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Final report

Small research and development activity

SRA

Vaccine business development in the Lao PDR

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1 Acknowledgments

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We would like to sincerely thank the staff from the Lao Department of Livestock and Fisheries who contributed to the research and deliberations and particularly their counterparts, Mr. Sengpheth Somsanith, the Deputy Director of VPC and Dr. Signa Kittiphone, Head of the VSU.

The significant support of the Deputy Director-General of DLF, Dr Somphanh Chanphengxay, and the Director of the VPC, Dr Sithong Phiphakhavong, is also greatly appreciated.

2 Executive summary

Currently the Lao Department of Livestock and Fisheries manufactures and distributes animal vaccines through its Vaccine Production Centre (VPC) and the Veterinary Supply Centre (VSU). These vaccines are mainly used by smallholders. There are no official channels operating for importing vaccines, other than through the VSU but commercial pig and poultry producers do buy vaccines in neighbouring countries.

ACIAR commissioned this small research project following its earlier review of the business operations of the VPC and VSU in 2006, Assessment of current and potential animal vaccine use in the Lao PDR. That review had identified problems in their operations and concluded that, to survive, there needed to be major changes in the way the vaccine production and supply business operated.

This project aimed to conduct background research and to hold high level discussions with stakeholders to develop and initiate the implementation of a new business model with the formal approval of the Lao Government.

The five-person team that undertook the project comprised a wide range of skills in animal health, vaccine manufacture and distribution, business development and rural development, both in Australia and Asia. Team members worked with the directors of the VPC and VSU as their counterparts and liaised closely with other senior officers in the DLF during 2007. The initial research into the supply of, and market for, animal vaccines was undertaken in Vientiane and two rural areas in February (Appendix 1). It reinforced earlier conclusions that the current Lao vaccine production and supply business conducted by the VPC and VSU was in a downward spiral towards collapse because:

- Demand for and sales of vaccine were falling.
- Despite some cost-cutting, costs for raw materials (which are imported) were gradually increasing.
- Prices charged for vaccines had been held at artificially low levels and do not cover the true cost of production.
- The VSU had a very large debt owed to it by customers and mostly by provincial governments.
- Staff numbers at the VPC were decreasing.
- Skills at the VPC had declined to a point where they are inadequate.
- Much of the donated equipment at the VPC was old, not operating and was not being repaired.
- The quality and effectiveness of some vaccines was declining.

Strategies to address many of these issues and other opportunities were identified through a SWOT analysis (Appendix 2) and a range of business options was developed, through to allowing an open unregulated vaccine market. These options

were presented and discussed at a meeting with senior government officers in July 2007 (Appendices 7 and 8). The meeting agreed on a mixed model of two options that allowed for improvements in the current manufacture and supply of VPC vaccines and improving the standard and management of imported vaccines.

The nine key elements of the preferred model were:

1. The establishment of a single *Animal Vaccine and Medicine Supply Centre* (AVMSC) that would be responsible for supplying the animal vaccine and animal medicine needs of Lao PDR.
2. Improved financial management.
3. A review and probable increase in prices.
4. Discontinuing production of some unprofitable vaccines.
5. Recovering long-standing debts.
6. Improving quality in production and introducing *Good Manufacturing Practice*.
7. Better marketing and brand identity.
8. Appointing a skills-based AVMSC Advisory Board.
9. Establishing a *Veterinary Medicine Regulatory Authority* (VMRA) to regulate of domestic and imported vaccines and medicines.

This model was endorsed by the Lao Government in November 2007 and, later that month, the team returned to Vientiane to work with the DLF to start the process of implementing the new model (Appendix 9). In addition to running workshops on financial management and marketing, team members, who are experienced in vaccine manufacture, audited the VPC buildings, staffing, equipment and operations. This identified a range of high priority issues to be addressed. The successful collaboration between with DLF colleagues developed:

- an Initial Audit and Quality Plan for the VPC (Appendix 10)
- draft terms of reference for the AVMSC (Appendix 11)
- a tentative structure and staffing plan for the AVMSC (Appendix 12).

These, and course notes on financial management and marketing, have been provided to the DLF.

The team believes that the long term capability of the AVMSC to effectively manufacture vaccines, even with the changes proposed in this report, is problematic. While it is technically possible to manufacture vaccines in a way that is consistent with GMP this will only happen with significant and ongoing investment in people, premises and equipment.

The Centre will still only be able to produce a limited range of vaccines and imports will be required to satisfy demand for vaccines for endemic and epidemic diseases, such as FMD and rabies. A range of other vaccines for commercial pig and poultry farms will largely continue to be imported and the increasing numbers of contract

rearers in the country will be supplied by the companies supplying the animals. It is very likely that imported vaccines will be less expensive and of equivalent or higher quality than locally produced vaccines. Continuity of supply of imports from a large number of possible manufacturers is also likely to be more reliable than local production. The AVMSC must decide whether to try to compete to supply the commercial sector or to concentrate on supplying quality assured vaccines to smallholders.

The setting of standards for vaccines that are produced by the Centre or imported is an essential step in managing the safety and efficacy of the vaccines used in Lao PDR. Establishing the capacity and processes to do this is a high priority. It is recommended that the proposed national registration system allows imports from manufacturers that are accredited by international organisations or by regional or other national authorities. Suppliers should have GMP accreditation and supply supporting documents for approval. The Centre may complement this by random evaluations of vaccines from time to time.

The particular challenges facing the AVMSC to become financially sustainable are to properly cost production, to increase sales and income and to manage debt. The current vaccination coverage of livestock populations in Lao PDR is very low and demand and sales will depend on significant increases in vaccination rates. This challenge is heightened by the low level of veterinary staff and infrastructure in the country, although some livestock development projects are trialling new approaches to providing animal health services to smallholders on a commercial footing.

Finally, successful implementation of the new model will require strong and enthusiastic leadership that is supported by the government, by the Advisory Board and by external expertise. Able leadership exists amongst the small number of senior DLF staff who have contributed to this project. In particular, we consider that success will depend heavily on the on-site leadership and technical and financial skills of the current Director of the VPC. ACIAR may consider it a worthwhile investment to support the managers' efforts by sponsoring technical support to improve quality vaccine supply and further guidance on development and implementation of the business management components of the new model.

3 Background

ACIAR Project, *Assessment of Current and Potential Animal Vaccine Use in the Lao PDR*, undertook an initial review of vaccine demand and supply in Lao PDR in mid-2006 as background to a proposed ACIAR project to improve the technical aspects of the production and distribution of the products of the Lao Government's Vaccine Production Centre (VPC) near Vientiane, Improved supply and quality of livestock vaccines in Laos (AH 2005/084).

This review concluded that:

1. The demand for vaccines by commercial livestock producers will increase steadily as the number and size of such enterprises increases.
2. Commercial producers can access vaccines from a number of sources and do not need to rely on the VPC. They will use vaccines that are of high quality, conveniently sourced, promptly supplied and appropriately priced for their production systems.
3. International distributors are already supplying an unknown quantity of vaccine in relatively small consignments and appear interested in supplying a larger market as it develops over the next 10 years.
4. Current imports have tacit government support at the national level and some provincial governments may be actively importing vaccine.
5. When they become active, regional TAD programs will increase demand for specific vaccines, of which classical swine fever (CSF) and haemorrhagic septicaemia (HS) vaccines are manufactured in Lao PDR.
6. Smallholders can buy animal vaccines or have their animals vaccinated on a fee for service basis through village veterinary workers who are supplied through the government vaccine distribution network.
7. Smallholders' access to vaccines and good animal health advice in remote areas is poor at this stage but should improve with rural development.
8. The current demand for vaccine from VPC by smallholders and the vaccination coverage of their livestock by VPC vaccines is low compared to the potential use.
9. Smallholders' vaccine use will probably increase slowly, driven by their ability to supply cash markets and their awareness and understanding of infectious animal diseases and the role of vaccination in protecting their investment in their livestock and the income from them.
10. Interested smallholders' awareness and understanding would be increased by more active and educated advisers.
11. Quality control in manufacturing at VPC and in distribution by VSU is compromised by inadequate government funding and poor cost recovery through underpriced sales and variable compliance with ASEAN standards of production.
12. There is significant potential to improve the quality and effectiveness of VPC vaccines through better quality control in production and distribution as proposed by the CSIRO/NAHC proposal to ACIAR.

13. The government policy of maintaining artificially low vaccine prices to encourage smallholder vaccination is not increasing demand and should be reviewed.

14. There are no major donors committed to funding the operations of the VPC/VSU in future.

15. A new business model for the VPC and VSU is needed to ensure financial and operational sustainability.

The review also recommended that:

- a new business plan for animal vaccine supply and distribution be developed with the Lao government
- the Lao government's commitment to local manufacturing of major animal vaccines at the VPC be established under the new business plan or an alternative sustainable model before the technical aspects of the proposed AH 2005/084 project proceed
- complementary field research investigates more closely the factors affecting smallholders' management of animal health, including vaccine use.

4 Objectives

In light of that review, ACIAR commissioned AusVet Animal Health Services to undertake this Small Research Project, AHA2006/155, in collaboration with Lao counterparts in the Department of Livestock and Fisheries, Ministry of Agriculture and Forestry, to help develop a new business model for the supply and delivery of animal vaccine in Lao PDR by:

1. Assessing the medium to long-term market for vaccines (type, total doses, geographical spread, indicative prices that are willing to be paid) by the various livestock industries/sectors in light of projected development and commercialisation in the cattle, buffalo, poultry and pig sectors.
2. Defining alternative suppliers of vaccines and the suitability of these vaccines (cost/dose landed, doses/vial, quality assurance, strain suitability, potential for distribution etc) at national, provincial and local levels. Define the necessary steps and critical issues for increased importation of vaccines
3. Providing an analysis of skills and equipment required for high quality business management and distribution and the gaps that exist.
4. Defining those vaccines that can or should be manufactured locally by the VPC and VSU and those that could be imported and distributed privately or by the VSU. This should include an analysis of the technical, financial, distribution and regulatory issues.
5. Defining a range, if possible, of funding and operations models for the VPC and VSU that are sustainable and independent of donor inputs.
6. Gaining endorsement of a preferred approach by the relevant government agencies in Laos.
7. Planning and introducing the new business model by gaining relevant government approval(s), appropriate training of senior VPC and VSU staff in managing the business, communication to key leaders at national, provincial level and inaugurating relevant administrative processes.

5 Methodology

AusVet coordinated a team of people with experience in animal health management in south-east Asia and Lao PDR and skills in business management, community development and veterinary chemicals and biologicals. The team comprised:

- David Kennedy, AusVet Animal Health Services (Team Leader)
- Scott Williams, SED Consulting
- Stephen Page, Advanced Veterinary Therapeutics
- Nancy Bourgeois-Lüthi, Agronomes et Vétérinaires sans Frontières, based in Vientiane, Lao PDR
- Richard Bevan, RE & HO Bevan Consulting Pty Ltd, who joined the team in November 2007 as a vaccine quality production expert and contributed to the implementation training workshops.

The team worked with two counterparts from the Lao Department of Livestock and Fisheries (DLF), Mr. Sengpheth Somsanith, the Deputy Director of VPC and Dr. Signa Kittiphone, Head of the VSU, who were in consultation with Deputy Director-General of DLF, Dr Somphanh Chanphengxay. The Director of the VPC, Dr Sithong Phiphakhavong, also took a lead role for the DLF.

Following a review of previous projects and the original CSIRO proposal, team members met with Dr Axel Colling in Geelong to discuss the current operations and the technical needs of the VPC. All team members then traveled to Lao PDR and participated in a one-day workshop with Lao stakeholders in Vientiane, on 16 February 2007, that was opened by the Director-General of DLF, Dr Bounkhouang Khambounheuang.

The main purposes of this meeting were to engage key stakeholders in the review and business development process and to gather key information about:

- Current trends and proposed developments in animal industries and disease control and in the supply, demand and distribution of vaccines
- Government policy and practice in relation to business management and investment and importation of vaccines.

Participants included representatives of NAHC and provincial officers of MAF who were responsible for livestock, managers of VPC and VSU and commercial livestock producers. Unfortunately representatives of NGOs that are involved with livestock development and of the national finance and importation offices were unable to attend but discussions were held with these people during the following week. Team members also briefed Dr Somphanh Chanphengxay on progress during this period.

Members of the team and counterparts undertook further information gathering that included:

1. Field visits to investigate status of and factors affecting demand and supply of animal vaccines in two major livestock production provinces, Champassak and Xieng Khouang
2. Closer investigation in Vientiane of the VPC/VSU business structure and the funding and regulatory environment in which vaccine suppliers would be operating in the short to medium term
3. Identifying and contacting alternative vaccine suppliers to south-east Asia and determining their interest, capacity and operational aspects of selling specified vaccines into Lao.

Field research findings were collated and analysed and alternative models for sustainable vaccine supply developed as outlined in detail in this report. Drs Kennedy and Williams returned to Vientiane in July to present and discuss options for a new business model to the senior officers of the DLF, including:

- Dr.Somphanh Chanphengsay, Deputy Director-General, DLF
- Mr Southchay , Planning & Cooperation Department, MAF
- Mr Phanthavong, Planning Division, DLF
- Mr.Bounthong Saphakdy, Head of Technical Division, DLF
- Dr.Bounlome Duangngun, Director of NAHC
- Dr.Siseng Khounsy, Deputy Director of NAHC
- Mr.Phouth Inthavong, NAHC
- Mr.Sengpheth Somsanith, Acting Director, VPC
- Dr.Signa Kittiphone, Director VSU

Dr. Bounkhouang Khambounheuang, DG of DLF and Dr.Sithong Phiphakhavong, DG of VPC were unable to attend the meeting.

The preferred business model was finalised in collaboration with the DLF officers during the following month and submitted to the DLF on 31 August 2007 together with the SWOT analysis and research findings presented above. The DLF translated the documented and submitted it to the Minister of Agriculture and Fisheries. The Lao government approved the new model on 17 November 2007.

The full team visited Vientiane for the final time during the week 26-30 November 2007 to meet with senior Lao officers and participate in workshops with them and with technical and administrative staff of the VPC and VSU. These workshops were aimed at facilitating implementation of the new model. The team included a vaccine manufacturing quality consultant, Richard Bevan, to assess the VPC and its practices, to recommend improvements and to work with the staff to develop a draft quality plan. Details and outcomes of the meetings and workshops are included in Section C5.

Project Team with DLF colleagues after the final meeting, 30 November 2007

Back: Nancy Bourgeois-Luthi, Scott Williams, Richard Bevan, Stephen Page.
Middle: Dr Sithong, Mr Chantaboune, Mr Sengpheth.
Front: Dr Somphanh, Ms Soukuna, Ms Kanthaly, Ms Soukphaphone, David Kennedy, Dr Signa.

5.1 Situation Assessment

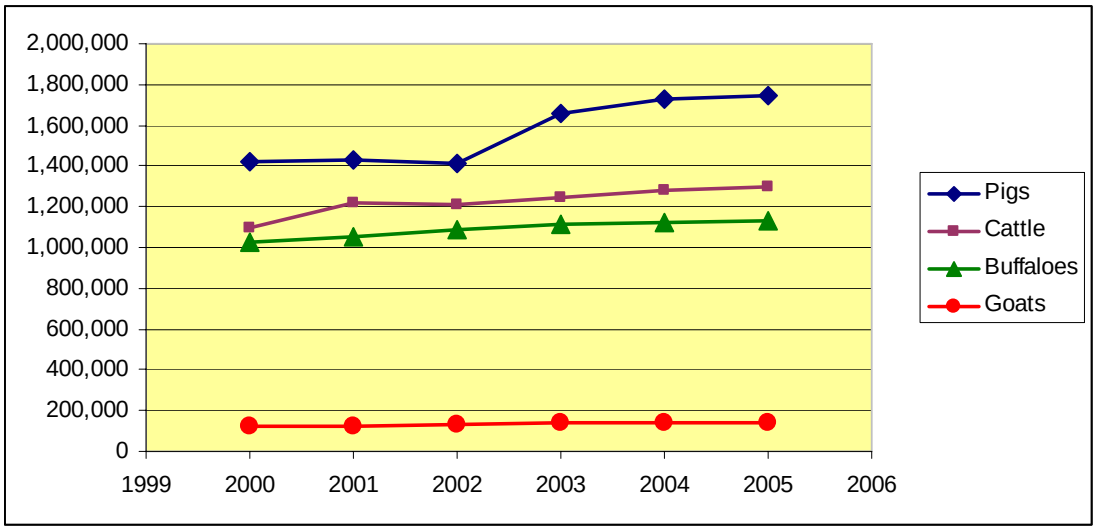
Material from 2006 ACIAR review*, Assessment of current and potential animal vaccine use in the Lao PDR, August 2006* and from the research undertaken in this project have been used in this section.

5.1.1 Demand

Livestock distribution in Lao PDR

The animal industries in Lao PDR comprise mainly grazing cattle, buffalo and goats and pigs and chicken production. Intensification is slowly occurring in the developing commercial pig and poultry industries, using hybrid breed stock and local and imported feeds. In 2005, FAO estimated the populations of chickens to have increased from 13 to 21 million and of ducks from 1.7 to 3.2 million from 2000 to 2005. Figure 1 presents the estimates for the larger livestock species populations over the same period. These are approximations only, probably based on extrapolations from the 1998-99 census and/or district estimates.

Figure 1. Estimated livestock populations, 1999-2005 (FAO Stat, courtesy Dr Colling)



A review of the livestock sector in Lao PDR by the United Nations Food and Agriculture Organization in 2004 observed that 89 percent of all farm households keep one or more types of livestock (Knips 2004), with chickens, the main type of poultry raised in Lao PDR, being a major source of protein and most households raising 20-30 chicken predominantly in scavenging systems with low growth rates and little egg production.

Pigs are also very popular with 64 percent of all households involved in pig production (Kaufmann et al 2003). Mainly indigenous breeds of pigs are kept by smallholders as a supplementary source of income for rice farmers with smallholder pig production accounting for 96 percent of the total pigs produced in Lao PDR. The number of pigs kept by household varies between an average of 1.4 and 3.7 animals, depending on the region. Thorne (2004) described three distinct pig production

systems which included (i) scavenging or free ranging, (ii) confined, and (iii) small scale commercial or semi-commercial. While there is a considerable overlap amongst these systems, and significant variations within the first two in particular, they account for around 60, 40 and <2 percent of the pig population respectively.

Cattle and buffalo are kept principally to provide draught power in paddy fields and are slaughtered locally for home consumption. The Agricultural census of 2000 found that cattle and buffalo were raised by 31% and 48% of households respectively. Dairy cattle are of minor importance in Lao PDR.

As noted by Stür et al (2002) there are few commercial pig, poultry and dairy enterprises and are all located in lowland areas near population centres such as Vientiane, where they are dependent on relatively high cost imported animal breeds and concentrate feeds from Thailand. Stür et al (2002) emphasised that disease is an important constraint to optimal animal production and can be associated with very high mortality rates in poultry, pigs and buffalo calves.

Based on information provided to FAO, the 2004 estimates of poultry, pigs, cattle, buffalo and small ruminant species in Lao PDR is presented in the Table 1. The distribution and density of the livestock population is also graphically presented in Appendix 13.

Table 1. Lao PDR Livestock Population by region and province, 2004 (FAO)

Area \ Species	Poultry	Pigs	Cattle	Buffalo	Small ruminants
NORTHERN REGION	7,066,400	665,400	246,600	298,600	79,000
Bokeo	420,400	48,700	24,000	21,300	4,500
Houaphanh	1,501,000	155,600	48,300	65,600	13,500
Luang Prabang	1,102,300	140,900	34,600	55,200	24,900*
Namtha	287,800	55,500	22,000	23,300	5,500
Oudomxay	1,683,000	89,900	33,600	37,200	20,800
Phongsaly	364,700	71,200	20,200	33,600	2,100
Sayabouri	1,707,200	103,600	63,900	62,400	7,700
CENTRAL REGION	8,157,600	699,700	753,800	539,900	37,700
Bolikhamsai	771,000	67,000	44,300	39,600	2,100
Khammouane	929,900	93,000	50,000	67,000	6,800
Savannakhet	1,998,300	279,400*	391,200*	282,700*	1,000
Vientiane	1,476,100	76,800	104,000	58,800	7,400
Vientiane (Munic.)	1,898,700	95,000	64,000	25,400	8,200
Vientiane 2	579,200	10,800	12,300	22,500	2,800
Xiangkhouang	504,400	77,700	88,000	43,900	9,400
SOUTHERN REGION	4,257,100	363,200	248,600	273,000	22,700
Attopu	250,000	20,100	12,100	44,500	2,200
Champassack	2,263,200*	100,700	126,000	120,100	3,100
Saravane	1,628,400	196,000	95,100	84,900	11,200
Sekong	115,500	46,400	15,400	23,500	6,200
TOTAL	19,481,100	1,728,300	1,249,000	1,111,500	139,400

* province with highest population of each livestock species

Livestock development policies and programs

The Lao Government is aiming to reduce poverty and increase smallholder incomes through increased commercialisation and improved animal nutrition, husbandry and disease control. The focus is on cattle and buffalo production in the northern highland areas and on pigs and poultry along the Mekong lowlands, closer to the larger city markets.

