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ASSISTANCE IN THE PRODUCTION OF VETERINARY DRUGS IN SADCC COUNTRIES

DP/RAF/86/012

LESOTHO

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

Prepared for the Government of the Kingdom of Lesotho
by the United Nations Industrial Development Organization,
acting as executing agency for the United nations Development Programme

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INTRODUCTION

Lesotho is situated in the mountainous region of Southern Africa, 31^{o}-38^{o} South, and is entirely surrounded by the Republic of South Africa. The topography is dominated by a number of high mountain ranges - up to 12,000 feet above sea level, even the lower plains being some 5,000-6,000 feet above sea level. As a result of this, the climate is essentially temperate.

The land area is about 30,344 sq.km.

The human population is estimated at about 1.5million with a growth rate of about 2.3% p.a.

1. LIVESTOCK POPULATION AND PRODUCTION TRENDS

Sheep	1.2×10^6
Goats	0.8×10^6
Cattle	0.5×10^6
Pigs	30,000
Chickens	1×10^6
(Layers 8,000)	
(Improved 35,000)	
Dogs	165,000

In none of the livestock sectors is there a trend towards increased numbers. The over-riding problem in Lesotho is of soil erosion and the low proportion of the land area which is suitable for agriculture.

There is, however, a policy of improving the productivity of livestock, thus the importation of Merino sheep, Angora goats, Brown Swiss and Freisian cattle are permitted.

The great majority of livestock are still kept in traditional systems, but the government has plans to develop poultry (meat and eggs), dairy production and pig production.

Of more significance is the plan to improve the production of wool and mohair in the traditional sector. This will be combined with a plan for extensive livestock production aimed at revegetation, controlled grazing and the control of stocking densities.

2. NATIONAL DISEASE CONTROL STRATEGIES

The most important disease strategies are to prevent the introduction of animal diseases, to control existing disease and to provide a clinical service through the country.

2.1 Sheep Scab. Sheep scab as a disease and the campaign to control it are completely dominant in veterinary activities in Lesotho. The disease was re-introduced from RSA in 1975 and since then the control of it has been the main preoccupation of the Veterinary Department in Lesotho. All sheep are dipped twice at an interval of 10-14 days between January and March. Dipping is controlled by Livestock Assistants using diazinon by a constant replenishment system.

There are 202 dipping tanks, 80% of them in working order. Eradication has not been achieved, possibly because of incomplete dipping, mising some animals or re-introduction via uncontrolled movements of animals across the border. The disease is notifiable and must be reported. Outbreaks are treated with Ivermectin (2 injections at 7 day intervals) with apparently good results. It is estimated that half the resources and cost of the veterinary department are devoted to this one disease.

2.2 Rabies. Rabies was introduced in 1982 and has remained endemic. The policy is to vaccinate and provide certificates for all dogs with a vaccine protecting for 3 years. However, the policy of charging the owner 1 Rand for vaccination has resulted in a reduction in the use of vaccine (only 20,00 doses in 1985) and an increase in human cases (16 in 1985). The official estimate of dogs in Lesotho is 160,000 but the true figure is probably much higher.

2.3 Newcastle Disease. NDV is endemic and a serious cause of losses in poultry. La Sota vaccine is produced locally, currently 3×10^6 doses p.a.

2.4 Blackquarter - local limited incidence.

2.5 Anthrax - absent.

2.6 TB - absent.

2.7 Brucellosis. Rare. Reactors are slaughtered.

2.8 African Horse Sickness, rare. Animals are vaccinated.

2.9 Blue tongue. Sporadic. Vaccine is used.

2.10 Ticks and tick-borne disease. Ticks are not of major importance. Anaplasmosis and pyroplasmosis cause losses, especially at the end of the winter.

2.11 Helminthiasis. This disease is second only to sheep scab in importance. Fluke and roundworms are both widespread and cause heavy losses especially in young lambs and kids.

3. ORGANISATION OF VETERINARY SERVICES

The services are headed by a Director of Veterinary Services, District Agricultural Officers, senior Livestock Attendants, and Livestock Improvement Centres staffed by Livestock Attendants.

There are also 7 veterinary clinics. The key staff are the Livestock Attendants who are responsible for organising disease control policies at the ground level.

