACTERIAL)
MYCOPLASMAS)
FUNGI)
SALMONELLA)
POTENCY, SAFETY)
STABILITY)
SAFETY IN CHICKENS 4 - 6)
WEEKS OLD)
IP MICE)
IP GUINEA PIGS)

FREEZE-DRYING
FINAL STOPPERING
CAPPING
LABELLING

STORAGE — +2 +6°C

ANNEX 5

NEWCASTLE VACCINE



NB* = MDV (Minimal Diseases Free) eggs are used.

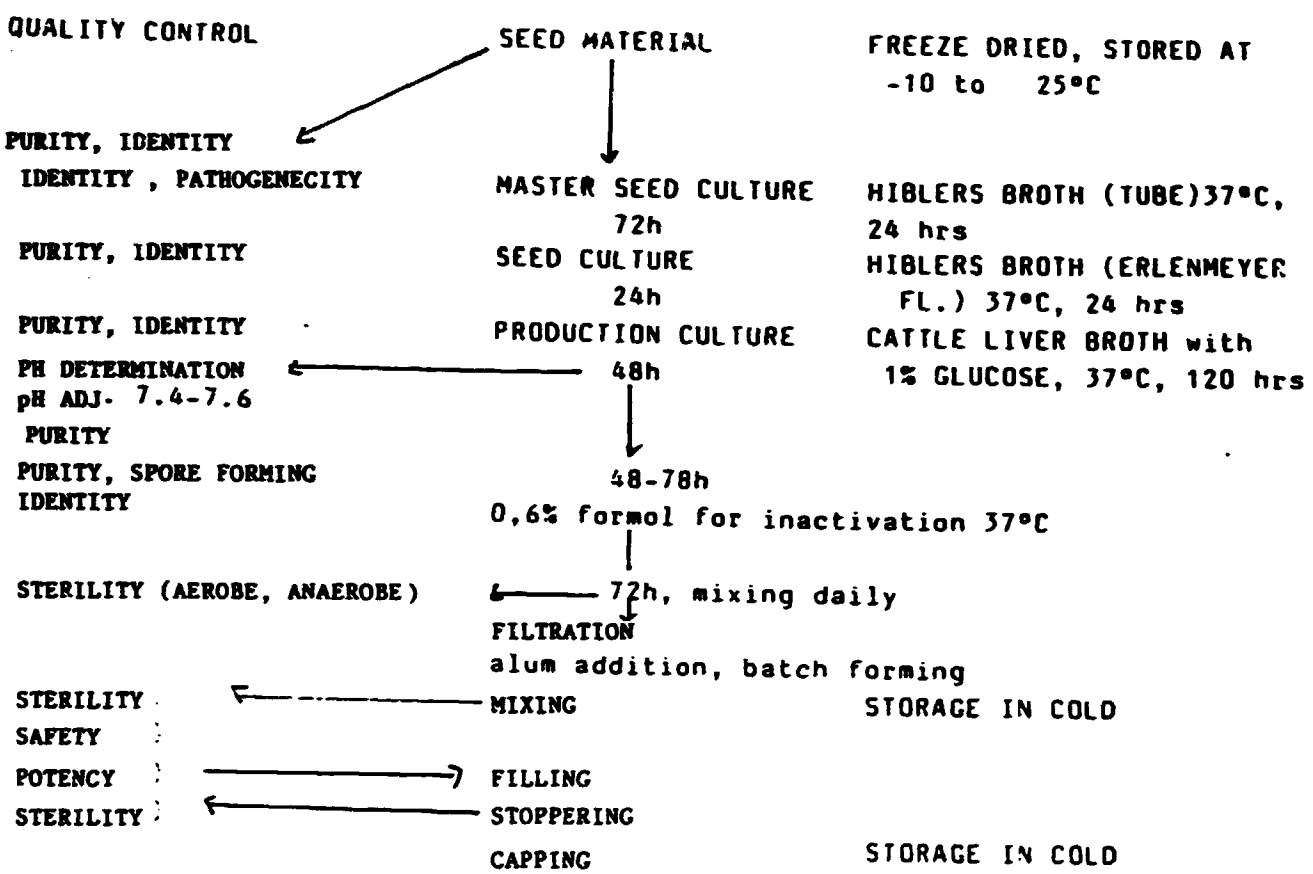
TUBERCULIN, MAMALIAN AND AVIAN

	SEED MATERIAL M. tuberculosis ANS (Bovine) D 4 (Avian)	Stonebrink, Lnewenstein-Middlebrook 7H10 Agar Dorset-Henley Agar at -10 to -20°C
PURITY ←	PRIMARY MASTER SEED CULTURE	SEE ABOVE, 37°C
	14-21 DAYS	
PURITY IDENTITY	SECONDARY MASTER SEED CULTURE	MIDDLEBROOK 7H10 AGAR
	7-10 days	
	FILLING THE SLANT UPTO THE MIDDLE	DORSET-HENLEY CULTURE MEDIUM
	7-10 DAYS	
	FINE PELLICLE ON SURFACE	
	SEED CULTURE	DORSET-HENLEY IN ERLENMEYER
	7-10 DAYS	
PURITY ←	PRODUCTION CULTURE	DORSET - HENLEY IN PENCILLIN FLASKS, 37°C
IDENTITY PURITY (VISUAL) ←	10-12 weeks (BOVINE) 7-10 weeks (AVIAN)	