In a recent presentation of the Strategic Vision for the Lao Agricultural Sector for 2006-2010 by the Ministry of Agriculture and Forestry (MAF) the state of development of lowland and upland agriculture was summarized as follows:

Lowlands

- transformation started
- commercial factors and product markets operating
- beginning of farming systems diversification.

Uplands

- subsistence rural economy
- limited markets
- endemic rural poverty
- traditional source of inputs and household consumption of outputs.

The constraints that have been identified in these systems include:

Lowlands

- insufficient flow of productivity-increasing cash crop technologies in more isolated rural areas
- institutional weakness at district and provincial levels affecting the capacity to deliver adaptive research, problem-solving and extension
- inadequacy of commercial credit facilities in many rural areas
- absence of commodity grades and standards
- insufficient market information and linkages
- non-existence of a post-harvest technology system.

Uplands

- heterogeneous topography inhibiting access and creating unique environmental hazards
- poor access to transport and road links
- lack of markets and market information flows
- high incidence of unsustainable shifting cultivation
- endemic rural poverty
- low intensity subsistence agriculture
- institutional weakness at district and provincial levels
- slow implementation of formal land tenure arrangements
- absence of productivity-enhancing technology flows
- low incidence of rural savings and investment.

The national vision is now to focus on a bottom-up approach where farmer demand drives research and extension in farming systems. Farming Systems Extension Workers (FSEW) at DAFOs will provide routine technical support to farmers and conduct field trials and demonstrations of new technologies with technical support provided by Subject Matter Specialists (SMS) at the PAFO level.

Within this environment, the priorities of the Ministry of Agriculture and Forestry (MAF) are to develop pig and poultry industry development on the lowlands and cattle and buffalo production in the upland regions. The relative importance of cattle and buffalo is decreasing where commercial cropping can be developed as farmers move to more mechanized land preparation.

The four areas in the Agriculture and Forestry Development Plan 2006-2010 are to address are:

1. Food Security and Food Production
2. Commodity Production
3. Slash and Burn Cultivation Eradication
4. Sustainable Forest Management.

Thirteen measures are being taken to address these, including the following which are of particular relevance to improving animal health and the use of animal vaccination:

- improve planning and production systems in different agro-ecological zones to increase income and alleviate poverty
- introduce improved plant and animal varieties
- improve agriculture extension services
- develop human capacity in order to increase productivity
- establish and develop village clusters in rural areas
- develop production groups and agriculture cooperatives
- increase efficient prevention and control of animal and plant diseases based on sanitary and phytosanitary (SPS) standard measures
- effectively manage and use financial support and investments from domestic and foreign sources and others.

Animal disease control and services

The Lao Government is aiming to reduce poverty and increase smallholder incomes through increased commercialisation and improved animal nutrition, husbandry and disease control. Animal disease control is managed from the National Animal Health Centre (NAHC) in the Department of Livestock and Fisheries (DLF), within the Ministry of Agriculture and Forestry (MAF) through provincial (PAFO) and district offices (DAFO). Field officers may specialise in one or more areas of livestock production (eg large livestock, poultry and aquaculture) depending on the local demand. The district staff also coordinate some of the work of Village Veterinary Workers (VVW).

Important infections of livestock species that occur, or have occurred recently, in the Lao PDR endemically or sporadically include the transboundary animal diseases, highly pathogenic avian influenza (HPAI), classical swine fever (CSF), foot-and-mouth disease (FMD) and haemorrhagic septicaemia (HS). The DLF aspires to have 70% of the cattle and buffalo population vaccinated against HS and about 40% of the pigs vaccinated against CSF.

It is estimated that there are about 50 active veterinarians in the country, most of whom are based in the capital, Vientiane. Commercial producers have some capacity to use private veterinarians and other private advisers to buy medicines and vaccines.

Most animal health operatives in the field are Village Veterinary Workers (VVW), who have been trained by the government or by livestock development projects to deliver animal health programs, including vaccinations during campaigns. They also provide basic veterinary services to smallholders such as voluntary vaccinations and treatments of sick animals for a variable fee. For instance, in the Vientiane Capital region the maximum fee for vaccinating cattle or buffalo for HS is 5,000 kip (or approx USD 0.50) but the fee appears to be about 1 to 2,000 kip in the other provinces visited. The DLF and donor projects have trained many VVWs over the past decade but it is believed that most of these are no longer active for a variety of reasons, probably the most important being a scarcity of income-generating work. One factor that is claimed to have contributed to this is the training of too many VVWs in some areas.

The intensity of animal disease surveillance and reporting in Lao PDR is low which in turn affects the general awareness and understanding of animal diseases among government services, VVWs and farmers.

Factors affecting demand for animal vaccines

The demand for animal vaccines comes from four sectors:

- Government animal health programs
- Private smallholders
- Commercial farmers
- Livestock development projects

Government

The degree of formal government involvement in animal disease control depends on the importance both of the livestock sectors that are affected and the impacts of the infection, as well as available funding. For instance, the government has actively intervened in trans-boundary animal disease (TAD) control in recent years to stamp out highly pathogenic avian influenza (HPAI) and to ring vaccinate to control incursions of foot and mouth disease (FMD).

The government's emphasis on forage improvement and on developing cattle and buffalo production results in provincial and district officers and VVWs encouraging smallholders to vaccinate against haemorrhagic septicaemia (HS). However this is voluntary and at the owners' expense and coverage is still low. The National Animal Health Centre has also been closely involved in development, promotion and evaluation of locally produced CSF vaccine in a small number of specific project districts.

Interestingly, although rabies is endemic, there is no national program of rabies control. VSU imported only 8,000 doses in 2006 in response to PAFO or DAFO requests for local programs.

Development projects

Vaccination is seen as a key component of most livestock development projects which may require that animals provided by the project are vaccinated against the major infections that cause deaths, such as CSF in pigs, HS in cattle and buffalo and ND and fowl cholera in chickens. In some projects, the vaccine is provided free of charge.

Commercial farmers

There are relatively few intensive commercial livestock enterprises in Lao PDR at this time, although the numbers are increasing. During this project and the 2006 vaccine review, we visited three intensive pig farms. Vaccine is an inexpensive investment for commercial pig producers who can quickly realise a profit on their investment from quicker growth and increased pig sales. One of the farmers near Pakse reported selling his porkers for between 12,000 and 14,000 kip per kilogram in 2006-2007. He sold weaners at 10kg for 400,000 kip. Another commercial farmer in Champassak told us that he sold 6 week-old weaners at 10 kg LW for 320,000 kip to small-holders near his farm. (The exchange rate at the time of writing the report was $US1=9,600 kip.)

These farmers vaccinated their sows and growers using a range of vaccines (including CSF, Aujeszky's disease, porcine parvovirus and mycoplasma) that are manufactured outside of Lao PDR and purchased from Thai retailers (see below).

Smallholders

The use of animal vaccines is very low among smallholders and is affected by:

- attitudes to their animals as regular income producers or as assets to cash in when needed
- relatively low importance of livestock on many farms compared to cropping
- limited awareness and understanding of the role of vaccines in health management
- attitudes towards the effectiveness of vaccines
- access to and price of vaccines
- ability to maintain their end of the cold chain
- animal grazing management and restraint facilities, especially for cattle and buffalo in extensive upland grazing systems.

Where smallholders can quickly realise a return on their investments in vaccine, there is more of an incentive to protect that income. Where smallholders can sell native Lao pigs into city markets, such as has developed with ACIAR's *Lao-Australian Animal Health Research Project* in project villages in Bolikhamxay and Xieng Khouang provinces, the interest in CSF vaccination is relatively high (also refer to theses on studies by J Conlan and T Vitesnik in 2006).

Where cattle and buffalo are important to household incomes or are used for land preparation for cropping, farmers are more inclined to have the VVW vaccinate them against HS. In upland areas, smallholder herds comprise usually only a few cattle that are considered assets that can be occasionally cashed when needed for celebrations or to meet other major family costs. In these circumstances, there is

generally lower interest in investing in improved husbandry, including vaccination. For instance, on the Bolivan plateau of Champassak where the farmers are primarily croppers, cattle have been displaced by machines for ploughing and they are now seen to have little importance by some farmers, although they are still a valuable asset. In one village near Phonsavan, the owner of a relatively large herd of 35 cattle told us that he and another owner of 30 head were the only ones of about 20 cattle owners in the village who vaccinated their cattle against HS. Most of the other owners had 5 to 10 head.

Although poultry are the most numerous livestock in the country, most are scavenging chickens that provide a low-input, inexpensive source of protein for smallholders. Although prevention of ND in other countries, including neighbouring Myanmar, has had dramatic effects on smallholder income and well being, there is little commercialisation of village poultry at this stage in Lao PDR and little financial incentive to invest in animal health. The added challenge of catching scavenging birds for vaccination is a further disincentive.

Not surprisingly, the active involvement of VVWs in smallholder communities appears to be very important factors in the attitudes and understanding of smallholders about animal health, disease causation and prevention. Traditional beliefs are prevalent, especially in more isolated regions. Active VVWs not only provide advice on animal husbandry and disease control, they often promote and organize vaccination campaigns, including collecting monies, traveling to vaccine resellers and bulk buying of vaccine from the PAFO and DAFO. They also often undertake the actual vaccination for a fee (from about 1,000 kip in Xieng Khouang to 5,000 kip near Vientiane), especially for large animals. This is a small charge compared to the value of a beast at 1.5 to 3 million kip.

Unfortunately many of the VVWs who have been trained by the government and projects are no longer active. For instance, only about a half of the 100 VVWs trained in 100 villages in the Paksong district are still active. Duties may include working for

livestock development projects or government programs (such as regular surveillance of poultry for HPAI) but VVWs are also heavily dependent on services and products that they can sell to smallholders such as animal vaccinations and treatments. VVWs leave the field largely because they cannot earn sufficient income from their activities. In some areas, it was felt that training too many VVWs was contributing to the low rate of retention and that some VVWs who had previously made a reasonable incomes were being squeezed out by the oversupply. As VVWs work largely in their local area, potential income can be affected by expectations that the VVW should provide services at little or no cost to friends and relatives.

Access to vaccine is limited for most smallholders. With vaccine resellers largely restricted to the provincial capitals, supplying vaccine to most villages requires the DAFO, VVW or the smallholder to undertake a special trip, which incurs both additional time (usually several hours) and transport costs. Although we found that resellers often provided ice, the need to maintain the cold chain during the transport and before use in the village probably provides another psychological hurdle to widespread smallholder vaccination.

Demand for vaccines that are not manufactured by the VPC

During the previous vaccine review project, we visited a large commercial piggery near Vientiane that imported all its vaccines from a Thai retailer, who had them delivered to the farm. These vaccines included Hungarian *CEVA* vaccines against CSF and Aujeszky's disease, a Dutch *Intervet* vaccine for porcine parvovirus and FMD vaccine manufactured by the Thai government institute at Pakchong.

On this project, provincial staff from Savannakhet and Khamoun reported that commercial piggeries commonly bought vaccines in Thailand. We also visited two small commercial breeding and growing farms in Champassak province that had been established in the past five years and had 25 and 40 sows. Both independently purchased vaccines from Thai retailers for a range of infections. One farmer took advice from an experienced pig farming friend in Thailand and purchased porcine parvovirus, Aujeszky's disease, haemophilus and mycoplasma vaccines from a shop in the city of Ubon, over 100 km away. The manufacturers of these vaccines included *CEVA* and *Boehringer-Ingleheim* The other farmer also vaccinated against Aujeszky's disease and porcine parvovirus and used a "multivalent" Taiwanese vaccine, but there was no packaging available to identify the manufacturers. This farm did use Lao CSF vaccine on piglets and weaners that was purchased at the PAFO in Pakse as it was cheaper than the vaccine that he could buy in Thailand.

There does not appear to be a significant demand for other imported vaccines in the absence of disease outbreaks or in areas that have a history of incursions. There is occasional low level demand for rabies vaccine by local authorities and projects and for FMD vaccine in areas when incursions occur, as in Champassak in 1999 and 2001.

The only vaccine for which there was a demand that was not satisfied by local or imported vaccine was for the clostridial infection blackleg or blackquarter in cattle, which is believed to occur sporadically in specific areas of Lao PDR.

5.1.2 Supply

VPC products

The role of the VPC is to produce vaccines to meet the requirements of Lao livestock producers. Table 2 shows the range of VPC vaccine products and its pricing:

Table 2. VPC vaccine range and wholesale prices (February 2007)

Product	Doses/ pack	Price/pack (kip)*	Price/dose (kip)*	Price/dose (US cents)
Haemorrhagic septicaemia (HS)	15	6,000	400	4.2
Haemorrhagic septicaemia (HS) in oil	10	12,000	1200	13
Fowl cholera (FC)	50	6,000	120	1.3
Newcastle disease (ND) F	100	5,000	50	0.5
Newcastle disease (ND) M	100	6,000	60	0.6
Newcastle disease (ND) I2 (heat resistant)	50	4,000	80	0.8
Classical swine fever (CSF)	10	8,000	800	8.3
Infectious bronchitis (IB)	100	6,000	60	0.6
Duck plague (DP	50	6,000	120	1.3
Fowl pox (FP)	100	5,000	50	0.5

*Price includes distilled water for reconstitution

VSU's role and dimensions

The role of the VSU is to ensure the national supply of veterinary products (pharmaceuticals as well as biologicals such as vaccines). The VSU acts as a not-for-profit wholesaler supplying intermediaries at various levels and also as a retailer to end-users. Any end-user can purchase stock direct from the VSU, and there is no difference between wholesale and retail pricing.

Total sales of *all* products (not just vaccines) for the VSU are around 750 million kip (approximately US$78,000) per year. Sales have grown slowly over the last three years (Table 3).

Table 3. Annual sales of all products by the VSU

	Sales (million kip)		
	2004	2005	2006
Vaccines	382	391	397
Other products	347	349	355
Total	729	740	752

The VSU distributed 17 vaccines in 2006, nine of which were manufactured at the VPC, to about 80 major customers that include the PAFOs and small retailers, all of which are situated either in Vientiane and in the provincial capitals. Vaccines are transported in cartons from the VPC to the VSU and then by foam boxes to customers. The various vaccines are secured in tight plastic bags (to help prevent breakage and loss of labels) and packed in clearly identified polystyrene foam boxes with ice. Used foam boxes are sourced from a cheese importing shop as far as possible because they are quite expensive (30,000 kip). Each standard foam box can carry 200 large bottles (15 doses) of FC or HS vaccine plus ice bags. Small foam boxes can contain only 100 vials (including ice bags). Customers are charged for new boxes (30,000 kip) because they are rarely returned.

The boxes are delivered to the Vientiane bus depot in the evening by the VSU Director himself and are transported overnight to the depot in the destination town from where they are collected by the retailer or the PAFO officer the following morning. The client is informed by the VSU about the shipment time and the identification number of the bus. In case of delay or problem, the VSU attempts find someone else to pick up and store vaccines as soon as possible.

The VSU charges 30,000 to 80,000 kip for the bus transport, depending on the distance from Vientiane. The cost of transport to the customer is approximately 150-1000 kip per bottle, depending on the size of the consignment and distance from the VSU. To save costs, the VSU encourages retailers to return the empty foam boxes that are in good condition to Vientiane for re-use (at an indicative cost to the retailer of about 10,000 to 20,000 kip). One retailer refunded customers 5,000 kip for returned boxes in good order. Although the boxes are reasonably fragile, only 2 to 3 consignments are returned due to damage per year. Vaccines used to be sent by air to more distant towns, such as Pakse, but this is now too expensive at approximately 100,000 kip per box compared to 50,000 kip by overnight bus.

Retail vaccine sales

During the field research trip to Champassak and Xieng Khouang provinces (see Appendix 1), we visited government offices in Pakse, Paksong and Phonsavanh, shops that sold vaccine in Pakse and Phonsavanh and a small number of farmers and VVWs near the main centres. A previous project had also included discussions with similar people in and near Vientiane.

In each of Vientiane, Pakse and Phonsavanh there are between 3 and 7 private shops that carry and sell animal vaccines. These shops usually also sell other animal products, such as feedstuffs, and may be known as 'feed shops'. They effectively operate as one-stop shops for animal supplies. Vaccines are stored in the shop's refrigerator/freezer and most retailers said that they provided ice for people who bought vaccines from them. As far as we could ascertain, no shops sell VSU vaccines in smaller centres away from these larger towns. Some farmers, DAFO staff and VVWs buy vaccine from PAFOs, DAFOs or private shops in these towns for their own use or to resell to smallholders. Private vaccine sellers said that most of their customers were smallholders, while PAFOs and DAFOs also supply livestock development projects.

Commercial farms in Lao PDR do use vaccines manufactured in Thailand and other Asian and European countries that are sourced in Thailand. They buy it personally from retailers during trips to Thailand or order it through retailers and have it delivered to the farm. Apart from the VSU, there do not appear to be any vaccine wholesalers or organized marketing of imported vaccines in the Lao PDR. We could not find any evidence of distribution networks used by foreign manufacturers or wholesalers. Vaccine retailers in Vientiane, Pakse and Xieng Khouang did not sell imported vaccine and said that they received no information or visits from other vaccine suppliers. So the remainder of this section relates to distribution of vaccine sourced from the VSU.

Shops that sell vaccines have no distinguishing features that otherwise differentiate them from other feed shops, and they appear to rely on word of mouth and proximity to markets and main roads to become known as vaccine retailers. This passive reputation could be volatile, as indicated in one of the provincial centres visited, where PAFO and DAFO staff advised against buying vaccine from some of the shops in the town in favour of buying from the PAFO and another shop operated by a colleague.

The prices that offices and shop owners said that they charged for vaccines purchased from the VSU varied widely, even within one town (Table 4).

Table 4. Retail prices for vaccines manufactured by the Lao VPC (in '000 kip, February 2007)

	HS **Alum**	HS **Oil**	CSF	NDm	NDf	FC	IB	DP	FP
VSU	6	12	8	6	5	6	5	6	5
Champassak									
Shop CH1	8	-	10	7	-	8	-	-	-
Shop CH2	10	-	12	9	-	10	-	10	-
Shop CH3	-	-	12	10	-	10	-	-	-
DAFO Paksong	15	15	13	14	12	12	-	12	12
Xieng Khouang									
PAFO	10	-	12	12	-	12	-	-	-
Shop XK1	15	20	15	15	-	15	-	-	-
Shop XK2	10	18	12	10	10	10	-	-	-

Key: HS: Haemorrhagic septicaemia; CSF: Classical swine fever; ND: Newcastle disease; FC: Fowl cholera; IB: Infectious bronchitis; DP: Duck plague; FP: Fowl pox

Imports through VSU

Although the formal requirements for import of vaccines for use in animals are onerous, vaccines are imported by the VSU and also by farmers directly from suppliers, most particularly from those based in Thailand. As well as distributing the full range of vaccines that are produced by the VPC (Table 2), the VSU also imports several lines (Table 5).