4. VETERINARY DRUG AND VACCINE MARKET (1985-86) AND ESTIMATED FUTURE REQUIREMENTS

4.1 The Veterinary Market (1985) is broken down as follows:

Product Groups	Unit	Value US $	%
Acaricides (mainly diazinon)	11,200 litres	115,897	43
Anthelmintics (mainly Valbazan)	-	108,394	40
Minerlas etc.	-	4,972	2
Antibiotics	-	21,645	8
Antiprotozoons	-	1,157	0.5
Vaccines Rabies	20,000 doses	8,000	
Blackquarter	67,500 doses	2,700	
Bluetongue	50,000 doses	4,000	
Others	-	3,015	6.5
	Sub-total	17,715	
	GRAND TOTAL	269,870	100

All drugs are purchased by the Veterinary Department and supplied through the Livestock Improvement Centres, and Clinics or used within the department (e.g. acaricides) in official campaigns.

4.2 Current use and estimated requirements of drugs and vaccines

These are indicated in A nnex 1. In view of the relative freedom from major diseases and the objective to concentrate on productivity rather than increase animal numbers, no greatly increased demand for drugs is anticipated in the forseeable future.

5. CONSTRAINTS ON DRUG AND VACCINE USAGE

There are no outstanding limitations to drug and vaccine usage. The budget is sufficient for drug purchase (via the revolving fund) but certain restrictions are apparent e.g.,

5.1 Transportation and repair of vehicles.
5.2 Repair of dip tanks.
5.3 Availability of trained Livestock Assistants. (A scheme is in hand to train a further 22 Livestock Assistants).

6. CONSIDERATION FOR LOCAL MANUFACTURE

6.1 Pharmaceuticals

Lesotho Dispensary Association (LDA) are manufacturing pharmaceuticals on a piece of land 30,000sq.m. at Mateteng which is 80 kilometres from Maseru. LDA work together with National Drug Stockpile Organisation (NDSO) who are on the

same site and are responsible for sale and distribution of the products. NDSO are also the official organisation for importation of drugs from Europe and South Africa. There are a few private importers in the country but the amounts imported are so small as to have no significance to overall strategy. LDA is officially classed as non profit making and normally show a loss whilst NDSO with a turnover of 3,000,000 Rands make a profit of 12 to 15%. NDSO are forecasting a profit increase of approximately 5% in the coming year. There is no manufacturing or distribution competition in the country. LDA are working at 50% capacity. Of total drugs handled 30% are imported and 70% locally produced. Sales to consumers of all types of drugs relate as follows: 60% exported, 40% home market. There are plans for expansion and segregation of work areas. Sales to SADCC countries are paid for either by Letters of Credit or on Tender documents but difficulties are experienced with payments from Angola.

6.1.1 Manufacturing Standards. These conform to BP and EP and to a large extent conform to GMP. The exceptions to GMP are the distinct possibilities of cross contamination whilst compressing tablets as the compressing cubicles are not under negative pressure. Neither is the entry air to the cubicles filtered to the correct degree. This situation is dangerously increased because antibiotics are processed in the same building using the same equipment as other products. Even a validated cleaning procedure of rooms and equipment cannot possibly eradicate all possibilities of cross contamination. As all tablet products are generic, no coding system on purchases exists. There is no bulk tablet store as such and confusion, unless stringently controlled, could occur in "look alike" products. A bulk tablet store should be created and products awaiting packing should be kept in lockable pallets. Sadly there is no central packing area, packing taking place at or near the scene of production. Under these conditions full control of packaging can never be perfect. On the credit side Q.C. monitor receipt of all received raw materials and monitor finished goods. Apparently only 1% of finished goods fail final analysis. A product recall system operates but in some cases due to the terrain of the country is dificult to implement. Sufficient documentation monitoring progress of production exists.

6.1.2 Site Services, Buildings and Plant.

There are four buildings on site.

1. Production building incorporating Q.C.
2. Raw materials for LDA (Store)
3. Divided building holding finished goods pending test from LDA and finished goods store of NDSO (Store).
4. Administration building catering for management, sales, accounts and purchasing department.

The buildings were erected in 1979, designed in conjunction with the Danish National Board of Health. The buildings in general are in good condition, have been well maintained and are kept clean. Some up-grading is now necessary to conform with the different requirements of GMP since 1979. In particular the production building has faults which require attention in air distribution systems, dust ledges and the use of wooden materials within the production area. In all other fields the buildings are satisfactory. It is intended to remove the activities of antibiotics to a separate area from other production. Extra separate processing equipment will be purchased to install in the separated area.