PURITY (VISUAL) IF NECESSARY USING CULT, MEDIA	KILLING LIVE MYCOBACTERIA	3h, 100°C, STEAM
	24h	REST PERIOD, ROOM TEMPERATURE
	SEPARATION & FILTRATION	BUCHNER FUNNEL, PAPER PULP NEGATIVE PRESSURE
	PRECIPITATION	10% TRICHLOROACETIC ACIC OF 40%
	2½h	
	1ST WASHING OF PRECIPITATE with	1% " "
	GRAVITATION	
	2h	
	2ND WASHING OF PRECIPITATE with	1% THRICHLERACETIC ACID
	GRAVITATION	
	16h	
	3RD WASHING OF PRECIPITATE with	" " "
	CENTRIFUGATION	
	30 min	2000 - 2500 RPM
	FLOCCULATION OF TUBERCULO-PROTEIN	NaCl sol of 10%
	CENTRIFUGATION	2000- 2500 RPM
	30 MIN	

	HOMOGENIZATION	
pH CONTROL & ADJUST TO 7.0	DISSOLUTION	BUFFERS, DIST WATER, ANTIBACT SOL.
	↓	
STERILITY TEST	STERILE FILTRATION	STERILE FILTER PADS
TUBERCULOPROTEIN	STORAGE	COLD +2 - +4°C
	↓	
STERILITY ———	FINAL DILUTION	GLYCERINATED-PHENOLATED SALINE SOL
TOXICITY	↓	
POTENCY	FILLING	
	STOPPERING	
STERILITY	CAPPING	
TOXICITY	LABELLING	
POTENCY		