Table 5. Vaccines imported by the VSU

Product	**Doses/pack**	**Price/pack (kip)***	**Price/dose (kip)***	**Price/dose (US cents)***
Rabies	1	7,000	7,000	73
FMD (cattle, sheep, goats)	20 (cattle) 40 (sheep/goats)	100,000	5,000 2,500	52 26
FMD (pigs)	75	450,000	6,000	63
Aujeszky's	10	40,000	4,000	42

*Price includes distilled water for reconstitution

The VSU distributed the following imported vaccines:

- Rabies vaccine (7,000 and 7,800 doses in 2005 and 2006)
- FMD vaccine for pigs (370 and 500 doses in 2005 and 2006)
- FMD vaccine for goats and cattle (8,000 and 8,500 doses in 2005 and 2006)

The only imported vaccines sighted in shops during our field work were rabies and canine parvovirus vaccines (that are imported and distributed by the VSU on demand) at the Paksong DAFO. Rabies vaccine was also carried at one Pakse shop.

However, commercial pig farmers in Champassak were also importing vaccines for the following infection from retailers in Thailand: Aujeszky's disease, porcine parvovirus vaccine, mycoplasma and haemophilus.

In addition, there was apparently a frequent request for a vaccine against blackquarter in cattle and buffalo but while the VPC has produced a vaccine in the past no vaccine is currently available in Lao PDR.

5.1.3 Distribution

Supply chain

Field visits to VPC / VSU customers showed that the vaccine supply chain is a complex one. The vaccine is purchased directly by the end-user (commercial farm, smallholder or village veterinary worker) or passes through the hands of one or more intermediaries: the various PAFO, DAFO, and private shops. These intermediaries buy from each other depending on local circumstances.

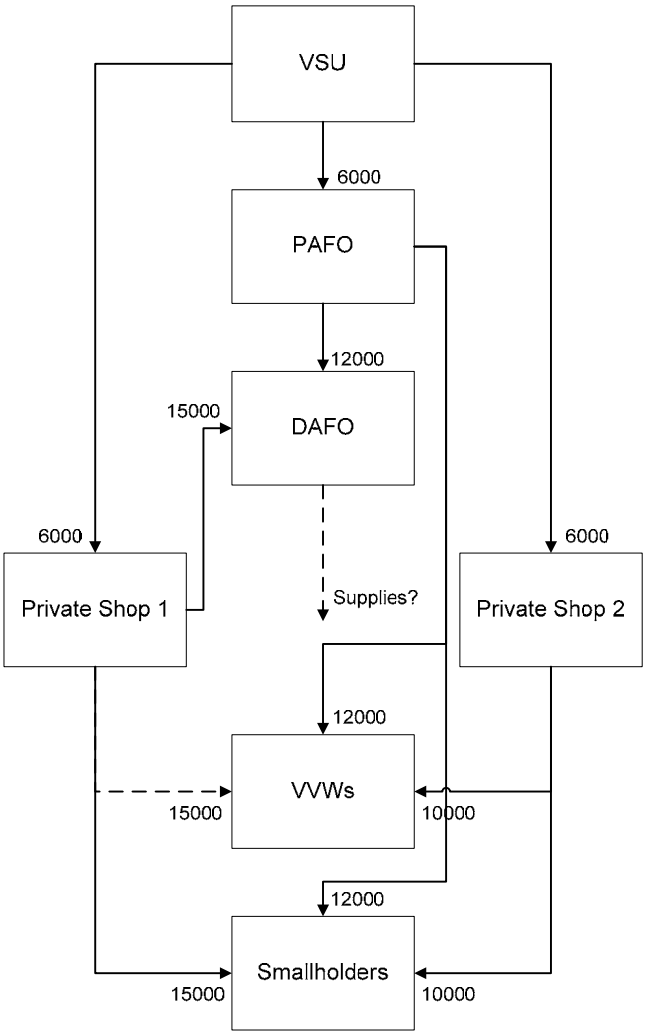
The destinations of selected vaccine product lines are shown in Table 6 (approximate estimates from VSU).

Table 6. Destinations of selected VSU vaccine product lines

	Provinces	Shops	Commercial farms	Other
ND (all)	60%	10%	20%	10%
FC	40%	30%	20%	10%
HS	60%	20%	10%	10%
IB	30%	30%	20%	20%
FP	40%	40%	10%	10%

An example of a local supply chain is shown in Figure 2. These are provided for illustrative purposes only, because there is no single supply chain defined for all areas, and this study examined only a sample of those supply chains in operation. A clear finding from the study, however, is that price mark-ups are generally high – much higher than would be expected in the Australian situation, for example, and considerably higher than could be considered reasonable for the value added by the various intermediaries.

Figure 2. Example supply chain: fowl cholera vaccine, Xieng Khouang Province (figures show the price in kip to the adjacent intermediary)



In this example, a bottle of fowl cholera vaccine is purchased for 6,000 kip from the VSU by one private shop in Xieng Khouang province and is on-sold for 15,000 kip to the end user. This is a retail mark-up of 150%. The shop adds value by:

- transporting the vaccine to the local area (costing around 3-400 kip per bottle, maybe more if turnover is too low)
- managing the financial transaction with the VSU for the vaccine (for example, there is a cost 15,000 kip per money transfer; the cost per bottle is unknown but would be small, because several payments are made at once)
- storing the vaccine (costs from depreciation of refrigerator, energy, opportunity cost of inventory)
- distributing the product, possibly with technical advice (incurring salary cost)
- providing ice for transport by customers

- absorbing the risk of product expiring or not being fit for purpose (difficult to quantify)
- reducing quality or other risks to the end-user by being government-licensed to distribute the product (incurring the cost of the licence, although this particular shopkeeper does not pay the licence fee)
- providing economy of scale in the purchasing process.

It is not possible to tell what an appropriate mark-up would be in this case without detailed figures. However, an Australian rural reseller would apply a mark-up of around 20-30% for a similar level of value-adding.

Not all resellers of vaccine are applying a 150% mark-up, although 50-100% is not unusual. End users can also purchase direct from the VSU and avoid the margins of the middle-men. Most do not purchase direct, however, because they do not know the option is available to them, or do not have the scale, or the financial or other resources to do so.

The fact that intermediaries appear able to apply unreasonably high mark-ups to the vaccines they sell suggests that the VPC is not charging enough for its product. Resellers can only charge what the market will bear. In the case of fowl cholera vaccine from the shop in Xieng Khouang province, for example, the reseller apparently believes that 15,000 kip is the price that optimises profit. In theory, the owner would reduce her margin and continue to sell at 15,000 kip if the VSU were to raise its price – unless she believes that the customer will pay even more for the product.

It was reported to the project team that VPC and VSU are expected to keep vaccine prices low in order to maximise demand from smallholders. The findings presented here show that the policy of keeping prices low ex-VPC / VSU is not ensuring the lowest possible price to the end user. The market is operating as expected to allow intermediaries to take advantage of the difference between the market equilibrium price and the artificially constrained supply price.

VSU business processes

The VSU has only three staff: the Director, a bookkeeper and an administrative assistant. In the fulfilment of orders, for example, the bookkeeper and assistant assemble the non-refrigerated products while the Director packs and seals the cold boxes and takes them to the bus for despatch.

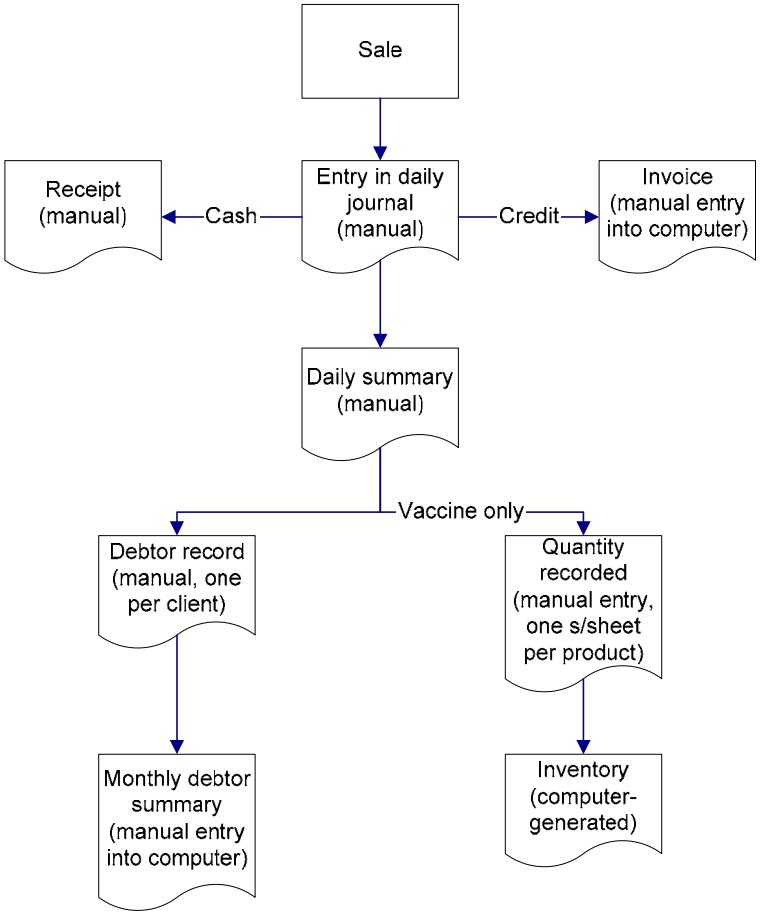
Customers who come directly to the VSU to collect vaccines or medicine pay in cash. Most vaccine, however, is distributed on credit to distant locations with the ordering procedure at the VSU office comprising the following steps:

- Order is placed at the VSU
- The consignment is prepared
- A computerized delivery and receipt form is filled

- The amount is transferred into the credit file (by hand)
- The amount is transferred into the computerized debt file (excel sheet).

One part of the workflow is shown in Figure 3. Note that the vast majority of sales are on credit.

Figure 3. Handling of sales at the VSU



Private retailers generally have good credit ratings with the VSU paying in full and promptly. On the other hand, the VSU also provides PAFO and DAFO offices with the vaccines on credit. Notionally, payment should be made when these government offices receive the proceeds from the sales however there is no guarantee of payment and the VSU has been instructed to continue to supply vaccine to some government offices for disease control purposes, despite long histories of non-payment. Some PAFOs and DAFOs have outstanding debts amounting to several million kip that have accumulated over two to three years. At January 2007, the total outstanding debt to the VSU was 357 million kip.

While PAFOs are indebted to the VSU, DAFOs may in turn have a significant debt with their respective PAFO. For instance, feed shops and private buyers pay cash for vaccines from the PAFO in Pakse but vaccines are supplied on credit for one to 3 months to government staff. In February, the Pakse PAFO was carrying a debt of about one million kip.

5.1.4 Lao Trade Environment

The trade environment of the Lao PDR, especially as it impacts on the importation of animal vaccines, is of particular interest if the country is to consider replacing some or all of the VPC's product range with imports.

Importing goods into Lao PDR

There are regular unofficial imports of vaccines into Lao PDR. These products arrive from across the Mekong and over land crossings (as distinct from airports), where inspections are less formal. Unofficial importations are tacitly accepted by authorities – in fact, the VSU imports vaccines through unofficial channels. CIE (2006) noted that 'in reality, there are no official imports – informally imported vaccine is relatively freely available and the government does not appear to make any serious attempts to limit informal vaccine importation'.

This project found that there are some official imports, although it is unclear precisely what laws and regulations are in place to control these. There are requirements at both national and provincial levels. For those imports arriving at airports and therefore needing to be managed 'officially', the process is onerous and lengthy, requiring permits from the DLF, the Trade Section of Vientiane municipality, the and Ministries of Finance and Customs, at both national and provincial levels.

The United Nations Traders' Manual for Lao PDR (United Nations 2005) provides a list of documents required by importers (Table 7):

Table 7. Documents required for imports (from UN Traders' Manual 2005)

Document	Body concerned
Bill of lading / air waybill	Shipping / airline company
Certificate of origin Form D (for ASEAN-CEPT treatment)	Ministry of Commerce / Lao National Chamber of Commerce and Industry
Commercial invoice	Importer
Single administrative document (customs declaration)	Customs department
Import permit	Line ministries*
Packing list	Importer
Other permits, as required	Ministries concerned

* DLF in the case of animal medicines

The Traders' Manual also advises that parties seeking to import goods must prepare a 6- or 12-month plan for each commodity to be imported. This plan must be submitted to the provincial Trade Section for acknowledgement and then to the Trade Section of the 'control unit' (not further defined) for import approval. A list of goods to be imported must also be supplied and it forms part of the import licence.
In short, the process to import animal medicines is complex – perhaps no more complex or onerous than that of any developed country, but undoubtedly more mired in unproductive bureaucracy than attempting to provide real benefits. For example, there seems to be far more effort expended in getting signatures on pieces of paper than demonstrating the safety of the product to be imported. There is presumably a mechanism within DLF for assessing the sanitary implications of vaccine imports as part of the issuing of permits, but that did not appear to be a major part of the importation process.

Animal vaccine imports

The project team was provided with a copy of a document entitled *Draft Veterinary Law (Version 20/5/2004)* by Dr Somphanh. The status of the document seemed unclear even to DLF officials but there was a clear expectation that it would be officially adopted in the near future.

The Draft Law regulates 'veterinary services' including 'commodities', which takes in 'products…for pharmaceutical or surgical use or for agricultural or industrial use…biological products and pathological material'. The Draft Law appears to provide strong support for domestic production of animal drugs, which presumably includes vaccines. Article 4 (*The promotion of the investment*) states that:

'The State has the policy of promoting all economic sectors, including domestic and foreign sectors, to invest in animal health and production activities.'

Similarly, Article 28 (*Licensing of animal drug production, veterinary drug shops and clinics*) in Part 3 states that:

'The Government strongly supports any individual, juristic person or organization intending to establish veterinary drug production facilities, veterinary drug shops and veterinary clinics. The production facility, shop or clinic must be authorized by the concerned bodies and meet the rules and regulations laid down by the Ministry of Agriculture and Forestry, Ministry of Health and urbanization (sic).'

On the other hand, there are no specific restrictions on the importation of vaccines by the DLF, except those for the usual sanitary reasons. Article 31 (*Import-, transit animal, animal products, and animal commodities*) states that:

'It is prohibited to import and transit animals, animal products and animal commodities through Lao PDR in case:

1. *There is an outbreak occur in the original export or transit countries. That outbreak is occurring during the same period of transportation.*
2. There is no health or sanitary certificate from the state vet*erinary services of the export countries.*

3. *The quarantine station veterinary officers suspect contamination with infectious diseases.*
4. *Suspect animals, animals products or by-products originating from animals except under conditions and certification to be determined by the Veterinary Services.*
5. *The importer not inform the concerned bodies in advance at least 15 days before the import date namely: date, quantity, means of transport, entry points.'*

The Draft Law codifies a significant role for the Veterinary Services. Article 21 (*Tasks and duties*) states that:

'The Veterinary Services contribute to the enforcement of the Veterinary Law, application decrees, rules and regulations pursuant to this law.
Moreover the Veterinary Services have the task and duty to

1. *assist in the preparation and definition of rules and regulations pursuant to the provisions of this law, comprising:*
    - *international trade and quarantine of animals; animal products and commodities destined for animal use*
    - *sanitary and quality norms for animal product and commodities destined for animal use.'*

More specifically in relation to the VPC and the VSU, Article 29 (*Management and control of animal drug production, veterinary drug shops and clinics*) states that:

'The state veterinarian is responsible for management and control of veterinary drug production facilities, veterinary drug shops and clinics in his/her responsibility area in order to meet the criteria that will be laid down by decree.'

The criteria to be 'laid down by decree', if they exist, are not known to the consultants. The provision for decrees appears to leave considerable latitude for the Government to vary the rules.

Notwithstanding the ambiguous nature of much of the document, the Draft Law appears to give a reasonable level of authority to the Director General of the DLF as head of the Veterinary Services. A major decision to switch from manufacturing to importing animal vaccines may only require his support.

Alternatively, the real decision-making may reside with the Minister of Agriculture and Forestry or even higher. This would probably not be known until it was tested.

As described above, the status of the *Draft Veterinary Law* (e.g. whether it is the latest draft and whether it accurately reflects the current views of the Lao Government) is not clear to either the consultants or, apparently, officers of the DLF. The confusion is not surprising. The Centre for International Economics (2006) noted that 'implementation of central government policy (in Lao PDR) is often quite weak: there is often a long delay in the issuance of key implementing regulations for new legislation'.

Human vaccine imports

The handling of human vaccines by the Lao Government provides an interesting comparison with the veterinary situation. There is no manufacture of human vaccines in Lao PDR. All vaccines are imported, in almost every case by a donor project or by private importers. The Government is not generally a purchaser of vaccines, although its Medical Product Supply Centre (which appears to be the equivalent of the VSU) did import some vaccines last year.

An importer is required to:

- Obtain registration for a new product from the Ministry of Health's Department of Food and Drugs, Division of Drug Control. We were told that applications for registration take no longer than 6 months to process and usually less (2-3 months), with the decision to grant registration in the hands of a committee. . Registration must be renewed every three years.
- Obtain a licence for each importation. Licences are also obtained from the Division of Drug Control. To obtain a licence the importer must supply a Certificate of Free Sale from the exporting country.

On taking possession of the imported product when it arrives in Lao PDR, the importer must show his licence to Customs and to inspectors from the Department of Food and Drugs Division of Drug Inspection. The inspectors ensure that the vaccine has been properly transported and stored and that it will be suitably transported from the port of entry.

The Division of Drug Inspection is responsible for monitoring vaccine activity 'post-marketing' (the Division's description). This includes compliance with regulations on product promotion. However, the Division has limited resources and can undertake only limited policing.

In summary, the process for importing human vaccines seem to match more closely that of Australia and other developed countries. There is a distinct product registration and compliance function that may not exist for animal vaccines in Lao PDR. The most interesting aspect, however, is the Government's apparent indifference to Lao PDR having its own production capability in human vaccines given the importance of manufacturing security as an argument put forward in support of maintaining local veterinary vaccine production capability.

External trade reform

According to a presentation of the Ministry of Agriculture's *Strategic Vision* for 2006-2010, reform of external trade is a major aspect of development of the agricultural sector, with new policies to:

- Fully support trade liberalization with minimal controls on exports and imports in concert with tangible trade liberalization measures by regional trading partners
- Gradual formalizing of informal cross border trade flows.

To achieve this, the Lao Government plans to

- Closely monitor tangible progress of regional trading partners in reducing/removing import/export permits and licenses and eliminating effective quantitative control over imports through licensing.
- Move toward trade liberalization in concert with parallel moves by regional trading partners.
- Operate, in concert with regional trading partners, to move many agricultural products and inputs to the ASEAN Free Trade Area (AFTA) inclusion list.

6 Achievements against activities and outputs/milestones

The planned research and activities were all undertaken successfully within the time frames planned. Significant achievements were

- Initial research visit completed with counterparts, February 2007
- Business options for future supply of animal vaccines presented, July 2007
- Preferred business model finalised and submitted to Lao DLF, August 2007
- Preferred option submitted by DLF to Lao government October 2007
- Government endorsed preferred model, November 2007
- Training workshops for new business model run, November 2007
- Supporting documentation forwarded to DLF 2007, December

7 Key results and discussion

7.1 Analysis

This section of the report aims to analyse the preceding information and identify the key issues that need to be addressed to develop a more successful model for the supply and use of animal vaccines in Lao PDR.