6.1.3 Present processing equipment is adequate for needs but there is no granule blender which limits batch sizes to the capacity of the Rollette mixer and the FBD. By blending a number of batches QC costs could be reduced. There is a scheduled maintenance system for process and service equipment which is recorded on a card

system. A standby generator exists and is functional. Steam, water and electrical services exist. A reverse osmosis plant is in operation.

6.1.4 There are 150 different products produced. In 1984 production was as follows:

71,000,000 tablets	All materials
60,000,000 capsules-antibiotics	obtained from
700,000 bottles of oral liquid	Europe and
130,000 tubes and jars	South Africa
400,000 dry mixture	Packing materials
600,000 powder sachets	exclusively
15,000 suppositories	from South Africa

The above represents 60% of full capacity. Each product has a master formula and relevant process operating instructions.

6.1.4 The technology is the International accepted standard and is well located within the premises except for the processing and packing of antibiotics. Production of other items and the equipment used including the methods is satisfactory. Samples are retained for 5 years.

6.1.5 Distribution of products is affected by NDSO to 19 hospitals and numerous out-stations staffed by nursing sisters. It was emphasised that due to the mountainous terrain delivery can sometimes be difficult. NDSO are in SW radio contact with all known outlets. A special person in reception continuously operates the equipment.

6.1.6 Staffing, Training and Administration. (Total staff LDA and NDSO 130 persons). The Managing Director of LDA is a pharmacist; the General Manager of NDSO is a pharmacist. The assistant to the GM is a pharmacist and a pharmacist is employed in the store area. The total staff at site is 130.

There are 3 supervisors in the Production Department who are classed as pharmacy technicians and who have undergone a course in Pharmacy of 18 months. They are responsible to the Production Manager.

A plan is in operation for "on-job" training for the large number of semi-skilled and unskilled operations in the plant and this is on-going. It is desirable that a full-time qualified pharmacist should be available in the production area.

The Control Lab. is well equipped and under the management of a Chemical Engineer. It has a staff of 12 persons most of whom are Chemistry graduates. The laboratory also offers an assistance service to Lesotho hospitals. The Manager of the QC Department is also Deputy Managing Director.

A Production Control System is in use for national orders but export orders are supplied emanating from a tender system. The objective of Production Control is to have a finished goods stock of 3 months.

Discussion

Production facilities are acceptable for present demand and with modificiations are suitable for future expansion. At all levels keeness and enthusiasm can be seen and the cleanliness of the premises and uniforms of the personnel are outstanding. As there is no sterile area production of injectables cannot be considered.

There are no facilities for veterinary pharmaceuticals in buik and as all raw materials would be imported they should not be considered.

6.2 Biologicals

6.2.1 In a room 4m x 5m the La Sato attenuated strain of Newcastle Disease Vaccine is produced, some 3,000,000 doses were made in 1985/86.

6.2.2 The specific pathogen-free embryonated hens eggs for production are imported from South Africa in six batches p.a. each of 360 eggs. Production is on a campaign basis between March and August each year.

6.2.3 Production does not meet international standards for example:

6.2.3.1 Quality control. The control tests are not carried out in SPF eggs, neigher are there intermediate product tests. The final vaccine is tested for EID50 by titration in embryos and haemagglutination inhibition.