ANNEX 7

BLACK-QUARTER VACCINE



ANNEX 8

ANTHRAX VACCINE

QUALITY CONTROL PURITY, IDENTITY	SEED MATERIAL B.anthracis 34F2	FREEZE DRIED, STORED AT -10 to - 15°C
	24h	
PURITY, IDENTITY SPORE FORMING	MASTER SEED CULTURE	BREWER AGAR (tube) 37°C
	24h	
	WASHING CULTURES	BREWER AGAR (MASON tube) 37°C LIVER EXTRACT of 1%
PURITY	SEED CULTURE	
	24h	STORAGE IN -4 to +8°C
	PRODUCTION CULTURE	150 ml BREWER agar/1l ROUX flasks
	72 - 96h	
SPORE FORMING PURITY (AEROBE, ANAEROBE)	HARVESTING	PHYS SALINE/ROUX Flask
	48h	STORAGE IN +4 to + -8°C
	BULK FORMATION, FILTRATION/GAUZE ADDITION EQUAL PART OF GLYCERINE, MIXING	STORAGE IN +4 to +8°C
	10 DAYS SHAKING DAILY	STORAGE ROOM TEMPERATURE (22-24°C) IN DARK
PURITY SPORE COUNT (24h) TRYPTOSE AGAR IN PETRI DISH	SAMPLE	STORAGE +4 to +8°C
	ESTABLISH FINAL DILUTION	PHYS, SAL 50% GLYCERINE 50% SAPONINE, PURE, WHITE 0,12% pH 7.0
PURITY SAFETY POTENCY	DILUTION FINAL	
	FILLING STOPPERING CAPPING	
PURITY	LABELLING	STORAGE IN COLD

ANNEX 9

BRUCELLA VACCINE

SEED MATERIAL — FREEZE DRIED, STORED AT -10 -15°C

(Brucella abortus, S 19)
st. physiological solution — POTATO-AGAR TUBES
96h

PURITY
IDENTITY
MISTER SEED CULTURE — POTATO-AGAR TUBES
48h

PURITY
IDENTITY
DISSOCIATION
SEED CULTURE — POTATO-AGAR (MASON) tubes
48h

IDENTITY
DISSOCIATION
HARVEST: BUFFERED PHYSIOLOGICAL SOLUTION
48
PRODUCTION CULTURE — 450ml LIQUID YEAST EXTRACT CULTURE MEDIUM/ 4L. ROUX FLASK HORIZONTAL SHAKING 37°C
66 - 72h
STORAGE +4 to +8°C
24h

PURITY
DETERMINATION OF VOLUME OF BACT. SUSPENSION
SUBGROUPS
ADDITION OF 10% CARBOXYMETHYLCELLULOSE OF 0.6 % — STORAGE +4 to +8°C

24h

PURITY
SUPERNATANT DRAINED
SEDIMENT COLLECTED, AND 25% FREEZE-Drying sol added — ASCORBIC ACID, 25%
THIOUREA 1,25%
SACCAROSE 25%