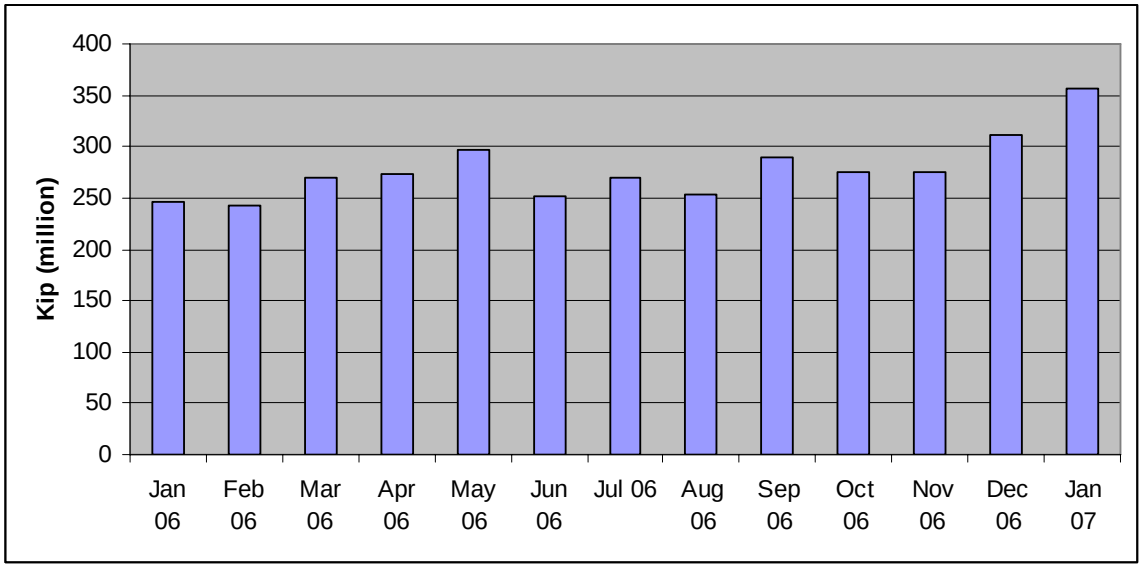
7.1.1 Strengths, Weaknesses, Opportunities and Threats

The field research undertaken in February 2007 identified a broad set of characteristics of the national vaccine supply business and factors that are affecting the supply and use of vaccines. These have been summarised and analysed in the table of Strengths, Weaknesses, Opportunities and Threats (SWOT) included as Appendix 2. The presentation of these is in a TWOS format which attempts to focus on the way forward in light of the various factors identified in the usual SWOT. Strategies to address weaknesses and threats and to take advantage of strengths and opportunities are described.

7.2 Business performance of the VSU

The reliance on manual systems means that it is not easy to obtain summary reports on the accounts. However, there is clearly a major problem with the level of debtors (see Figure 4).

Figure 4. Cumulative value of VSU debtors, January 2006-January 2007



As at 31 January 2007, accounts receivable from 110 customers totalled 357 million kip. This compares with total sales in 2006 of 752 million kip. In other words, outstanding debt currently represents nearly 50% of annual turnover.

The average length of time these amounts have been outstanding is not known, but several examples of very longstanding individual provincial government debts (2 years or more) were provided. Three examples are given in Table 8.

Table 8. Examples of bad debts at the VSU

	Amount owing (kip)	**Date of last payment**
Customer A	5,348,000	12/7/04
Customer B	10,942,000	13/10/04
Customer C	1,770,000	16/5/03

Managing debtors is a significant challenge for the Director of the VSU. He can refuse to supply any further product to parties with outstanding invoices (as he has done in the case of customer C). However, he takes the risk that a major disease outbreak will occur and he may be held accountable because he would not supply vaccine. In cases where phone calls and other requests for payment are not complied with, the Director will seek advice from the DLF, but this does not appear to solve the debtor problem to any degree.

Vaccines are still supplied to customers A and B and the bad debt is considered to be unrecoverable. The debts were somehow ‘cleared’ in their own accounts by these PAFOs. Apparently, new people took over the vaccine purchases and were not considered responsible for recovering the money, so each PAFO has simply determined that it no longer has an obligation to pay the amount owing.

A further complication within the PAFO offices is that the responsibility for vaccine purchase may be split between ‘Technical’ and ‘Finance’ sections. It appears that orders may be placed by those administering animal health without clearance from the Finance section, with the result that Finance does not feel obliged to pay.

While it is not clear how much of the debt owed to VSU is recoverable, the situation is very poor and not sustainable for a business.

There is a sense that the staffing at the VSU is insufficient for the current demands. It appeared, from a limited inspection of the books and from discussions with the Director, that tasks are being completed just in time or after hours. Other aspects of the business are just not done. For example, there appears to be limited management of inventory, particularly for those products other than vaccines. They are simply re-ordered when it is noticed that stocks are low. The VSU store contains considerable stocks of out-of-date product which has yet to be disposed of.

A major reason for the apparent understaffing is that work processes are inefficient. For example, the paper trail associated with product sales is largely manual and involves multiple entries of the same data. Invoices are numbered, but the numbers may not always be captured for later tracking of orders.

There is no reason for manual systems when off-the-shelf financial and inventory management software packages are readily and inexpensively available for small businesses. In fact, VSU already has a custom-made software program built in

Microsoft Access® that was developed by the last EU project. The program is installed on the Director's computer, but it is not used, although there are some data entries from about two years ago. The program appears to be well-designed and easy to use (although VSU staff think that a "bug" in the system needs to be fixed). Although the Director recognises its value, he has had difficulty making the time to implement it.

The creator of the program has been identified. He moved to another area of government after the EU project finished, but could be retained for a day or two to check the program and possibly to provide training in its use.

The VSU also has only two computers at present, one of which was described as very old and lacking in memory. The 'good' computer is used only by the Director and has a monitor that is unlikely to last long. There would need to be a computer with reasonable specifications available to the bookkeeper and administrative assistant, with appropriate network and backup.

7.3 Business performance of the VPC

Information on the operation of the VPC gathered for this project came principally from Dr Sithong and Mr Sengpheth, with additional material from reports of previous projects concerning the VPC (AusVet 2006, Guilloteau 2002).

Dr Sithong has been the Director of the VPC but he has also recently taken up the position of Director of the EU Livestock Farmer Support Project. Mr Sengpheth, the Deputy Director and Chief of the Bacteriology Section, is currently managing the VPC. These are two of only three personnel with formal technical training at the VPC and the problem of loss of skilled staff has been referred to in previous reports (for example, Guilloteau 2002: EU Project ALA/96/19, Report of the Vaccine Laboratory Specialist Feb-Apr 2002).

It was difficult to fully understand the finances of the VPC. Financial records in the conventional international format (i.e. statement of financial performance / profit and loss, and statement of financial position / balance sheet) were not provided and business literacy is limited, although it appears that previous EU projects have established systems to allow some budgeting and tracking of expenditure.

For the purposes of this report, the following generic chart of cost accounts is used:

- Cost of goods sold
- Marketing
- Finance and administration
- Salaries.

Cost of goods sold

Cost of goods sold (COGS) varies directly with the quantity of vaccine produced. Actual expenditure figures for these items were not available for this review, but

rather standard costings per batch of vaccine aggregated up to the total production, with an allowance for an additional 10% due to wastage. It has not been possible to verify how closely the standard costings match the actuals.

Nor has it been possible to verify the batch costings. One or two obvious anomalies were found (for example, a batch of 3,500 bottles of CSF vaccine requiring 4,200 bottles, caps and stoppers), but the overall impact of these is unknown. For the purposes of this report, we have assumed the batch costings to be reasonably accurate.

Major cost items are non-SPF fertile chicken eggs (for the viral vaccines), culture media (for the bacterial vaccines) and bottles (both). The latter two are purchased from overseas and are therefore expensive and dependent on accessing foreign exchange.

In 2006[1], the total cost of goods sold was estimated 393,493,524 kip (US$40,988)[2], including the 10% allowance for wastage. However, as explained above, this is a planned rather than an actual figure, and its relation to actual expenditure is not available.

Marketing

No marketing costs are identified by the VPC. The marketing function is assumed by the VSU.

Finance and administration

These costs include electricity, fuel, telephone, water, animal feed, clothing, and repairs and maintenance (water, gas and waste removal were not listed as costs). Some of these items would be variable or semi-variable (i.e. they will increase or decrease to some extent with the level of production) and others would be fixed.

There do not appear to be any finance costs, so all overheads are referred to in the VPC accounts as ‘administration’. According to Dr Sithong, the 2006 administration figure includes those components shown in Table 9.

Table 9. Components of ‘administration’ in VPC accounts

Item	Cost (kip)
‘Incentive for Government’ and basic salary for seconded staff (hired by the VPC)	32,929,200
Office running costs	48,279,000
Transportation and packing ‘and others consumable’	35,875,400
Maintenance and ‘small repair’	62,364,000
Total	179,447,600

The total administration cost of 179,447,600 kip is equivalent to US$18,692.

[1] *Note that the Lao financial year runs from 1 October to 30 September. Certified statements of accounts obtained by the consultants are dated October.*
[2] *The exchange rate at the time of writing the report was $US1=9,600 kip*

Administration does not include the costs of electricity and telephone which are paid by Government (as are the salaries of regular staff). Government-funded costs are estimated as shown in Table 10.

Table 10. Government-funded costs of running the VPC

Item	Cost (kip)
Basic salaries for 13 staff	80,000,000
Electricity	25,000,000
Telephone	10,000,000
Total	115,000,000

If these costs were added, the total 'administration' figure would be 294,447,600 kip (US$30,672).

It is also important to note that administration includes only a basic level of repairs and maintenance, and that depreciation is not recorded as an expense. This reflects the fact that there is no substantive maintenance carried out. The lack of maintenance and equipment renewal is clearly a major problem (see Appendix 9). At the time of visiting the VPC for this project, several important items of equipment were not functioning because there was no money for repairs or spare parts. These items included autoclaves, a minus 70^{o}C freezer for vaccine seed storage and a water heater. Some of the non-functioning equipment was supplied by the most recent EU project and is very new. Older pieces of equipment, such as the minus 20^{o}C freezer, appear to be deteriorating and drawing close to the end of their useful lives.

The administration cost provided here should not therefore be regarded as the 'true' cost of running the facility because it makes no allowance for the real depreciation on equipment, nor those items covered by Government.

Salaries

The VPC has 18 staff, 13 of which are classed as 'Government' and 5 'seconded'. According to the Director, this is about as low as staff numbers can reasonably go. He argues that, in any case, there are no gains to be made by reducing staff numbers because salaries are only a 'very petty part of the expenditure' at 25-30,000,000 kip/year (seconded staff only).

Salaries contribute approximately 16% of total VPC costs. This is consistent with the 14% estimated by the EU Specialist in 2002. At the time of the 2002 report there were 25 staff. The EU Specialist regarded the staffing at the time as the minimum possible and that, in fact, the Centre was suffering from a lack of suitably qualified personnel. This appears to be the case today.

Summary

VPC costs for 2005/06 are shown in Table 11.

Table 11. Summary of VPC costs 2005/06

Item	Before Gov't subsidy (kip)	After Gov't subsidy (kip)
Cost of goods	393,493,524	393,493,524
Marketing	0	0
Finance and administration	184,447,600	149,447,600
Salaries	110,000,000	30,000,000
Total	687,941,124	572,941,124

It was beyond the scope of this project to analyse the technical aspects of the VPC's operations and therefore any opportunities to reduce the cost base. The EU Vaccine Laboratory Specialist B. Guilloteau (2002) found a few such opportunities, although these only offered minor savings (Table 12). One of those opportunities involved increasing demand rather than cost-cutting.

In short, it can be concluded that there is limited scope for the VPC to generate a surplus purely by improving efficiency of production. In fact, the EU Specialist noted that fixed costs were already at a minimum. These fixed costs did not include anything more than basic maintenance of equipment. If anything, costs are likely to rise if the VPC is to meet ASEAN or other quality standards.

Table 12. Recommendations for cost savings at VPC from EU Specialist (Guilloteau 2002)

Recommendation
Reducing variable costs
Dilute bacterins to save on cost of medium
Compare cheaper bacterin media with current
Consider 200-dose (cf 100-dose) packs for avian vaccines to save on packaging
Improve coordination of planning between VPC, Provinces and Districts to allow larger lots of raw material to be purchased
Become self-sufficient in rabbits for CSF vaccines to save on purchases
Increase batch size to reduce QA costs
Increasing prices
Review prices, but with comparison against prices of imported vaccines
Increasing sales
Encourage smallholders to vaccinate

7.3.1 Relative profitability of product lines

The VPC monitors the cost of production and contribution margin for each product by allocating to each product a proportion of the administration cost.

There is no fixed formula for this allocation, which appears to be decided on a case-by-case basis taking into account:

- Number of batches produced per year (HS, FC and CSF are the most commonly produced lines)
- Cost of time, labour and other inputs (HS, FC and CSF have higher input costs)
- Cost of transport to the field (HS and FC are more costly due to their weight)
- Acceptability to the market (the market is least price-sensitive to HS and CSF, and most sensitive in the case of poultry vaccines).

It is not entirely clear whether the allocations of administration are optimal as a basis for activity-based costing. Certainly, the last of the allocation criteria (acceptability to market) would appear to be an unsuitable basis for allocating overhead costs and should be taken into account when setting price rather determining cost of production. Similarly, consideration of the cost of transport in the field may not be relevant given that customers pay freight costs from the VSU.

Notwithstanding these comments, the allocation of administration costs appears to line up reasonably well with the proportion of total packs contributed by each line.

A breakdown of the costs and revenues for each product line (at August 2006) is shown in Table 13.

The summary shows that some product lines, notably the poultry vaccines, with the exception of NDF and NDM, are not contributing a sufficient surplus to meet their share of administration, although all cover their cost of goods sold. CSF and HS vaccines are the most profitable lines and are 'carrying' the other products. Ironically these may be the products with the most questionable value; CSF because of critical cold chain hurdles and the HS vaccine due to the expected brief duration of immunity of the aluminium adjuvanted line.

Overall, there is an apparent surplus of 94,786,415 kip (US$9,874) after all expenses have been paid. As noted above, however, this figure does not include depreciation and it does not include the costs covered by Government (115,000,000 kip). On these figures the VPC could not meet the costs currently met by Government if it had to meet those costs and if it continued to manufacture loss-making products. Nor would it, in all likelihood, be able to meet its depreciation costs.

However, it should also be noted that the surplus shown in the summary is not a 'real' figure, because the cost of goods as shown are planned rather than actual. For example, there is a 10% surcharge placed on the budgeted cost of raw materials for each product line to allow for damage and loss. This cost is not real. Also, not all the doses produced were sold. The Director's estimate is that around 3,640,000 doses were sold rather than the 4,448,055 shown in the figures (82%). This may not impact the profit and loss statement of the current financial year (the following year may show difficulties) but there would be negative effects on cash flow.

*Table 13. Costs and revenues for each VPC product line**

Item**	No. doses	% all doses	Raw material cost	Admin cost allocation	Total cost of production*** [A]	Cost /dose	Cost /pack	Selling Price/dose	Selling Price/pack	Total sales [B]	Total surplus (kip) [B-A]	Surplus as % of sales
HS	505,185	11%	110,822,667	53,834,280 (30%)	181,122,642	359	5,378	400	6,000	202,074,000	20,951,358	10.4%
HS oil	73,550	2%	30,185,175	10,766,856 (6%)	45,047,235	612	6,125	1,200	12,000	88,260,000	43,212,765	49.0%
FC	771,100	17%	81,000,130	25,122,664 (14%)	116,735,073	151	7,569	120	6,000	92,532,000	(24,203,073)	(26.2%)
ND F	847,600	19%	15,819,691	14,355,808 (8%)	33,193,049	39	3,916	40	4,000	33,904,000	710,951	2.1%
ND M	1,313,400	30%	24,399,163	14,355,808 (8%)	42,630,468	32	3,246	40	4,000	52,536,000	9,905,532	18.9%
ND I2	120,000	3%	4,115,640	5,383,428 (3%)	10,448,975	87	4,354	60	3,000	7,200,000	(3,248,975)	(45.1%)
SF	252,600	6%	76,043,462	35,889,520 (20%)	123,126,280	487	4,874	700	7,000	176,820,000	53,693,720	30.4%
IB	195,750	4%	3,762,256	5,383,428 (3%)	10,060,252	51	5,138	50	5,000	9,787,500	(272,752)	(2.8%)
DP	195,100	4%	8,165,676	8,972,380 (5%)	18,851,862	97	4,831	80	4,000	15,608,000	(3,243,862)	(20.8%)
FP	173,770	4%	3,407,525	5,383,428 (3%)	9,670,048	56	5,564	40	4,000	6,950,800	(2,719,248)	(39.1%)
Totals	4,448,055	100%	357,721,386	179,447,600	590,885,885					685,672,300	94,786,415	

* All prices in kip
** Product abbreviations Key: HS: Haemorrhagic septicaemia; CSF: Classical swine fever; ND: Newcastle disease; FC: Fowl cholera; IB: Infectious bronchitis; DP: Duck plague; FP: Fowl pox
*** Includes 10% allowance for damage and loss

7.4 Potential for further vaccine imports

A study of livestock vaccines available in 6 countries in South East Asia revealed more than 1,000 products manufactured by more than 100 companies either within SEA or abroad. Examples of the variety of products available are presented in the Appendix 3 where 59 CSF vaccines and 36 HS vaccines are identified. With respect to the poultry vaccines (especially ND, IB and FP) there are even more potential sources. In many cases the cost of the vaccines is no greater than that of products manufactured by the VPC.

A critical issue becomes the process of selection of a product for import. The most important selection criteria should include:

- Quality of product (is it manufactured according to a recognised code of GMP?)
- Suitability (will the vaccine protect against challenge with local strains of the disease agent?)
- Stability (will the product withstand the prevailing conditions to the end-user - is it cold chain robust?)
- Other important but less critical criteria may include:
  - cost
  - reliability of supply
  - shelf life
  - dose regimen (dose volume, number of vaccinations)
  - unit size (number of doses per container)
  - adverse events (site reactions, anaphylaxis etc).

With respect to the two examples of CSF and HS vaccines the following comments are pertinent.

7.4.1 Classical Swine Fever Vaccines

- Of the 59 sources, at least five are manufactured by GMP (vaccines 4, 15, 25, 26, 42)
- Two of these products are subunit vaccines
- Three products are living
- Each of the living products can be stored between 2 and 8^0C for at least 12 months
- Each batch of these products is released on the basis of identity, sterility, safety, purity, potency and stability tests.

It must be recognised that the study by Conlan (2006) of the stability of a single batch of the VPC CSF vaccine revealed that it was not stable if stored at 4^oC and of limited stability (less than 4 months) if stored at -20^0C. These findings need to be replicated but nonetheless suggest that effective vaccination of pigs is unlikely. The study of Vitesnik (2006) demonstrated that when the cold chain was bypassed pigs did respond serologically to vaccination with the VPC vaccine. However the titre of the vaccine under study was not determined and no challenge studies or assessment of duration of immunity was carried out.

Mariner (1997), who was head of the successful Pan African Rinderpest Campaign, Thermostable Rinderpest Vaccine Transfer of Technology Project, emphasised that

freeze-drying is a critical step in the vaccine manufacturing process. Product formulation and vacuum settings used during lyophilization affect product potency, stability and portability. He further stated that it is:

'…important to remember that vaccine costs represent less than 10 percent of the cost of vaccinating an animal and that vaccine quality is the single most important determinant of vaccination success or failure. A poorly packaged and lyophilised product may be a cent cheaper per dose, but is much more prone to cold chain failures. Veterinarians and paying consumers will insist on products that work and are cost-effective in the field. The optimal efficacy and portability of a well lyophilised product is essential for success in the market.'

7.4.2 Haemorrhagic septicaemia vaccines

- Of the 36 products listed only one (#32 in the list from Vaksindo in Indonesia) is manufactured under a code of GMP.
- One product, that from Advanced Biologicals in Myanmar is a lyophilised living product that is reported to be stable at 30 – 36^0C for 3 years and to provide a high level of protection for 12 months.
- Other products from India and Pakistan are reported to be stable for extended periods at room temperature.

The significant benefits of selected thermostable products should be closely examined and a decision made as to the positive impact on animal health if selected vaccines were imported.

If Lao PDR should choose to continue manufacturing vaccines at the VPC, it is recommended that a program of improving the thermal stability of each vaccine be developed and implemented.

7.5 Vaccine quality standards

In a review of the production and quality control of veterinary vaccines for use in developing countries Soulebot et al (1997) noted that "…the inherent variability of biological agents and materials and the relative inefficiency of quality control tests in providing adequate reassurance for final products means that the roles of the QA system and GMP are of the utmost importance" and further that "the need to maintain control over all aspects of GMP cannot be overemphasized".

Radlett (1997) described the general design and operating requirements for vaccine manufacturing establishments and noted that "the essential requirement for a manufacturing plant is that it should produce a sufficient quantity of good quality, safe and effective product in an economic manner. The objectives of optimum plant design and the concepts of good manufacturing practice and total quality management are intended to ensure that these requirements are met on a routine basis". He further stated that "(the principles of GMP) are applicable to any manufacturing situation and where they can be effectively integrated into the design and operation … it is frequently advantageous to do so." He concluded that "manufacturing operations in which live agents such as vaccine seeds are handled under conditions in which sterile materials are exposed to the environment represent one of the most difficult challenges in the design of facilities which satisfy modern manufacturing requirements."