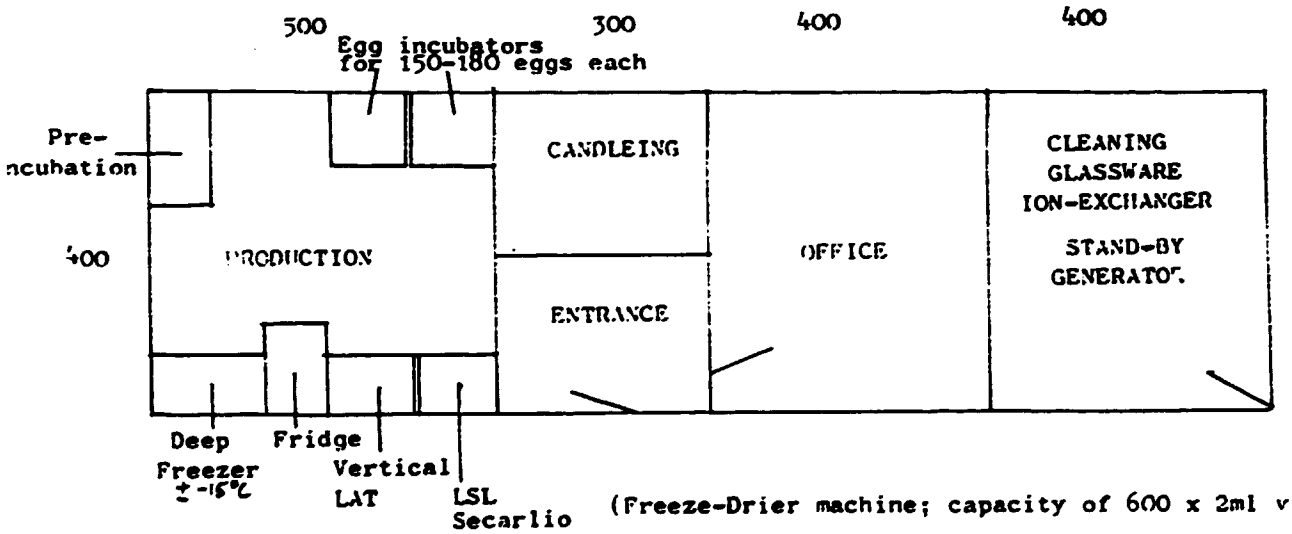
6.2.3.2 Not every batch is safety or potency tested in chickens.

6.2.3.3 Sterility tests are made on blood agar and agar with no special media for the detection of mycoplasma, salmonella or fungi.

6.2.3.4 On the final product there is no moisture determination on the freeze dried vials.

6.2.3.5 The tests which are carried out on batches are not properly recorded, neither are proper records maintained of numbers of vials and doses issued. There are also deficiencies regarding the written instructions for use and the labelling of the vials.

6.2.4 Plant and Equipment



Conditions in the room are extremely hygienic but are neither ari conditioned nor mechanically ventilated. One operator carries out the whole production function and final cleaning of the area. Equipment used is as follows:

1. 1 - Mini freeze dryer
2. 1 - Horizontal laminar flow cabinet
3. 3 - Egg incubators
4. 2 - Deep freezers
5. 1 - Laboratory type incubator
6. 2 - Small portable sterilisers

6.2.5 Communication and Distribution. Hearing requisitions of field veterinarians and poultry advisers adequate doses are produced in advance, stored and hand carried or posted to them. Laboratory production is informed on outbreaks via Central Veterinary Services.

6.2.6 Only one professional carries out all the phases of production including cleaning, cleansing as well as having Diploma of Agricultural College (local), Poultry Husbandry Course, (1 year, the Netherlands) and Laboratory Technician training (6 months, Israel). There are no trainers.

6.2.7 Discussion

It is doubtful whether the production is truly economic as the eggs used for production (SPF) are imported from RSA at Rand 0.2 each. Also on the base of the information obtained it seems clear that the producing unit does not meet International Standards and is unacceptable even for national purposes.

7. RECOMMENDATIONS

7.1 Segregate the production and packing of antibiotics to a separate area (N.B. this is in this years budget).

7.2 Create a lockable bulk tablet store complete with lockable pallets.

7.3 Consideration be given to a central packing area to allow greater control on finished packs.

7.4 Fit filters to the grills on the doors of the compressing cubicles.

7.5 Although a dust extraction system is fitted to the turret and pressure points of the compressing machine, a separate extraction system with filtered outlet should be fitted in the room to keep the room free from dust particles and at negative pressure to the corridor.

7.6 The system of self production of self-adhesive labels is not suitable for an operation of the size of LDA. Self production should be confined to applying batch numbers and expiry dates on bought-in labels.

7.7 The whole operation of tablet is dependent on one compressing machine. A stand-by should be purchased as soon as possible.

7.8 In the field of cost-saving it would be advisable to purchase a 350kilo cone blender to cut down on QC costs (tablets and powders).

7.9 Filtration of liquids is by a plate filter press. All pads are imported and with a long delivery. Consideration should be given to the purchase of a cartridge type filter from either PALL, MILLIPORE or GUNA ZETA.