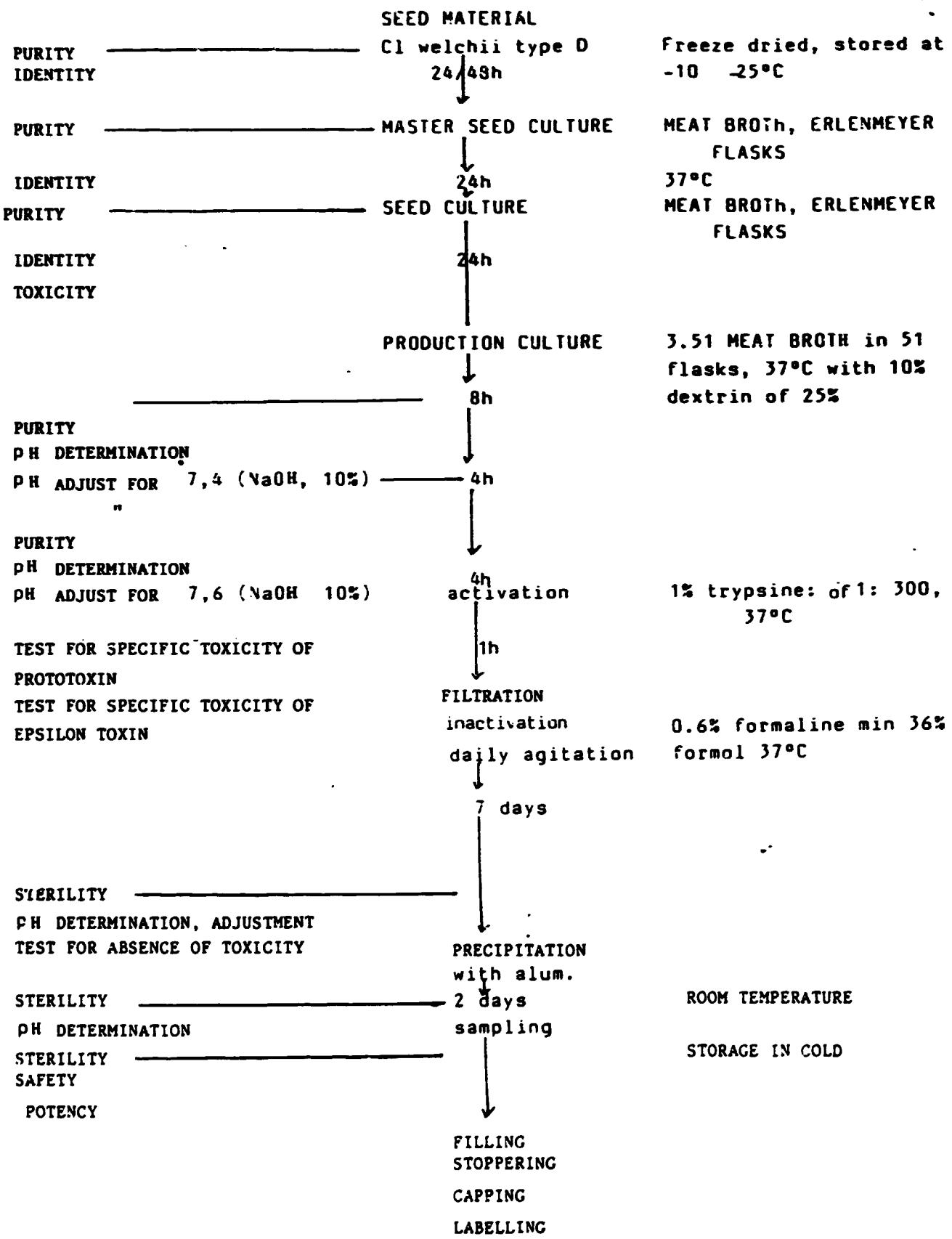
FILLING, STOPPERING

FREEZE DRYING

24h

PURITY
VIABILITY
SAFETY
DISSOCIATION
CAPPING
LABELLING — NITROGEN ATMOSPHERE
STORAGE +4 to +8°C

PULPY KIDNEY VACCINE



BRUCELLA ABORTUS AGGLUTINATING ANTIGEN

	SEED MATERIAL Brucella abortus 1119-3	FREEZE-DRIED, STORED AT -10 - -20°C
	↓	
PURITY IDENTITY	MASTER SEED CULTURE 72 - 96h	37°C POTATO AGAR TUBES
	↓	
PURITY IDENTITY	SEED CULTURE 48h	37°C POTATO AGAR TUBES [MASON]
PURITY IDENTITY	HARVESTING 48h	PHYS. SALINE. SOL.
	PRODUCTION CULTURE	37°C, 150 ml POTATO AGAI IN ROUX FLASKS OF 1 LITI
	↓	
PURITY	72h DISCARD RESIDUAL OF SEED,	
PURITY IDENTITY DISSOCIATION	HARVESTING, SUB-GROUPS ↓ 5 days	PHYS, SALINE SOLUTION STORAGE AT +2 +6 °C
	↓	
THERMOAGGLUTINATION STERILITY IDENTITY	INACTIVATION 70 min	95°C WATER-BATH + 0,5% PHENOL
	↓	
	STANDARDIZATION	INTERNAL STANDARD SERUM NATIONAL STANDARD ANTIGE
	↓	
STERILITY IDENTITY STABILITY	DILUTION	PHYS. SAL. SOL. with 0,5% PHENOL
	↓	
	STORAGE	+2 +6°C
	↓	
STABILITY STERILITY IDENTITY	FILLING STOPPERING CAPPING LABELLING	
	↓	
	STORAGE	+2 +6°C

ANNEX 12

FOWL TYPHOID ANTIGEN