The OIE Regional Workshop on International/Regional Harmonisation of Veterinary Medicinal Products (Bogor, Indonesia, 6-10 November 2006) was attended by participants from throughout SEA and importantly, included the Directors of the VPC and the VSU (Dr. Sithong and Dr. Signa). The workshop considered that

- The improvement of animal health is an essential factor for the development of the agriculture/livestock sector and poverty reduction by reducing human and animal health risks.
- Veterinary medicinal products are essential in animal disease prevention, control and treatment, and those will provide satisfactory results only when they are produced and controlled in compliance with international standards and used in an effective way.
- There are existing mechanisms in participating ASEAN Member Countries of registration of veterinary medicinal products. However, the official control of veterinary drugs is vested in various national organisations that differ in their approach to ensuring the quality, safety and efficacy of the products.

- Veterinary drugs with low or doubtful safety and efficacy often prevail for users in some part of the region, and under this condition, illegal trades have been identified.

The workshop recommended that:

- More attention should be paid to further strengthening functions of Veterinary Administrations in some countries for ensuring a national government mechanism of control and registration of medicinal products for veterinary use.
- International cooperation should be continued for the region in order to support and strengthen activities of National Veterinary Administrations in conjunction with ensuring effective mechanisms of veterinary drug registration and quality control of veterinary drugs, either locally produced or imported. The cooperation should focus on the development of human resources who are involved in veterinary drugs control and registration in the forms of training on information, risk analysis of veterinary drugs, registration and drug assay at the laboratory, to meet international requirements and standards.
- The regional networks should be developed to exchange information on veterinary medicinal products in order to improve quality assurance for veterinary vaccines marketed in the region and veterinary medicinal product registration. In particular, there should be regular organisation of regional seminars/workshops as well as electronic communication.

The operation of the VPC has been the subject of study and report by experts from the European Union (Jetteur 1998; Guilloteau 2002; Anon 2004) and recommendations for enhancement of quality management have been proposed. The principles of Good Manufacturing Practice (GMP) are set out in Appendix 4.1 and form a universally accepted model that could readily form the basis of practice at the VPC. Vaccine monographs and standards developed by various international agencies for vaccines similar to those manufactured at the VPC are identified in Appendix 5 and should be considered when developing a code of GMP for the VPC.

As a result of the research it was recommended that the future business model for vaccine supply include the following elements:

Quality Management

A code of GMP, developed and appropriately customised to the needs of Lao PDR for implementation at the VPC. Consultants with experience in vaccine manufacture, GMP and the needs of different countries are available and could readily adapt a standard for adoption by the VPC. The process could look comprehensively at the VPC and identify and implement all necessary processes and procedures. The exercise would result in uniform and reproducible manufacturing processes that would ensure a consistent high quality product is produced. As the master seeds have not been examined for many years the consultancy could also evaluate the current status of the seeds and introduce new seeds as necessary. The subject of CSF vaccine quality could also be the subject of investigation and a systematic review undertaken with an objective to improve shelf life and storage conditions.

Independent review

An advisory panel to review VPC practices and provide advice on manufacturing and supply issues.

National Regulatory Authority

An independent authority to control the quality of domestically produced and imported veterinary medicines. Assistance from within ASEAN is available and also from consultants in Australia.

7.6 Trends for future vaccine supply and distribution

Future vaccine supply and distribution is dependent on the types of diseases considered by farmers and their advisors as important constraints to animal health and the welfare of communities, the incidence of these diseases, the availability and technical characteristics of accessible vaccines (thermostability, immunogenicity, quality) as well as the motivation and willingness of livestock owners to vaccinate.

As described by Stür et al (2002), Thorne (2004) and ADB (2006) a major constraint to increasing livestock production in Lao PDR is the high incidence of livestock disease. For example, farmers in Luang Prabang and Xieng Khouang reported that more than 80% of all chicken die every year (FLSP 2002) and epidemics of pig diseases often occur killing many or most pigs in a village in a single outbreak (Hansen 1997, FLSP 2002, Thorne 2004). The rate of mortality caused by diseases is lower in cattle and buffalo, except for high mortality of buffalo calves (30-40%) due to internal parasites, especially *Toxocara vitulorum*.

As part of a regional study of livestock diseases (Perry et al 2002), local experts rated the diseases listed in Table 14 as the most significant in Lao PDR.

Importantly, not all the significant diseases are amenable to prevention by vaccination. However, simple and effective interventions are available for these diseases and as Stür et al (2002) pointed out death of buffalo calves from toxocarosis can be completely prevented by an inexpensive anthelmintic administered at the appropriate age. The immediate and obvious improvement in health associated with such treatment could be used to help win the trust and confidence of villagers in other animal health measures such as vaccination.

The origin of the high incidence of disease is multifactorial and includes:

1. poor nutrition and sanitation
2. uncontrolled movement of animals
3. movement of diseased animals
4. incorrect diagnosis of disease and inappropriate treatment
5. poor access to information on how to control and treat diseases
6. restricted coverage by and ineffective vaccines
7. weak veterinary support services
8. inappropriate livestock management practices.

As reinforced by Thorne (2004) a well designed and integrated approach to disease control is necessary and unless each of the above interacting factors is satisfactorily addressed the impact of improved availability and quality of vaccines will not be maximised.

Table 14. Top ten diseases of livestock with greatest impact on the poor in Lao PDR (Perry et al 2002)

Disease	Livestock at risk	Importance in Lao PDR	Impact		
			Lost production	Mortality	Trade barrier
Vaccine-preventable diseases					
Classical swine fever	Pigs	High	+	+++	+
Newcastle disease	Chickens	High	+	+++	
Haemorrhagic septicaemia	Buffalo and Cattle	High	++	++	
Foot and mouth disease	Buffalo and Cattle	Medium	+		+
Duck plague	Ducks	Medium	++	++	
Fowl cholera	Chickens	Medium	+	+++	
Fowl pox	Chickens	Medium	++	++	
Diseases requiring non-vaccine prevention measures					
Toxocarosis	Buffalo	High	+	+++	
Ectoparasites	All	Medium	+		
Gastrointestinal helminthosis	All	Medium	+	+	

Other critical considerations with an impact on future vaccine supply and distribution include the cold chain, vaccine duration of immunity, emergence of new diseases and development of new vaccines.

7.6.1 Thermostability

A significant issue in Lao PDR that has been reported repeatedly over the last 20 years (Ballard 1995; Blacksell 2001; Anon 2004; Conlan 2006; Vitesnik 2006) is the extreme difficulty in maintaining a cold chain from the VPC to the villages in which vaccines are to be administered.

Lao PDR is not alone. In almost all countries in which the performance of the vaccine cold chain has been assessed inadequacies have been identified. Appendix 6 identifies investigations in 33 countries (including Australia) that have revealed poor management of the cold chain. In a large number of cases vaccines have been frozen, an unexpected issue that is increasingly described. The solution in the future is likely to be the development of vaccines that are not as dependent on cold storage.

In recognition of the sometimes insurmountable obstacles in establishing a reliable cold chain there have been many investigations exploring approaches to the development of vaccines that are less dependent or even independent of the need for refrigeration.

Experimental approaches to improved stabilization include:

- Substitution of deuterium oxide (D_2O) for water in the final blending stage of vaccine production (Ikizler and Wright 2002, Crainic et al 1996, Wu et al 1995, Milstien et al 1997, Melnick 1996) has been associated with dramatically improved thermal stability of a variety of live viral vaccines.

- Promising approaches to thermostabilization include sugar glass encapsulation of live vaccines (Nicholls 2004) and vaccine antigen immobilisation onto the surface of L-glutamine micro-crystals via a rapid dehydration method, resulting in the production of a fine free-flowing powder (Murdan et al 2005).
- Enhanced thermostability of protein antigens has been achieved by a number of protein engineering approaching including the elimination of a partially unfolded state (McHugh et al 2004) and addition of a disulfide bond (van den Akker et al 1997).

Commercially successful thermal stabilization has also been achieved by the following methods:

- A thermostable Newcastle disease vaccine based on the I_2 strain was produced after the strain was identified in a program of selection for antigenicity and thermostability of a collection of field isolates (Bensink and Spradbrow 1999).
- Systematic investigations of lyophilization combined with stabilizers (for example lactalbumin hydrolysate-sucrose, Weybridge medium, buffered gelatin-sorbitol, or trehalose dihydrate) and reconstitution of vaccine (with for example distilled water or 1M $MgSO_4$ or 0.85% NaCl) has been applied successfully to the stabilization of a number of vaccines (Sarkar et al 2003, Jou et al 1996). An experimental form of lyophilization based on an ultra rapid method for the dehydration and preservation of live attenuated rinderpest and peste des petits ruminants vaccines (Xerovac) has been described (Worrall et al 2000).

However, one of the most successful examples of improved vaccine development is that which arose from the Thermostable Rinderpest Vaccine Transfer of Technology Project. The enhanced vaccine resulted from a detailed optimisation of lyophilization and is a powerful example of what can be achieved (Mariner et al 1991).

7.6.2 Duration of immunity (DOI)

When the rate of vaccination is low, and rates of revaccination presumably even lower, the duration of protective immunity becomes an even more important issue. Currently there is no readily available information that characterises the duration of immunity of any of the vaccines produced by the VPC. Vaccines with extended DOI are likely to play an important role in the future. Increasing the potency of vaccines or the development of novel formulations that allow repeated and sustained immunogen release from the site of administration are both methods currently employed or under investigation.

7.6.3 Emergence of new diseases

There are two principal types of disease emergence that could precipitate the need for new vaccines in Lao.

The first and immediate type of emergence is due to endemic diseases that become obvious and important as a consequence of intensification of livestock management and the realisation of effective control of the first priority diseases by vaccination and other means. Lower priority endemic diseases identified in the study of Perry et al (2002) included IBR, anthrax, blackquarter and *Brucella abortus* infection in cattle; infectious coryza, Gumboro disease, salmonellosis and mycoplasmosis in poultry; and *Brucella suis* infection in pigs. Already, pig farmers are (informally) importing vaccines for the control of parvovirus infection, *Haemophilus* infection and Aujezsky's disease which can also be added to the list of endemic diseases. Vongthilath and Blacksell (2000) identified *Salmonella choleraesuis* and *Erysipelas rhusiopathiae* as disease agents likely to have a huge impact. An insight into other endemic diseases that should be considered is gained by reviewing the vaccines currently available and in use in other South East Asian countries such as Vietnam, Philippines and Indonesia. While there are more than 1000

vaccines (single agent plus various combination products) available commercially in these countries (Page 2007), there are around 61 target diseases, 19 in pigs, 19 in poultry and 24 in ruminants as summarised in the following table. In addition to this list there are vaccines available for a number of other diseases, such as those caused by *Streptococcus suis*, *Lawsonia intracellularis* and *Brachyspira hyodysenteriae*.

Table 15. Vaccines available in Indonesia, Philippines Or Vietnam **(*diseases in bold are those for which vaccines are made by the Lao VPC)**
Pig Disease Agents (19)
Actinobacillus pleuropneumoniae
Bordetella bronchiseptica
Aujezsky's disease
*Classical swine fever**
Escherichia coli (K88, K99, F41, 987P and other antigens)
Foot and mouth disease
Haemophilus parasuis (Glasser's disease)
Leptospirosis (L canicola, L grippotyphosa, L hardio, L icterohaemorrhagiae, L pomona, L bratislava)
Mycoplasma hyopneumoniae (enzootic pneumonia)
Parvovirus
Pasteurella multocida
Porcine reproductive and respiratory syndrome (PRRS)
Salmonella choleraesuis
Swine influenza
Poultry Disease Agents (19)
Avian encephalomyelitis
Avian rhinotracheitis ('Swollen head syndrome'; SHS, pneumovirus)
Chicken anaemia virus
*Duck plague**
Egg drop syndrome
Coccidiosis
*Fowl cholera (Pasteurella multocida)**
*Fowl pox**
Haemophilus paragallinarum (Coryza)
Infectious bronchitis
Inectious bursal disease (Gumboro)
Infectious larynotracheitis
Mareks disease
Mycoplasma gallisepticum

Mycoplasma synoviae
*Newcastle disease**
Reovirus (viral arthritis; tenosynovitis)
Salmonella enteriditis
Salmonella gallinarum
Ruminant Disease Agents (23)
Bacillus anthracis (anthrax)
Bovine respiratory syncytial virus (BRSV)
Bovine virus diarrhoea (BVD)
Clostridial species (perfringens, novyi, septicum, chauvoei, tetani)
Coronavirus
Corynebacterium pyogenes
Foot and mouth disease (FMD)
*Haemorrhagic septicaemia**
Infectious bovine rhinotracheitis
Leptospirosis (L canicola; L pomona; L grippotyphosa; L hardjo; L icterohaemorrhagiae)
Orf
Parainfluenza Type 3
Pasteurella (Mannheimia) haemolytica
Rotavirus
Salmonella typhimurium

The second form of emergence is associated with the introduction of new diseases by uncontrolled transboundary animal movements, animal imports and bird migration. Already highly virulent PRRS in pigs and HPAI in poultry have been introduced in this way. It should be anticipated that further diseases will emerge, particularly if border controls are not strictly enforced.

7.6.4 Development of new vaccines

The large size, projected growth and highly competitive nature of the vaccine market combine to motivate a huge investment of more than US$300 per annum in vaccine technology. Global sales of veterinary vaccines were US$3.2 billion in 2004, representing 20% of global animal health product revenue. The combined sales of vaccines in Brazil, France, Germany, Japan, Spain, United Kingdom and the United States account for almost two-thirds of the global total. The five leading vaccine businesses (*Boehringer Ingelheim*, *Fort Dodge*, *Merial*, *Pfizer* and *Schering-Plough* generate three-quarters of all sales in the sector. The focus of considerable research is in immunogen identification, antigen presentation, formulation improvements and novel delivery methods. Recent reviews (for example those by Meeusen et al 2007, Azad and Rojanasakul 2006, Ulmer et al 2006, Pashine et al 2005, Wack and Rappuoli 2005, Shams 2005, Pastoret and Jones 2004, Carter 2003, Singh and O'Hagan 2003) have described advances in mucosal immunity, DNA vaccination, reverse vaccinology, conjugation technology, molecularly defined subunit vaccines, new approaches to attenuation of disease agents (especially by selected gene deletion) to produce improved modified live vaccines, vector vaccines, plant vaccines, immune system targeted adjuvants, vaccines against zoonotic food-borne pathogens, antigen loaded dendritic cells as vaccines, and synthetic vaccines.

There has also been much focus on new approaches to DIVA (differentiation between infected and vaccinated animals) vaccines for classical swine fever. Beer et al (2007) described five strategies (immunogenic CSFV peptides; DNA vaccines; viral vectors expressing CSFV proteins; chimeric pestiviruses; and trans-complemented deleted CSFV genomes [replicons]) to allow specific serological markers of vaccination. However, it is possible that each of these approaches may face the same problem of lower immunogenicity as faced by the current marker vaccines. Indeed the need for novel DIVA vaccines may be rendered superfluous if concurrent improvements in detection methods can be validated. For example, Li et al (2007) developed a multiplex nested RT-PCR for the detection and differentiation of wild-type viruses from C-strain vaccine of classical swine fever virus. Such a method may satisfy the demands of a DIVA strategy and allow C strain vaccines, widely accepted as the gold-standard of protection from CSF, to continue to be used.

It is anticipated that vaccines with improved stability, enhanced immunogenicity and easier delivery combined with an acceptable cost will progressively emerge over the next 10 to 15 years but in the short term conventional vaccines will continue to dominate.

Haigh (1997) reviewed the role of private industry in the transfer of vaccine technology to developing countries and noted that “the single most quoted justification for technology acquisition by developing countries is self-sufficiency followed closely by a cheaper product which saves hard currency by avoiding import of commercial vaccine. Unfortunately the facts do not generally support this justification. The benefits of scale are lost. …the validity of investing in traditional vaccine technology rather than continuing to import becomes very doubtful.”

The current portfolio of vaccines is unlikely to satisfy future demand for animal health. Because of the large number of possible sources of vaccines and the variation in quality, it is recommended that a National Registration Authority (NRA) is established to control the import of vaccines and other veterinary medicines, with particular attention to manufacturing quality and evidence of efficacy and safety.

7.7 Future options for Lao management of animal vaccine supply and distribution

7.7.1 Objectives of a new model

The following discussion of alternative options for a Lao animal vaccine business model assumes two prime objectives:

1. Use of vaccines by livestock owners in a manner that optimises the economic benefit to the owner and to other livestock owners
2. Delivery of objective (1) in a manner that minimises the cost to the Lao Government.

Objective 1 has two elements:

- Use of vaccine is *optimal* rather than *maximal*, i.e. vaccine is used when there is a genuine need for protection of livestock against a particular disease, which is not necessarily the entire population of the species in question.
- Vaccination by an individual owner of livestock sometimes has implications for other owners, because it reduces the overall challenge by the disease being protected against. Thus, individuals who do vaccinate provide some benefit to other owners, while those who do not vaccinate may free-load to some extent from those who do.

Lao authorities may also consider that a third objective is important:

3. To maintain a capability in vaccine production within Lao PDR.

However this report does not accept that this is a legitimate objective for a new business model for the following reasons:

- The argument that capability in animal vaccine production is a national security issue is weak. The international animal vaccine market is highly competitive worldwide and there are many sources of animal vaccines. It seems highly unlikely all or even many of these would become unavailable due to conflict or other factors. Also, it seems inconsistent to argue for protected domestic animal vaccine production when human vaccine production has no such protection (see also A4.3).
- Protection of Lao vaccine production is potentially in conflict with Objective 2: that is, imported vaccines may be more cost-effective than locally-produced vaccines. In fact, this is almost certain to be the case, as Lao PDR does not have the economies of scale to produce vaccines inexpensively (unless it increases production and seeks to export). Thus, additional costs will be incurred, either by the Lao Government or by the purchasers of the product.
- Furthermore, a desire to maintain local production may even conflict with Objective 1 if local product is unable to meet the quality parameters required to optimise the benefit to the user. Again, this is almost certainly the case, because the VPC does not have the scale to afford even the minimum standards of quality control practised by large vaccine companies.
- Even if the maintenance of national vaccine production capability is considered important, there are ways of managing this without engaging in full production – for example, by preserving seed stocks that could be used if needed, developing and keeping full production documentation and maintaining a small number of trained and experienced personnel.

7.7.2 A picture of a successful business model

A successful business model for animal vaccines in Lao PDR will be built upon the elements shown in Figure 5. The figure is explained in further detail below.