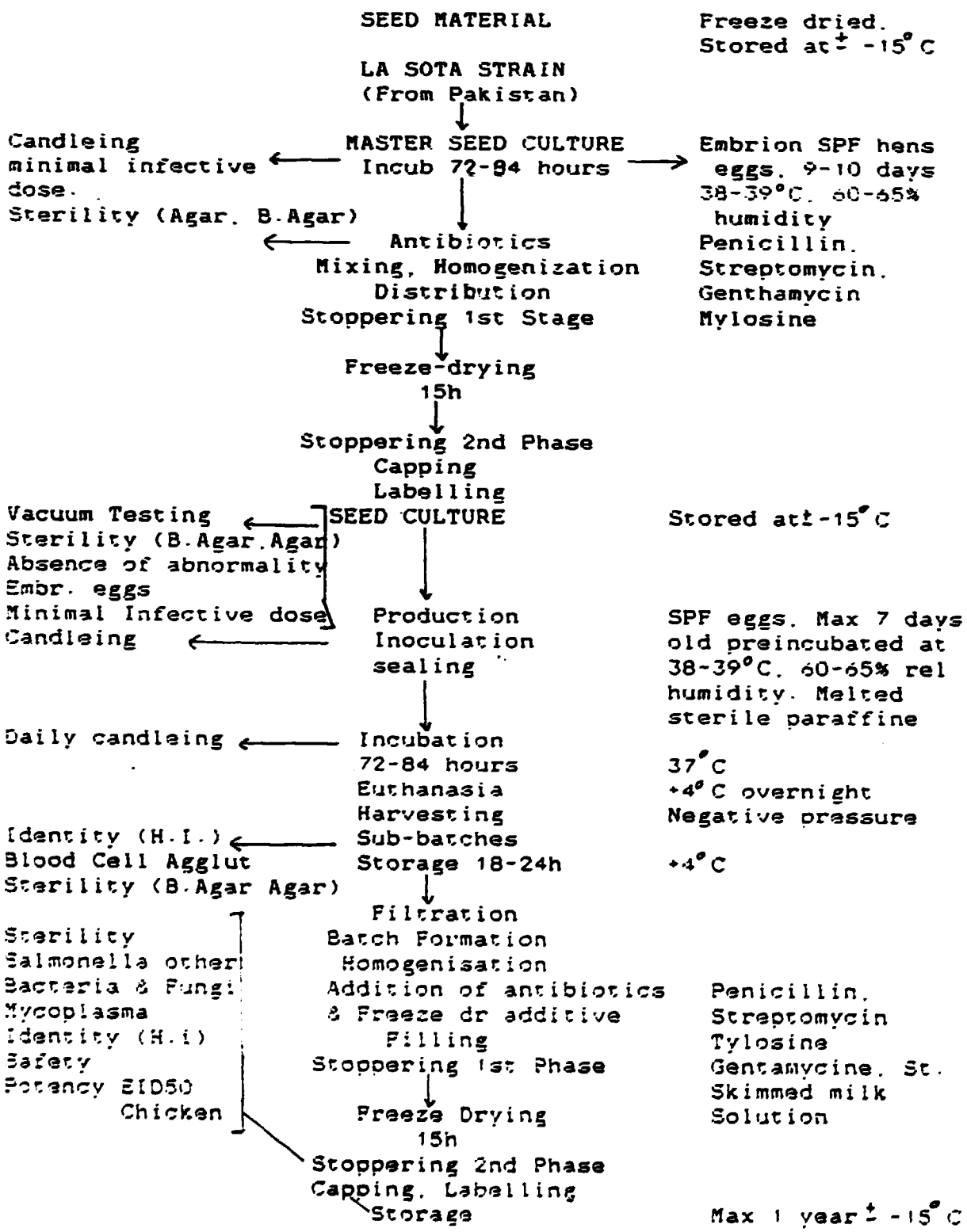
7.10 Newcastle vaccine production should cease since deficiencies of technique/records/plans involves potential hazards for animals inoculated with vaccine produced there. The existing staff should be used for the quality control of the imported vaccines.