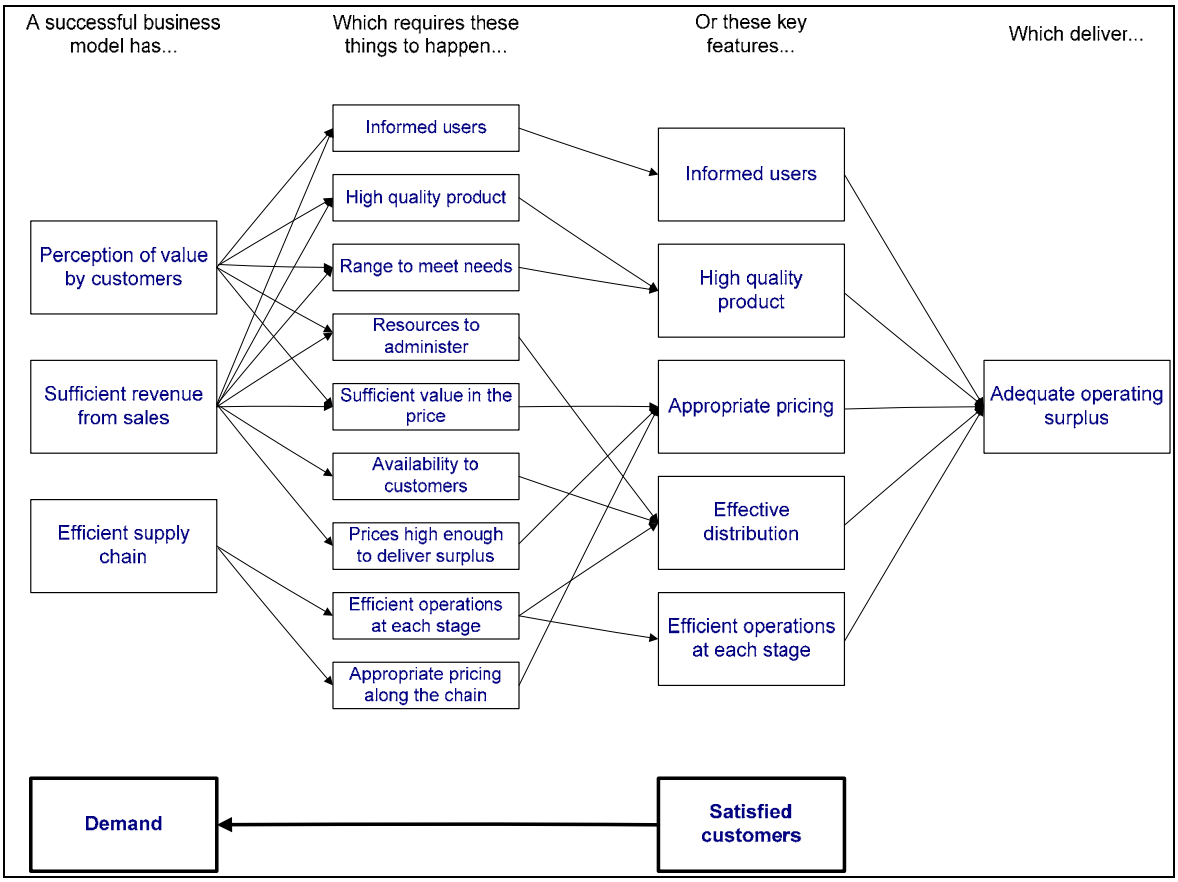
7.7.3 Perception of value by customers

In a successful model, VPC/VSU or ‘Approved Imported’ vaccines are valued by customers because they understand the benefit of vaccination (i.e. better productivity and fewer deaths) and they trust the quality of the product. This creates strong demand. This requires:

- Informed users
  - Education of end-users (including appropriate use of vaccines, the need to investigate apparent failures or adverse effects, etc)
  - Promotion
  - Informed intermediaries in the supply chain
- High quality product (including appropriate processes of transport, storage and supply)
- Resources available to administer vaccines
- A range of vaccines to match perceived disease needs
- Pricing that leaves a financial surplus for the end-user (i.e. it costs less to vaccinate than to suffer the losses)

- Continuous improvement of products to meet changes in customer expectations
- Ongoing technical support.

Figure 5. Elements of a successful business model for animal vaccines



7.7.4 Sufficient revenue from sales

In a successful model, there is sufficient revenue from sales to cover all costs of the supply chain, plus provide a sufficient surplus to allow investment in new technologies and growth of the business. This requires:

- High demand – related to the above (quality, value)
- Availability to customers
- High enough prices.

7.7.5 Efficient supply chain

In a successful model, the supply chain is efficient, with each player earning a return commensurate with the size of their investment, the risk inherent in their investment and the value they add to the chain. This requires:

- Efficient operations at each stage (production, storage, distribution, marketing, financial management etc)
- Appropriate pricing decisions along the chain
- Coordination along and between members of the supply chain
- Supply being responsive to changes in demand.

Gap analysis

Desired state	Current situation	Remedial measures
Informed users	• Understanding of the value of vaccination is low, but being addressed by various projects and some DLF material • Little or no promotion, branding etc anywhere along the chain • No sales force or marketing personnel	• Education of intermediaries, including resellers, VVWs, and end-users – tie-in with projects • Promotional activity – branding of product, signage • VVW or other SQP trained to monitor response to vaccination and rapidly investigate any suspected adverse effects
High quality product	• Uncertain, but evidence to suggest quality is poor • Insufficient return on sales in the business to allow high standard of QA or QC	• Consider importation of higher-quality product, with VPC providing QA role (also consider VPC specialises in key vaccines and imports others to fulfil needs) • Ensure available vaccines match disease needs of each target species • Generate greater returns and strengthen QA/QC at VPC
Appropriate pricing	• Appears that pricing at VPC/VSU might be too low – high mark-ups further down the chain suggest VPC/VSU price has little to do with demand • Little information on price elasticities of demand but field mark-ups indicate potential for increase in VSU prices • Constraints from government who require low cost product • Constraints with ability of smallholders to generate cash from livestock assets	• Test different pricing strategies – increase prices gradually • Work with projects assisting smallholders to generate cash from assets • Introduce different payment methods (eg explore options for ‘vaccine bank’, revolving funds)
Effective distribution	• Some regions are not well serviced • Question over integrity of cold chain	• Evaluate impact of current transport temperature profiles on vaccine quality • Only supply vaccines that match available / achievable cold chain. • Monitor quality of transported vaccine and have recall / replacement plan

Efficient operations at each stage	• VPC appears to be operating as cheaply as possible (too cheaply – lowest cost may equate to lowest quality) • Likewise VSU – shoestring budget and poor debt recovery but e.g. inefficient use of Director's time • No control over intermediaries	• Examine options to increase economies of scale • Consider establishing distribution hubs and/or accredited resellers in key areas for greater control • Examine merging of VPC/VSU operations • Credit management

7.7.6 Recommendations for a new business model

Options for a the future model of the Lao vaccine business were developed and a team comprising David Kennedy and Scott Williams presented background information in the form of a SWOT analysis (Appendix 2) and these options to a meeting of senior Ministry and DLF staff (Appendix 7) in Vientiane in late July 2007.

The team highlighted that:

- demand for and sales of vaccine are falling
- despite some cost-cutting, costs for raw materials (which are imported) are gradually increasing
- prices charged for vaccines have been held at artificially low levels and do not cover the true cost of production
- the VSU has a very large debt owed to it by customers and mostly by provincial governments
- staff numbers at the VPC are decreasing
- skills at the VPC have declined to a point where they are inadequate
- much of the donated equipment at the VPC is old, not operating and not being repaired
- the quality and effectiveness of some vaccines is declining.

The meeting acknowledged that the vaccine business was on a spiralling towards collapse.

Five options were presented and discussed frankly at the meeting which agreed that a combination of Options 2 and 4 be described more fully and submitted to the government. The options considered and the preferred new business model are described in Appendix 8 but the preferred model comprised the following:

1. An *Animal Vaccine and Medicine Supply Centre* (AVMSC), responsible for supplying the animal vaccine and animal medicine needs of Lao PDR.
2. Improved financial management in costing, forecasting, computerised accounting system.
3. A review and possible increases in price for some or all vaccines.
4. Production of unprofitable vaccines to be discontinued.
5. The recover of long-standing debts.
6. Improved quality in production and introduction of Good Manufacturing Practice.

7. Better marketing, including the establishment of a brand identity.
8. Establishment of a skills-based Advisory Board to the AVMSC.
9. Establishment of *Veterinary Medicine Regulatory Authority* (VMRA) to set standards for imported and locally produced vaccines and medicines.

These elements of a new business structure were finalised in collaboration with the DLF officers during the following month and submitted to the DLF on 31 August 2007 together with the SWOT analysis and research findings presented above. The DLF translated the documented and submitted it to the Minister of Agriculture and Fisheries. The Lao government approved the new model on 17 November 2007.

7.7.7 Implementation of the new model

A larger team visited Vientiane again during the week 26-30 November 2007 to conduct meetings with senior Lao officers on how to implement the new business model endorsed by the Lao Government on 17 November 2007. Workshops were also run with senior managers and with technical and administrative staff of the VPC and VSU to assess current systems and propose improvements.

The training aimed to help senior DLF staff to develop:

- Ownership of the model and of the changes required
- Confidence that they could implement the changes
- Skills, tools and guidelines to help them with planning and implementation.

The program for the week and the expected outcomes of the main components are outlined in Appendix 9.

Implementation Framework Meeting

The opening meeting on the Monday afternoon was attended by most of the senior animal health officers and a senior planning officer from the Ministry . The new model was affirmed and information provided on quality management and establishing a regulatory authority. The roles of the proposed Animal Vaccine and Medicine Supply Centre (AVMSC) Advisory Board were discussed and it was agreed to develop draft terms of reference during the week. It was also agreed that senior Lao officers would lead discussion at the closing Implementation Meeting on the Friday as part of the process of taking ownership of the implementation.

The benefits of developing and implementing a Lao National Regulatory Authority for veterinary medicines (vaccines and veterinary pharmaceuticals such as the antimicrobial and antiparasitic agents) was presented and discussed during the opening meeting. The regulatory mechanisms could be modelled on the Lao approach to human medicine imports. It was proposed that a high level task force be assembled to prepare a plan for consideration by Government decision makers. Adopting key elements of the WHO medicine procurement guidelines could be very beneficial and would rely on manufacturing quality audits conducted by selected overseas regulators and other reliable authorities (Refer: Regulation of vaccines: building on existing drug regulatory authorities' (http://whqlibdoc.who.int/hq/1999/WHO_V&B_99.10.pdf.)

Vaccine manufacturing and storage

Over the next two days team members reviewed manufacturing processes, procedures and records and inspected and assessed production and storage facilities and operations at the VPC with the Director and other staff. At the start of this phase of the workshop, the

Director, Dr Sithong, presented an overview of issues at the VPC in response to the discussion on quality production at the initial meeting.

In addition to the four team members who participated in the first visit in February 2007, the team included a highly experienced quality consultant in vaccine manufacturing, Richard Bevan. With Stephen Page, Richard assessed the personnel, premises, equipment and processes at the VPC and recommended improvements in a preliminary quality plan. At the Friday meeting, the following frank conclusions were presented including:

Current VPC staff are motivated, enthusiastic and very capable and it was recommended that:

- Staff need
  - Training in standard operating procedures (SOP) to capture all parts of production
  - Training in other responsibilities such as labelling
  - New production QC testing procedures
  - Specific rules for production processes
- Additional staff are needed
- Quarantine release system should be established
- Labelling system and QA release need to be improved.

Good Manufacturing Practice at the VPC could benefit from refining its operation in respect to:

  - Cleanliness
  - Traceability
  - Documentation
  - Labelling
  - Product release

There are a number of major technical issues that need to be addressed:

- VPC is:
  - Old
  - Run down
  - Microbiologically contaminated
- VPC is in need of:
  - Refurbishment
  - Maintenance
  - Upgrading for the future
  - Addressing capacity issues for future production

Tasks that need to be undertaken soon include repairing and painting rooms with epoxy paint to ease cleaning, systematic and defined cleaning and disinfection of production rooms; and repairing electrical systems, water system, autoclaves, egg incubators, freezers and fridges.

New equipment that is required in the short term were itemised as follows:

- Generator
  - Buy starter battery for standby generator

- Cold storage
  - 3 domestic fridges / freezers to replace unreliable and 20 year old units in viral, bacterial and QC areas
    - Guarantee bacterial seeds
    - Guarantee WIP viral process for CSF vaccine
    - Guarantee QC reference preparations
- Water
  - Acquire 500 litre stainless steel tank to hold distilled water.
  - Tank to have heater to keep water hot before use.
- Moisture meter
  - To determine moisture content of freeze dried vaccines
- Freeze drier - chart recorder
- pH meters
- Autoclaves - chart recorders (optional)
- Temperature recording and validation
  - Standardised thermometer for calibration
  - Maximum / minimum thermometers on fridges, freezers, incubators
- New autoclave
  - Consider vacuum cycle autoclave to sterilise clothing for use in aseptic processes
- Additional needs:
  - Separate challenge cultures from production cultures in -70^{0}C freezer
  - Back up master cultures stored elsewhere
  - New -70^{0}C freezer
  - New -35ºC freezer to hold bulk viral antigen
  - Retention sample testing principles
  - Product stability profiles to be undertaken
  - Preservatives for inactivated products (thiomersal).

This information was presented to the DLF on 30 November and is supplemented by more detailed information on Initial Audit and Quality Plan that was sent to DLF on 19 December 2007 (see Appendix 10). The DLF felt that, following an encouraging meeting with the Vice-Minister during the week of the Implementation worshops, it was an appropriate time to report on the outcomes of the implementation workshops and their plans for implementing the new business model.

7.7.8 Financial management

A financial management workshop was also run at the National Animal Health Centre for administrative and accounting staff over two days. Administrative and accounting staff from both the VPC and VSU attended with the Directors of both units. The principles of accounting and financial management were presented by Scott Williams and discussed and applied to examples of Lao vaccine manufacture. Topics included:

- Estimating and allocating direct and indirect costs
- Gross margins and operating profit as measures of financial performance
- Budgeting, planning, forecasting and monitoring performance
- Invoicing and debt management
- Recovery of debt from provincial government customers
- Potential accounting software.

The current systems at the VPC do not adequately record transactions of manufacturing inputs such as raw material receivals and transfers from store that are needed to accurately estimate direct production costs. Several participants, however, including the VPC Director, understood the workshop well and demonstrated a good understanding of accounting principles. A comprehensive set of slides that were used in the presentations (and improved following the workshop) were sent to the DLF.

7.7.9 Marketing

On the last morning a marketing workshop covered the basic principles of marketing and emphasised the importance of the two-way relationship between a business and its customers. It identified market segments for animal vaccines in Lao PDR and outlined how a marketing plan could be developed to address these (eg government offices, livestock development projects, commercial pig and poultry producers and smallholders). A set of slides from the presentation, which included the outline of a marketing plan, were sent to the DLF.

7.7.10 Final Implementation Meeting

On the final afternoon, the team met with senior DLF officers and with the MAF Director of Planning(?) to review the outcomes of the week and to propose the way forward. The Director of the VPC presented his views on improving financial management and the future structure and responsibilities of managers. The meeting developed a draft organisational structure of the new AVMSC (Appendix 11) and Draft Terms of Reference were also agreed for the AVMSC Advisory Board (Appendix 12). The DLF was keen to present these to the Vice Minister, with whom discussions had been held recently. As previously noted, the Draft Quality Plan would be useful to the DLF in the near future as it presents a frank assessment of what steps the VPC needs to take to satisfy the minimum standards of a specifically adapted code of GMP developed for the Lao VPC. It also recommends a range of high priority improvements, some of which would require significant capital expense.

8 Impacts

The project will only make a significant impact if the new business plan for vaccine supply is implemented by the Lao government. The following sections assume that this will occur.

8.1 Scientific impacts – now and in 5 years

There has been no significant scientific impact from the project yet but in the medium to long term, the quality and effectiveness of animal vaccines and other medicines that are manufactured in Lao PDR or imported should gradually improve.

8.2 Capacity impacts – now and in 5 years

The capacity of managers and staff to improve production and the management of supply and marketing of animal vaccines has been significantly improved by the project. Managers and senior DLF officers developed their appreciation and understanding of business management and the potential improvements that could be made. The capacity to produce vaccines and manage the business should be enhanced through implementation of the business plan with further technical input on vaccine quality management and business guidance from the proposed Advisory Board.

8.3 Community impacts – now and in 5 years

The Lao government is planning expansion and diversification of the smallholder livestock production sector. The rural community and the country should benefit from more efficient and effective animal production and better animal products resulting from better disease prevention and control.

8.3.1 Economic impacts

Better management of vaccine supply should lead to better range of high quality animal health products being available at competitive prices. The direct economic impacts should be on reduced animal deaths from diseases such as CSF and HS and increased livestock production and turn-off as young animals survive longer. The indirect effects should follow as smallholders increased their capacity to sell their surplus stock and markets develop to buy that surplus, household income should increase with flow on effects for rural communities.

At the national level development of quality procedures that result in vaccines of international quality could potentially lead to small exports for specific products such as HS and CSF vaccines.

8.3.2 Social impacts

Significant social improvements should follow improved the economic situation for smallholders allowing spending of cash income on housing, education and health.

8.3.3 Environmental impacts

No direct environmental impacts are anticipated from. Indirect impacts may result from changes in animal management that follow improved disease prevention and control.

8.4 Communication and dissemination activities

It had been proposed that some commercial and provincial government people would participate in the November training workshops however the DLF decided to focus on the staff of the VSU and VPC. It is now proposed that communication of changes in the animal vaccine business will be undertaken through marketing and normal government channels.

9 Conclusions and recommendations

9.1 Conclusions

The long term capability of the proposed Animal Vaccine and Medicine Supply Centre (AVMSC)-effectively manufacture vaccines, even with the changes proposed in this report, is problematic. While it is technically possible to manufacture vaccines in a way that is consistent with GMP this can only happen with significant and ongoing investment in people, premises and equipment.

The Centre will still only be able to produce a limited range of vaccines and imports will be required to satisfy demand for vaccines for endemic and epidemic diseases, such as FMD and rabies. A range of other vaccines for commercial pig and poultry farms will largely continue to be imported and the increasing numbers of contract rearers will be supplied by the companies supplying the animals. It is very likely that imported vaccines will be less expensive and of equivalent or higher quality than locally produced products. For instance, it probably costs a large manufacturer less than USD 1.00 to produce a bottle of 1,000 doses of SPF Newcastle disease vaccine which could be sold for as little as USD 2.00, depending upon the market. The VSU currently sells its 100 dose non-SPF ND vaccines for approximately USD 0.50-60 which are onsold to farmers at a significant markup.

In addition, continuity of supply of imports which may be supplied from a large number of possible manufacturers is likely to be more reliable than local production which will be susceptible to equipment or product failure with little potential for backup in times of crisis or critical need. The greater the value of vaccine and medicines that are imported, the greater the bargaining position of the Centre will be to gain a better price. The Centre must decide whether to try to compete to supply the commercial sector or to concentrate on supplying quality assured vaccines to smallholders. Currently, equipment is production limiting; for instance, one freeze dryer is being used to produce small volumes of five different viral vaccines and one 40 litre fermentor produces the two bacterial vaccines. This pales in comparison with the multiple 1,000 litre fermentors that large vaccine manufacturers use. Profits from vaccine sales will not cover the costs of replacing these with larger equipment. In addition, the VPC production is currently totally dependent on one aging autoclave remaining operational; to supplement or replace it would cost between AUD 250,000 and AUD 500,000. As it is also unlikely that the Lao Government would buy such equipment, any expansion would depend on the generosity of donors.

Whatever the decision, the setting of standards for vaccines that are produced by the Centre or imported is an essential step in managing the safety and efficacy of the vaccines used in Lao PDR. Establishing the capacity and processes to do this is a high priority. It is not recommended that the Centre become a testing facility for imported vaccines, as this would become logistically and bureaucratically very difficult with issues such as quarantine before release, testing capabilities of the Centre, failure in testing procedures and cost recovery. Reputable suppliers would be reluctant to sell legally into Lao PDR which could also lead to avoidance of the system by smuggling.

A better approach (and consistent with international practice) will be to develop a national registration system with clear approval requirements and to import from manufacturers that are accredited, by international organisations (such as OIE or FAO) or by regional or national authorities (such as the European Union, United States, Thailand or possibly China). The proposed Lao veterinary medicine registration authority would require suppliers to have GMP accreditation and supply supporting documents for approval. The Centre may complement this by random rather than routine evaluations of vaccines from time to time.

The AVMSC's supply of appropriate vaccines and medicines for Lao PDR must not only be technically sound but financially sustainable. The particular challenges facing the Centre in this area are to properly cost production, to increase sales and income and to manage debt. The vaccination coverage of livestock populations in Lao PDR is very low and demand and sales will depend on significant increases in vaccination rates. A recent meeting on animal health services in Vientiane was told that less than 1% of cattle and 2% of pigs were vaccinated in three districts in the Vientiane municipality. Current vaccine distribution would suggest that this is an underestimate for the country as a whole, but it highlights both the challenge and the potential for a significant market increase. This challenge is heightened by the low level of veterinary staff and infrastructure in the country. The current SADU project in northern provinces is trialling a new approach to basing animal health services to smallholders on a commercial footing and early results on uptake and vaccination coverage in a pilot are reportedly encouraging (Source: j.connell@cgiar.org, LaoFAB, 9 Dec 2007).

Finally, successful implementation of the new model will require strong and enthusiastic leadership that is supported by the government and by the Advisory Board and by external expertise. Able leadership exists amongst the small number of senior DLF staff who have contributed to this project. In particular we consider that success will depend heavily on the on-site leadership and technical and financial skills of the current Director of the VPC, Dr Sithong Phiphakhavong.

9.2 Recommendations

ACIAR may consider it a worthwhile investment to support the new AVMSC managers' efforts by sponsoring technical support to improve quality vaccine supply and further guidance on development and implementation of the business management components of the new model.

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10.2 List of publications produced by project

Not applicable

11 Appendixes

11.1 Appendix 1 Initial Team Visit to Lao PDR, 14-25 February 2007

Date	Activity
Wed 14 – Thurs 15 Feb	Australian team members travel to Vientiane
Thurs 15 Feb	Initial discussions with AVSF team member and DLF counterparts
Fri 16 Feb	Stakeholder workshop 25 participants from DLF, PAFO from selected provinces, private sector etc., Lao Plaza Hotel, Vientiane
Mon 18 – Fri 23 Feb	Field research • Vientiane at VPC, VSU, DLF and other government offices • Champassak and Xieng Khouang provinces (see below)
Sat 24 – Sun 25 Feb	Australian team members return to Australia

Field Research Activities – Vientiane	
Team Members: S Williams and S Page (to 19 Feb). Counterpart: Sengpheth Somsanith	
Mon 19	Meet Dr Khamphy Tkhammavon, DLF Deputy Director General Meet Jamie Conlan at NAHC
Tues 20	Meet Dr Sithong Phiphakhavong and Dr Michael Handlos at NAHC Meet Dr Somphanh Chanphengxay, DLF Deputy Director General, with Drs Kennedy and Bourgeois-Luthi
Wed 21	Visit VSU with Drs Kennedy and Bourgeois-Luthi Meet Dr Ricarda Mondry of the FAO
Thurs 22	Visit VPC, meet Dr Sithong and Mr Sengpheth Telephone discussion with Dr Rod Lefroy, CIAT
Fri 23	Meet Mr Southavanh Thephasy, Deputy Chief of Food and Drug Control Division Visit Department of Customs (contact unknown) Meet Mr Santipharb Phomvihane, Director General, Ministry of Finance

Field Research Activities – Champassak & Xieng Khouang Provinces	
Team Members: D Kennedy and N Bourgoise-Luthi. Counterpart: Signa Kittiphone	
Sun 18	Champassak province: • travel to Pakse • visit of 3 “one stop” shops selling veterinary medicine, animal vaccines, chemicals for crop protection and agricultural implements • visit of a private pig farm (60 sows) in the outskirts of Pakse town

Mon 19	Champassak province: • visit of a private pig farm (45 sows) in Paksong district • visit of a government cattle farm (400 ha, 130 heads) in Paksong district, Boloven Plateau • visit of Paksong DAFO storing and issuing veterinary medicine and animal vaccines • visit of a private small-holder farm (20 cattle heads, some chickens and pigs) in Paksong district • visit of 1 village veterinary worker (VVW) • visit at 2 shops selling veterinary medicine, animal vaccines, chemicals for crop protection and agricultural implements
Tues 20	Champassak province: • visit at PAFO • travel back to Vientiane • short meeting with the whole team in Vientiane • meeting with Dr. Somphanh, DLF
Wed 21	Vientiane and Xieng Khouang province: • visit of VSU • travel to Xieng Khouang • meeting at PAFO
Thurs 22	• meeting with Ms. Oumma, PAFO staff and owner of a private veterinary shop • meeting with a district livestock officer • visit of PAFO veterinary shop and laboratory • visit of a private “one stop shop” selling veterinary drugs and vaccines, as well as animal feed agricultural implements and chemicals • visit of a government cattle farm (600 ha, 80 heads), established under IFAD cow bank project • visit of a VVW
Fri 23	• visit of a poultry farm (layers) belonging to the Lao Airforce • visit of a small-holder farmer (cattle, pigs, poultry) • visit of a commercially oriented cattle farmer • travel back to Vientiane • closing dinner

11.2 Appendix 2 SWOT Analysis

Internal Factors ►	*Strengths*	*Weaknesses*
External Factors ▼	• Vaccine supply can meet much of current low level of demand. • Lao vaccines cover most of the diseases that have been classified as important by the DLF. • Government in-principle support for local production. • Government currently allows importation of other vaccines to supplement supply. • Commercial farmers informally import other vaccines they need from Thai retailers. • A distribution network is established to provincial capitals. • The VPC is a purpose built and equipped facility. • There is competition among multiple outlets in some provincial towns. • Profitable retail outlets. • Vaccine retail outlets and PAFO/DAEFO have fridges and freezers for cold chain. • Commercial farmers, VVWs, retailers understand uses and limitations of vaccines. • Some projects, VVWs and village heads organise vaccination campaigns (eg HS) • Revolving funds have been established to support some village vaccination programs (eg CSF).	• Very low vaccine coverage of national livestock population. • Heavy reliance on one local manufacturer (VPC). • Numbers and skill level of staff declining at VPC. • Maintenance of VPC equipment is inadequate. • VPC is dependent on imported production materials. • Quality of Lao vaccines is uncertain as there is no independent assessment. • VPC QC and manufacturing practice is inadequate at some times. • VPC is financially dependent on donor funds for equipment and training. • Inconsistent supply of some vaccines (eg HS oil vaccine). • Unavailability of Lao or suitable imported Blackleg vaccines. • There is no official standard for imported vaccines. • Low level of business skills in manufacture and distribution system. • There is no public catalogue of vaccines availability. • There is very little marketing of vaccination and vaccines (ie promotion, branding, sales analysis, etc). • VSU has large debt and long list of long standing debtors. • Prices not covering production costs of some vaccines. • Accounting and stock recording/reporting system is labour intensive and limited. • Government financial support for national vaccination programs is inadequate. • The cold chain is variable with no measures of effectiveness. • The cold chain is not extensive and dependent on refrigeration/electricity. • Storage is inadequate for some vaccines (especially Lao CSF vaccine that requires -20^{0}C). • Diagnosis and surveillance and reporting of diseases of smallholder livestock is poor and the relative and absolute importance of various diseases is uncertain. • Current demand for most vaccines is very low. • Ability to access vaccine in remote areas is very low. • Many smallholders see livestock as asset or secondary activity and not as business and do not market surplus animals. • Smallholders do not vaccinate if disease has not occurred recently. • Smallholders are largely unaware of animal disease and the role of vaccines. • Local and national cost-benefit of vaccination is not known or appreciated. • There is little or no monitoring of vaccine efficacy. • Training and ongoing support/mentoring of VVWs is largely dependent on donor projects • Many VVWs leave jobs as there is not enough work/returns. • VVWs expected to vaccinate family's, friends' and neighbours' animals free of charge.

Opportunities	SO Strategies	WO Strategies
• Government increasing support for livestock industry development. • Ministry vision of farmer driven programs. • Government support for business development. • Government interest in commercial partnerships with private companies. • Government priority to open up external trade • Livestock Development projects wanting to improve animal health • Lao involvement in regional animal health programs such as SEAFMD • Other producers of quality vaccines are manufacturing and/or distributing in other countries in the region. • Thermostable vaccines less dependent on cold chain. • Lao vaccine is recognized by farmers and retailers. • Existing computerised VSU management and accounting system has been developed. • Private retailers are keen to develop their businesses. • There is potential for price increases at VPC/VSU without having significant impact on price to smallholders • External expertise available to help develop and implement GMP. • New vaccine technologies developing. • Lao Health Ministry has established import and registration procedures. • Revolving funds operate for human drugs and CSF vaccine in Lao PDR.	*Using Strengths to take advantage of Opportunities* • Engage government as a customer for "public good" vaccines (eg HS programs). • Evaluate success of developing sustainable VVW models (eg SADU). • Accredit informed and quality vaccine retailers and VVWs. • Accredit quality vaccines – Lao and imported. • Market Lao vaccine better – brand (eg LaoVax), slogan, fridge stickers, shop signs. • Obtain support from vaccine manufacturers to ensure VPC production is world class. • Integrate high quality vaccine (and other veterinary medicines) imports with high quality local production. • Export of selected vaccines from VPC to neighbouring (and more distant) countries. • Combine vaccine supply with other animal health measures (health checks, disease surveillance, nutrition advice etc). • Run animal vaccine programs at same time as human vaccination programs in remote communities. • Demonstrate field effectiveness of animal health treatments/vaccination. • Adapt Lao health vaccine import and registration model. • Collaboration on vaccine and drug production with neighbouring countries.	*Taking advantage of Opportunities to overcome Weaknesses* • Identify true costs of production and set prices accordingly. • Stop producing unprofitable vaccines. • Introduce continuous improvement principles and GMP culture • Introduce ongoing technical training program of VPC staff with international support. • Use external business management skills. • Differentiate government, commercial and smallholder markets. • Collect provincial and other debt to VSU with national government support. • Establish a national registration authority to assess and control quality of imported and local products. • Combined medical / veterinary vaccine transport and storage (cold chain) as well as vaccination campaign (eg Chad model) • Encourage programs that support commercialisation of smallholder livestock production. • Promote understanding and cost benefit of vaccination as a component of animal health insurance. • Identify and allocate marketing jobs within VSU and train or appoint appropriate staff. • Implement computerised management system and train VSU staff in its use. • Improve thermostability of existing vaccines. • Develop/import thermotolerant vaccines.

• Threats • Business failure of the VPC/VSU because they are unable to recover debt. • Donor projects promote dependency through providing free vaccine. • Potential poor standards of some vaccines imported by commercial farmers. • High level political support for supply is not matched by funding. • PAFO/DAFO advise against private shops because of alleged poor vaccine handling and storage. • Inadequate temperature control of cold chain leads to ineffective vaccine. • Disease outbreaks due to poor quality vaccine/contamination. • Training too many VVWs threatens livelihood of existing active VVWs. • Endemic diseases become more important with more intensive livestock management. • Introduction of new diseases (eg virulent PRRS). • Inability to import required vaccine.	***ST StrategiesUsing Strengths to avoid Threats*** • Establish quality and other criteria for mix of imported and local vaccines • Report and manage VSU debt with government back-up • Continuing education of and investment in active and effective VVWs through projects, regional and national meetings, forums etc to keep them informed, increase motivation and share experiences. • Projects promote cost effectiveness/value for money of vaccination and • Utilise imported vaccines to complement local production. • Promote role and credibility of accredited retailers.	***WT Strategies Strategies to minimise Weaknesses and avoid Threats*** • Develop and monitor quality standards for manufacturing and distribution. • Develop vaccines with less stringent cold chain requirements (eg CSF). • Gain government commitment to establish sustainable import processes. • Improve diagnosis and surveillance and reporting to the field of occurrence of major diseases. • Engage national and provincial government as customers which have to pay for the product they require. • Improve selection process of VVW with a view to maximising retention on the job. • Develop standards and regulation to allow rapid import of quality vaccines as needed.

11.3 Appendix 3 Sources of Classical Swine Fever and Haemorrhagic Septicaemia Vaccines

11.3.1 Classical Swine Fever Vaccines

59 Vaccines described from 32 Countries.

- Chinese lapinized strain: 26
- GPE- strain: 11
- Thiverval strain: 3
- LOM strain: 4
- subunit DIVA vaccines: 2
- other strains: 3
- unknown strain: 10

#	COUNTRY	MANUFACTURER	DETAILS	USE IN CILMPV*
1	Myanmar	Advanced Biologicals	Strain not described	Myanmar
2	Argentina	Agrofarma S.C.A.	Chinese (lapinized)	
3	Russia	Agrovet	LK-VNIIVVIM live K live	
4	France	Bayer	Subunit (E2 antigen) [Oil]	
5	Singapore	Bestar Laboratories	GPE live	Vietnam
6	Peru	BFV Laboratorios S.R.L.	Chinese (lapinized)	
7	Mongolia	Biocombinat	Strain not described	
8	Nepal	Biological Products Division	Chinese (lapinized)	
9	Peru	BIO-TONG S.A.	Chinese (lapinized)	
10	Czech Republic	Bioveta	TVM-1	
11	Philippines	Bureau of Animal Industry	Chinese (lapinized)	Philippines
12	Thailand	Bureau of Veterinary Biologics	Chinese (lapinized)	
13	Venezuela	C.A. Laboratorios Asociados	Chinese (lapinized)	
14	Hungary	CEVA	Thiverval strain	Philippines
15	France	Ceva Sante Animale	Chinese (lapinized)	Philippines
16	Japan	Chemo-Sero-Therapeutic Research Institute	GPE live	

17	Japan	Chiba Serum Institute	GPE live	
18	Korea	Choong Ang Animal Disease Laboratory	Strain not described (combination vaccine with swine erysipelas)	Vietnam
19	Korea	Daesung Microbiological Labs	LOM Live	
20	Colombia	Empresa Colombiana de Productos Veterinarios S.A.	Chinese (lapinized)	
21	Taiwan	Formosa Biomedical	Lapinised Philippine Cornell (LPC) strain	Philippines
22	Brazil	Fort Dodge Saúde Animal	Chinese (lapinized)	Philippines, Indonesia, Vietnam
23	Argentina	Instituto de Sanidad Ganadera S.R.L.	Chinese (lapinized)	
24	Argentina	Instituto Rosenbusch S.A.	Chinese (lapinized)	
25	Netherlands	Intervet International B.V. (Porcilis CSF Live)	GPE live	Philippines
26	Netherlands	Intervet International B.V. (Porcillis pesti)	Subunit (E2 antigen) [Oil]	Philippines
27	Italy	Istituto Zooprofilattico Sperimentale	Chinese (lapinized)	
28	Korea	KBNP	LOM Live	
29	Japan	Kitasato Institute	GPE live	Indonesia, Vietnam
30	Korea	Komipharm International Co., Ltd.	LOM Live	
31	Korea	Korea Microbiology Lab	LOM Live	Vietnam
32	Japan	Kyoritsu Seiyaku Corporation	GPE live	
33	Japan	Kyoto Biken Laboratories, Inc.	GPE live	Indonesia
34	Cuba	LABIOFAM	Chinese (lapinized)	
35	Argentina	Laboratorio de Diagnostico Y Prevencion Veterinario	ATCC 131-VR	

36	Paraguay	Laboratorio de Producción de Biológicos	Chinese (lapinized)	
37	Peru	Laboratorios Caletti S.C.R.L.	Chinese (lapinized)	
38	Peru	LASAVET S.A.	Chinese (lapinized)	
39	Argentina	Lauda Laboratorios Unidos de America S.A.	Strain not described	
40	Myanmar	Livestock Breeding and Veterinary Department (LBVD)	Strain not described	Myanmar
41	Japan	Matsuken Pharmaceutical Industry Co., Ltd.	GPE live	Philippines
42	France	Merial (Pestiffa)	Chinese (lapinized)	Philippines
43	Argentina	Merial Argentina S.A.	Chinese (lapinized)	Indonesia Vietnam
44	Slovakia	MEVAK a.s. Nitra	Strain not described	
45	Malaysia	MVP	GPE live	Philippines
46	Mexico	National Biologicos Producer Veterinarios	Strain not described	
47	Vietnam	Navetco	Chinese (lapinized)	Vietnam
48	Japan	Nisseiken Co., Ltd.	GPE live	
49	Romania	Pasteur Institute	Chinese (lapinized)	Philippines
50	Indonesia	Pusvetma (Hogsivet)	Strain not described	Indonesia
51	China	Qingdao Yebio Bioengineering Co., Ltd./Yebio Products	Strain not described [Combination vaccine with swine erysipelas & pasteurellosis]	
52	Germany	Riemser Arzneimittel AG	Chinese (lapinized)	
53	Romania	ROMVAC Company SA	Thiverval strain (RP 93 Live)	
54	Japan	Scientific Food Laboratory Co., Ltd.	GPE live	
55	Taiwan	Ta Foong Veterinary Biological Laboratories	Strain not described	Philippines

56	Peru	Tecnología Química Y Comercio	Chinese (lapinized)	
57	Lao PDR	Vaccine Production Centre (VPC)	Chinese (lapinized)	Lao PDR
58	Croatia	VETERINA Animal Health Ltd.	Chinese (lapinized)	Philippines
59	Thailand	Veterinary Biologics Center	Chinese (lapinized)	

CILMPV: Cambodia, Indonesia, Lao PDR, Myanmar, Philippines, Vietnam

11.3.2 Haemorrhagic Septicaemia Vaccines

36 vaccines
Pasteurella multocida, serotype B :2 or E :3

#	COUNTRY OF MANUFACTURE	MANUFACTURER	VACCINE DESCRIPTION
1	Myanmar	Advanced Biological	
2	India	Animal Vaccine Institute, Gandhinagar, Gujarat	
3	Mongolia	Biocombinant	
4	India	Brilliant Industries	
5	Philippines	Bureau of Animal Industry	B:2 aluminium potassium sulfate
6	Thailand	Bureau of Veterinary Biologics	B:2, Oil adjuvant
7	Sudan	Central Veterinary Research Laboratories	
8	Spain	CZ Veterinaria S.A.	B:2 aluminium hydroxide
9	India	Haryana Veterinary Vaccine Institute, Hisar, Haryana	
10	India	Indian Immunologicals, Hyderabad, Andhra Pradesh	oil adjuvanted (OA) aluminium hydroxide
11	India	Indian Veterinary Research Institute (IVRI), Uttar Pradesh	
12	India	Institute of Animal Health & Production, Patna, Bihar	
13	India	Institute of Animal Health & Veterinary Biologicals, Mhow, Madhya Pradesh	
14	India	Institute of Animal Health & Veterinary Biologicals, West Bengal	
15	India	Institute of Animal Health and Veterinary Biologicals (IAH&VB), Nandinagar, Bidar	
16	India	Institute of Animal Health and Veterinary Biologicals, Thiruvananthapuram, Kerala	P52 Paraffin / lanolin
17	India	Institute of Veterinary Biological Products, Pune, Maharashtra	
18	India	Institute of Veterinary Biologicals, Guwahati, Assam	
19	India	Institute of Veterinary Biologicals, Lucknow, Uttar Pradesh	
20	India	Institute of Veterinary Preventive Medicine, Ranipet, Tamil Nadu	

21	India	Intervet, Pune, Maharashtra	Aluminium hydroxide gel
22	Philippines	Lakpue Drug	B:2 aluminium potassium sulfate
23	Malaysia	Malaysian Vaccines and Pharmaceuticals (MVP)	
24	Philippines	National Institute of Molecular Biology & Biotechnology	B:2 aluminium hydroxide
25	Myanmar	National Vaccine Production Laboratory	
26	Nigeria	National Veterinary Research Institute	B:2, E:3, 4
27	India	Orissa Biological Products Institute, Bhubaneswar, Orissa	
28	India	Punjab Veterinary Vaccine Institute, Ludhiana, Punjab	
29	Indonesia	Pusvetma	
30	India	Regional Veterinary Biological Unit, Jaipur, Rajasthan	
31	Lao PDR	Vaccine Production Centre (VPC)	Oil adjuvant Aluminium hydroxide
32	Indonesia	Vaksindo	
33	India	Veterinary Biologicals & Research Institute, Hyderabad, Andhra Pradesh	
34	Turkey	Veterinary Control and Research Institute	
35	Malaysia	Veterinary Research Institute	Type B:2, double adjuvant
36	Egypt	Veterinary Serum and Vaccine Research Institute	Oil adjuvant

11.4 Appendix 4 Good Manufacturing Practice Principles

Veterinary medicines are subject to a registration process that requires them to be fit for their intended use and to not place treated animals or users at risk due to inadequate safety, quality or efficacy. Veterinary medicines must be manufactured in such a way that they comply with their registered particulars and that there is batch-to-batch consistency.

The ultimate responsibility for attaining these quality objectives lies with senior management, but their attainment also requires the participation and commitment of all staff, at all levels, within the manufacturing organisation. In order to achieve these objectives, the manufacturer must have in place a comprehensively designed, adequately resourced and correctly implemented system of quality assurance, incorporating the principles of good manufacturing practice (GMP).

Quality assurance is a wide-ranging concept covering all aspects of the manufacturing process that individually or collectively influence the quality of a manufactured product. It is the sum total of the arrangements made to ensure that veterinary medicines are consistently manufactured in an appropriate manner to the quality standards required for their intended use. Quality assurance therefore incorporates both GMP and quality control as well as other factors outside the scope of this Code of GMP such as environmental and occupational safety controls.