VETERINARY DRUGS AND VACCINES USED (1986) AND ESTIMATED FUTURE 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
					Litres	
Ectoparasiticides						
Diazinon	11,200 (Litres)	116	11,200	120	12,000	130
Anthelmintics		108		120		130
Antibiotics		21		25		25
Antiprotozoons		1		1		1
Feed Additives		5		8		10
SUB-TOTAL		251		274		296
Biologicals						
FMD						
Rinderpest						
Rabies	20,000 (doses)	8	40,000	16	60,000	30
Poultry vaccines						
Other viral vacc. (Rift Valley Fever						
African Horse Sickness etc)						
Blackquarter	68,000	3	80,000	4	80,000	4
Anthrax						
Brucella						
Pastuerella						
Botulism						
Others		7		8		10
SUB-TOTAL		18		28		44
TOTAL		296		304		340

Annex 2

NEWCASTLE VIRUS VACCINE, LIVE
(Flow diagram based on technology protocol obtained)



Annex 3

RABIES IN LESOTHO

Rabies was reported to have broken out in the Northern district of Lesotho (Leribe). In 1982 the first animal to have a laboratory confirmed diagnosis was a cow from the same district. Before this outbreak there had been several reported rabid animals in The Republic of South Africa.

From Leribe the epidemic in the dog population spread to Berea and its high lands then to Maseru and Thaba-Tseka. It goes without saying that wherever there was an epidemic of the disease in animals, many people were also exposed to rabid animals. A total of 579 people were exposed to rabid animals. See table: 1 - 2

Number of people exposed to rabid animals by type of animal August 1983 - October 1984.

Table:1

Number of People	Type of Animal
537	Dogs
21	Cows
7	Cats
3	Donkeys
2	Foxes
9	Unspecified
TOTAL 579	

93% of people were exposed to dogs while 0.2% were exposed to foxes

Table: 2 Table two shows number of people exposed to rabid animals by disticts.

Table:2

Districts	Number of people	Percent
Leribe	117	20.2
Berea	91	15.7
Maseru	317	54.7
Thaba-Tseka	25	4.3
Quthing	28	4.8
Butha-Buthe	1	0.2
TOTAL	579	

As can be seen from the above table, incidence of people bitten by sick animals is predominately in the northern and central districts. Only in August 1984 rabies was reported to have broken out in animals at Mafeteng and in September 1984 was reported in Quthing district.

Due to lack of knowledge on the part of people bitten by (mad dogs) as it is locally termed and shortage of anti rabies vaccine, there are people who have died from rabies. From 1983 up to October 1984 sixteen people have been reported to have died from rabies.

Table: 3 Shows number of human deaths from rabies by districts.

District	Number of People
Leribe	3
Berea	5
Maseru	5
Thaba-Tseka	3
TOTAL	16

Of the sixteen people who died twelve were males while four were females. Four people were below 10 years of age, seven were below 30 years of age, while five had no ages specified. Nine of the people who died from rabies were said to have been bitten by stray dogs (56.3%) while seven (43.7%) were bitten by domestic animals.

Control Measures

The Ministry of Health together with the Ministry of Agriculture have embarked on a control programme of the disease in the country. The necessary support for implementation of this programme has been given by WHO and FAO.

Rabies is primarily an animal disease and it is transfered to humans when he is bitten by a sick animal. Prevention of the disease is therefore the responsibility of the Ministry of Agriculture. This Ministry through its livestock division is vaccinating animals against rabies throughout the country. Vaccinated animals are issued a vaccination certificate which is valid for 3 years after which the animal should be re-vaccinated. Only a minimum charge of M1.00 is required to vaccinate an animal.

The Ministry of Health through its disease control unit is distributing human diploid anti rabies vaccine to all health facilities in the country. Up to now free vaccination is given to people bitten by rabid animals, in all a person gets 6 shots of single dose anti rabies vaccine. This costs the Ministry of Health M120.00 per person bitten by a rabid animal.

Judging by the increasing number of human dealths from rabies, it is obvious that our campaign is not doing well. The live-stock division is now intersifying its vaccination campaign in areas where incidence of dog bites is high. All health facilities are supplied with stand-by human anti rabies vaccine. Several health talks on rabies have been given over Radio Lesotho and at Pitso's to educate people about the disease, point out the importance of thorough cleaning of the wound after dog bite and vaccination against the disease.

By thorough cleaning of the wound we hope to remove virus deposited through saliva of a sick animal on the wound. By vaccination we hope to prevent development of rabies in man and prevent death. It is a well known fact that once the disease has developed in man there is no cure, the only outcome is death.

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