Quality assurance requires manufacturers to have in place a quality management system encompassing the organisational structure, responsibilities, procedures, instructions, processes and resources necessary for implementing quality management. That system must ensure that facilities and equipment are suitable for the types of products made, that there are sufficient competent personnel and that appropriate procedures are in place to ensure appropriate quality standards are met. In addition, the system must ensure that all materials involved in the manufacturing process (including raw materials, intermediate materials or samples from any material relevant to product quality) are checked and tested, where necessary, to ensure that they meet required quality standards before they are released for use. Procedures must be in place to ensure that the finished product has been made correctly and meets all the required quality tests before it is released for supply or sale.

The quality management system must be relevant to the needs of the product. It must be fully documented, monitored for effectiveness and incorporate an element of continuous improvement.

Good manufacturing practice (GMP) is the part of quality assurance that ensures that products are consistently manufactured to the quality standards appropriate for their intended veterinary use and in accordance with their registration particulars and specifications. GMP is concerned with both production and quality control. It is a means of giving consumers confidence that the products meet the required quality standards and are safe and reliable for the purposes for which they are intended.

The basic requirements of GMP are that:

1. all manufacturing processes are clearly defined, are systematically reviewed in the light of experience, and shown to be capable of consistently producing veterinary medicines that comply with their specifications and the required quality standards
2. critical steps of manufacturing processes and significant changes to the processes are validated
3. all necessary facilities for GMP are provided, including:
    - appropriately qualified, trained or experienced personnel

- adequate premises and space
- suitable equipment and services
- correct materials, containers and labels
- approved procedures and instructions
- suitable storage and transport.

4. instructions and procedures are written in an instructional form in clear and unambiguous language, specifically applicable to the facilities provided
5. operators are trained to carry out procedures correctly
6. records are made manually and/or by recording instruments during manufacture which demonstrate that all the steps required by the defined procedures and instructions were in fact taken and that the quantity and quality of the product was as expected; any significant deviations are fully recorded and investigated
7. records of manufacture, including distribution, that enable the complete history of a batch to be traced are retained in a comprehensible and accessible form
8. a system is available to recall any batch of product from sale or supply
9. complaints about marketed products are examined, the causes of quality defects investigated and appropriate corrective and preventive measures are taken in respect of the defective products and to prevent re-occurrence.

Quality control is the part of GMP that is concerned with specifications, sampling and testing, and with the organisation, documentation and release procedures that ensure that the necessary and relevant tests are carried out so that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory.

Compliance with GMP ensures that quality is built into the product at the time of manufacture. It requires products to be consistently manufactured in a safe and clean environment, by specified methods, under adequate supervision, with effective quality control procedures, and with a documentation trail that links starting materials, through the various manufacturing processes, to the finished product.

11.4.1 Manufacturing Principles

Quality Management

- Manufacturers of veterinary medicines must have in place a quality assurance system to ensure that finished products are fit for their intended use, comply with registration requirements and do not place treated animals or users at risk due to inadequate quality, safety or efficacy.
- The quality assurance system must ensure that:
  - appropriate procedures are in place to ensure that relevant quality standards are met
  - all materials involved in the manufacturing process comply with required quality standards before they are released for use in manufacture
  - there are measures designed to prevent cross-contamination
  - there are safeguards and controls in place designed to prevent the occurrence of foreseeable errors or process failures

- finished products have been made and stored correctly, and they comply with required quality standards before they are released for supply.

- The quality assurance system must be relevant to the nature and intended use of the product. It must be fully documented, monitored for effectiveness and provide for continuous improvement.

Personnel and Training

- Veterinary medicines must be manufactured under the management and supervision of appropriately qualified, trained or experienced persons who:
  - understand the specialised technical, quality and legal requirements relating to the manufacture of veterinary medicines for which they have responsibility
  - have their duties and responsibilities clearly defined by the manufacturer.
- Manufacturing staff must be trained to a satisfactory level of competency in:
  - the basic principles of good manufacturing practice
  - the specific duties, in connection with the manufacture of veterinary medicines, that they are required to perform.
- There must be a sufficient number of competent personnel to carry out all required tasks.

Buildings AND Grounds

- Veterinary medicines must be manufactured in buildings that are located, designed, constructed, maintained and utilised to:
  - suit the operations carried out in them
  - ensure protection of the veterinary medicines from contamination
  - permit effective cleaning and maintenance, including cleaning after processes have been completed
  - minimise the risk of manufacturing error.
- The products must also be manufactured in an environment, or in equipment fitted with precautionary measures, that:
  - ensures a standard of hygiene appropriate to the class of veterinary chemical product being manufactured
  - minimises the risk of cross-contamination of the finished product, or of materials or components that are used or manufactured at the premises
  - ensures the safety of operators and protects the outside environment.

Equipment

- Equipment used in the manufacture of veterinary medicines must be suitable for its intended purpose and appropriately operated, maintained and cleaned. Equipment must be correctly installed and operated in accordance with written instructions that are appropriate for the equipment.
- The design and layout of equipment must be such that:
  - the risk of manufacturing error is minimised

- effective cleaning and maintenance are possible, in order to avoid cross-contamination of either intermediate materials or the finished product, the buildup of dust or dirt and, in general, to avoid any adverse environmental effect on the quality of the product.

Documentation

- Manufacturers of veterinary medicines must establish and maintain a system of documentation, document control and record keeping that:
  - provides precise specifications for starting materials, intermediate materials and finished products, manufacturing formulae and instructions, and operating procedures for associated manufacturing and quality control activities
  - provides a complete history of each item, batch, or quantity manufactured in a specified timeframe, of veterinary chemical product produced at the premises
  - establishes a traceable connection between raw materials and the finished product.

Computer Systems

- Where, in any step of manufacture, a computer is used for any activity that may affect the quality, safety or efficacy of a product, then the computer system must be subject to quality system management principles to ensure operational suitability.
- The introduction of computer systems into any manufacturing process, including materials control, processing control, quality control and product distribution, must not adversely affect product quality or quality assurance.

Production

- Veterinary medicines must be manufactured to specifications in accordance with manufacturing information supplied as part of their application for registration including any subsequent approved variations.
- Production operations must follow documented procedures that have been clearly defined by the manufacturer.
- Any critical manufacturing process and any change to that manufacturing process, must be validated and formally approved by an authorised person. Where a change in the manufacturing process affects the registered specifications of the finished product, formal approval of such changes must be obtained from the registering authority before the affected product is released for supply.

Quality Control

- Manufacturers of veterinary medicines must have in place an effective quality control system which is designed to ensure that before products are released from manufacture for supply they meet specifications and have been manufactured in accordance with the manufacturer’s documented procedures.
- The person responsible for quality control must be sufficiently independent of other aspects of the manufacturing operation to allow effective implementation of the quality control function.
- Manufacturers must ensure that analytical laboratories and animal testing facilities used in a step of manufacture follow the principles of good laboratory practice.

Contract Manufacture

- Where all or part of the manufacture of a veterinary chemical product is contracted to another party, the licensed manufacturer must ensure that before manufacture commences all parties have signed a written 'GMP Agreement' that clearly specifies each party's responsibility in relation to every aspect of the manufacturing process, assurance of product quality and consistency with product registration particulars.
- Arrangements for contracted steps of manufacture must not compromise the quality of the product.
- Where a contractor is authorised to manufacture under the licence of another manufacturer, the licence holder must exert direct control and oversight of the quality management of the contracted step.

Internal Audits

- Manufacturers of veterinary medicines must regularly and systematically carry out internal audits of all aspects of their manufacturing operations, as well as of their quality assurance program, in order to monitor compliance with their authorised procedures, standards and requirements and ensure product quality. Steps must be taken to implement any necessary corrective and preventive action identified by those internal audits and to assess the outcomes.

Complaints and Product Recalls

- Manufacturers of veterinary medicines must have in place a system of handling complaints regarding products they have manufactured or otherwise handled on the licensed premises. There must be a documented system of recording, investigating and, where appropriate, acting upon all complaints that may be related to product quality.
- Manufacturers must also have in place a documented and effective procedure for recalling from the marketplace product that is known to be defective, or is suspected of being defective.

Immunobiologicals and Other Products of Biological Origin

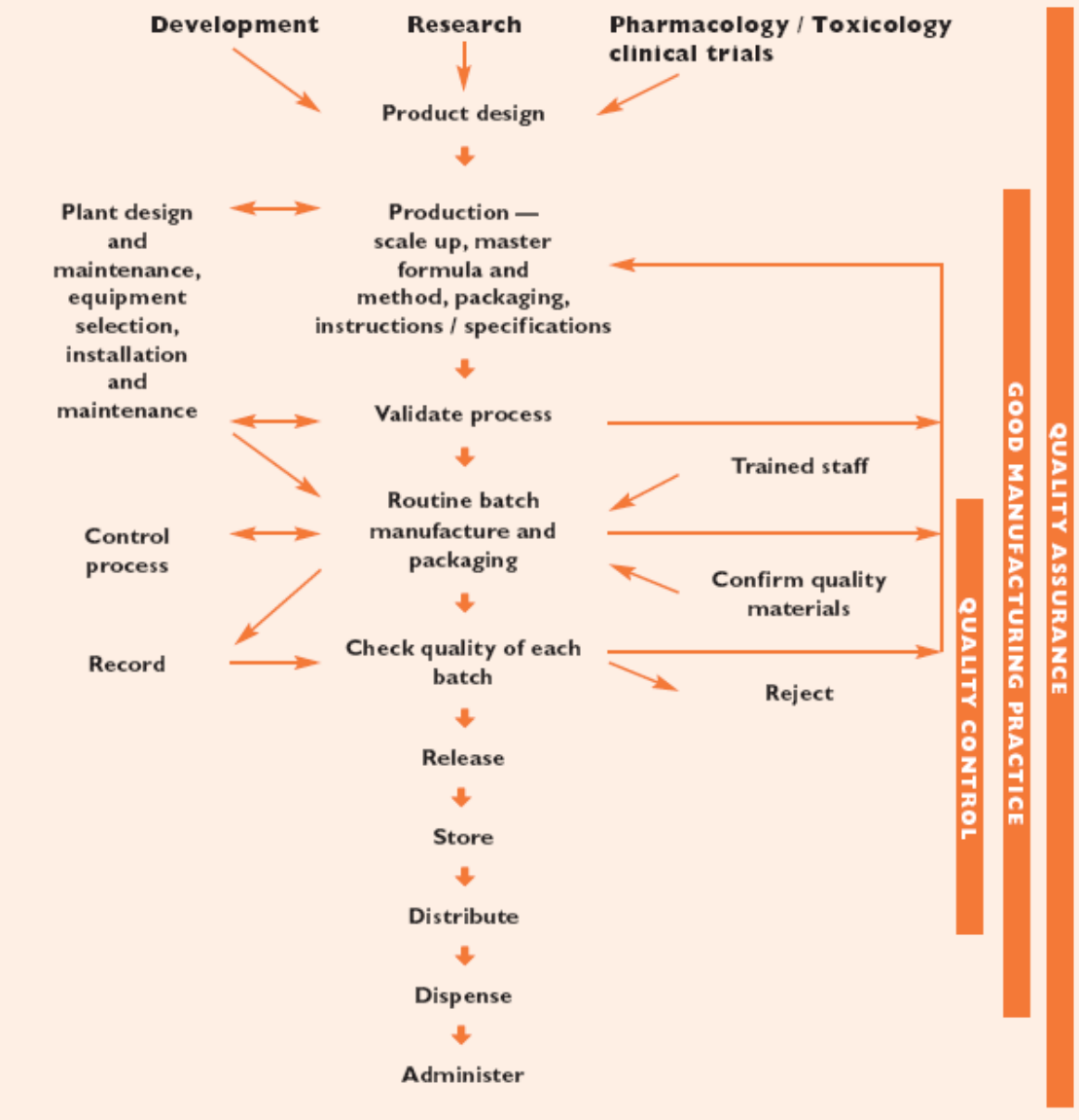
- Veterinary immunobiological products and other medicines of biological origin including those that are manufactured using a specified biological process must be manufactured:
  - using only biological starting materials that are, or are derived from biological materials demonstrated to be as free as practicable from adventitious contamination
  - in premises designed, constructed and maintained so as to provide an appropriate level of containment of the biological or microbiological agents being handled and to permit effective decontamination from these agents or from toxic residues by procedures that:
    - are established and validated by the manufacturer
    - maintain the safety of personnel.
  - in cases where uniformity of product depends on deriving batches from a seed lot
    - by maintaining the lots in secure and protective storage
    - by keeping meticulous records of their origin and disposition.

Manufacture of Sterile Products

- Veterinary medicines that are required to be, or are represented as being sterile, must be manufactured:
  - in separate, controlled areas in the premises that have
    - high standards of hygiene
    - a system of controlling particulate contaminants appropriate to the class of veterinary chemical product being manufactured.
  - with special care and attention to detail
  - in accordance with procedures established and validated by the manufacturer.
- The manufacturer must establish procedures and have equipment available (or in the case of bioburden, have access to equipment) to adequately monitor:
  - the microbiological status of the environment in production areas
  - the microbiological burden of the veterinary medicines that are to be sterilised.

References

- APVMA - Australian Code of Good Manufacturing Practice for Veterinary Chemical Products http://www.apvma.gov.au/qa/gmp_code_veterinary.pdf
- Guide for Good Manufacturing Practice for Medicinal Products, September 2003 edition, published by the Pharmaceutical Inspection Convention Cooperation Scheme (PIC/S) http://www.picscheme.org/index.php



USP (2005).Ensuring the Quality of Medicines in Low-Income Countries. An Operational Guide. The United States Pharmacopeial Convention, Inc (USP)

11.5 Appendix 5 Standards for vaccines manufactured by the VPC

European Pharmacopoeia 5th Edition 2004

Veterinary Vaccine Monographs include:

- Avian Infectious Bronchitis Vaccine, Living
- Duck Plague Vaccine (Live)
- Fowl Cholera Vaccine (Inactivated)
- Fowl Pox Vaccine, Living
- Newcastle Disease Vaccine, Living
- Swine Fever Vaccine, Living

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2004

(Updated: 21.11.2006)

- Classical swine fever (hog cholera) http://www.oie.int/eng/normes/mmanual/A_00036.htm
- Newcastle disease http://www.oie.int/eng/normes/mmanual/A_00038.htm
- Haemorrhagic septicaemia http://www.oie.int/eng/normes/mmanual/A_00063.htm
- Avian infectious bronchitis http://www.oie.int/eng/normes/mmanual/A_00107.htm`q
- Duck virus enteritis http://www.oie.int/eng/normes/mmanual/A_00111.htm
- Fowl cholera (avian pasteurellosis) http://www.oie.int/eng/normes/mmanual/A_00112.htm
- Fowl pox http://www.oie.int/eng/normes/mmanual/A_00113.htm

Manual of ASEAN Standards for Animal Vaccines

Livestock Publication Series- 2A Second Edition http://www.aseansec.org/agr_pub/ls2.doc

Veterinary Vaccine Monographs include:

- Avian Infectious Bronchitis Vaccine, Living
- Duck Plague Vaccine (Live)
- Fowl Cholera Vaccine (Inactivated)
- Fowl Pox Vaccine, Living
- Newcastle Disease Vaccine (lentogenic strain)
- Newcastle Disease Vaccine (mesogenic strain)
- Swine Fever Vaccine (lapinised)

11.6 Appendix 6 Cold Chain Failures

COUNTRY (33)	REPORTS OF INADEQUATE VACCINE COLD CHAIN*
Africa (various countries)	Pabst and Taylor (1988)
Australia	Barrand et al (1991), Burgess and McIntyre (1999), de Campo and Lester (1998), Fisher (1996), Gavranic (1994), Gold et al (1998), Gold et al (1999), Guthridge and Miller (1996), Hazelton et al (2002), Jeremijenko et al (1996), Lewis et al (2001), Liddle and Harris (1995), Miles (1993), Miller (1994), Reimer and Lewis (1998)
Bolivia	Nelson et al (2007)
Canada	Milhomme (1993), Weir and Hatch (2004), Yuan et al (1995)
Chile	Carrasco et al (1982)
Ethiopia	Berhane and Demissie (2000)
Ghana	Lloyd (1977)
Hungary	Lugosi and Battersby (1990)
India	Goel et al (2004), Goel and Swami (2004), Mukherjee et al (2004), Subramanyam (1989)
Indonesia	Nelson et al (2004), Otto et al (1999)
Ireland	Finnegan and Howell (1996)
Italy	Grasso et al (1999)
Lao PDR	Kuroiwa et al (2001)
Malaysia	Hanjeet et al (1996)
Mexico	Camacho-Amor et al (1990a), Camacho-Amor et al (1990b)
Mongolia	Edstam et al (2002), Edstam et al (2004)
Mozambique	Village Reach, MOH & PATH. (2004)
Nepal	Jha et al (2003)
New Zealand	Baker et al (2002), Beauchamp and Mansoor (1992), Ford and Gibbs (1990)
Nigeria	Adu et al (1996), Omilabu et al (1999)
Pakistan	Parviz et al (2004), World Health Organization (1990)
Papua New Guinea	Bass (1993), Wirkas et al (2007)
Russia	Smirnov et al (2004)
Scotland	Cherivan (1993)
South Africa	Benade (1994), De Swardt et al (1987), Schoub and Cameron (1996)
Spain	Ortega et al (2002)
Sri Lanka	Senanayake and de Silva (1997)
Taiwan	Pai and Ko (1999)
Thailand	Techathawat et al (2007)
UK	Briggs and Ilett (1993), Fernando (2004), Finn and Crook (1999), Haworth et al (1993), Hunter (1989), Jeremijenko et al (1996), Thakker and Woods (1992), Wawryk et al (1997), Wilcock (1996)

USA	Bell et al (2001), Bishai et al (1992), Borkow (1975), Casto and Brunell (1991), Frankel (1979), Gazmararian et al (2002), Hayden (1979), Kendal et al (1997), Krugman et al (1974), Lerman and Gold (1971), Setia et al (2002), Woodyard et al (1995)
Vietnam	NEPI, PATH & UOM (2003)

* References included in Page (2007)

11.7 Appendix 7 Presentation Visit to Lao PDR, 23-26 July 2007

Team: David Kennedy & Scott Williams

Date	Activity
Sun 22 - Mon 23 July	Australian team members travel to Vientiane
Tue 24 July	Discussions about business options with DLF counterparts
Wed 25 July	Presentation of options to senior DLF officers and discussions
Th 26 July	Revise and refine preferred option in light of discussions
Th 26 - Fri 27	Australian team members return to Australia

Senior DLF Officers' Meeting

Lao Plaza Hotel, Vientiane, 25 July 2007

Participants	Position
Dr.Somphanh Chanphengxay	Deputy Director General, DLF (Chairman)
Mr Southchay	Planning & Cooperation Department, MAF
Mr Phanthavong	Planning Division, DLF
Mr.Bounthong Saphakdy	Head of Technical Division DLF
Dr.Bounlome Duangngun	Director, National Animal Health Centre
Dr.Siseng Khounsy	Deputy-Director, National Animal Health Centre
Mr.Phouth Inthavong	National Animal Health Centre
Mr.Sengphet Somsanith	A/Director, Vaccine Porduction Centre
Dr.Signa Kittiphone	Director, Veterinary Supply Unit
Dr Scott Williams	ACIAR Consultant
Dr David Kennedy	ACIAR Consultant

Apologies

- Dr. Bounkhouang Khambounheuang, Director-General, DLF
- Dr.Sithong Phiphakhavong, Director, VPC

11.8 Appendix 8 Recommended Model for Vaccine Business Development in Lao PDR

11.8.1 Background

The population of Lao PDR is heavily dependent on livestock production for income, food and draught power. The Lao Government is committed to improve livestock production and animal health to help alleviate poverty, to improve the standard of living in the country and to increase external trade.

Endemic animal disease limits livestock survival and productivity in Lao PDR, and with zoonotic agents posing a threat to human health. Lao PDR is also a partner in regional control programs for transboundary animal diseases (TADs) such as foot-and-mouth disease, classical swine fever and highly pathogenic avian influenza. Given its location in south-east Asia it is also at risk of severe impacts from new or emerging animal diseases such as fatal porcine reproductive and respiratory syndrome that is reported to have recently spread from China.

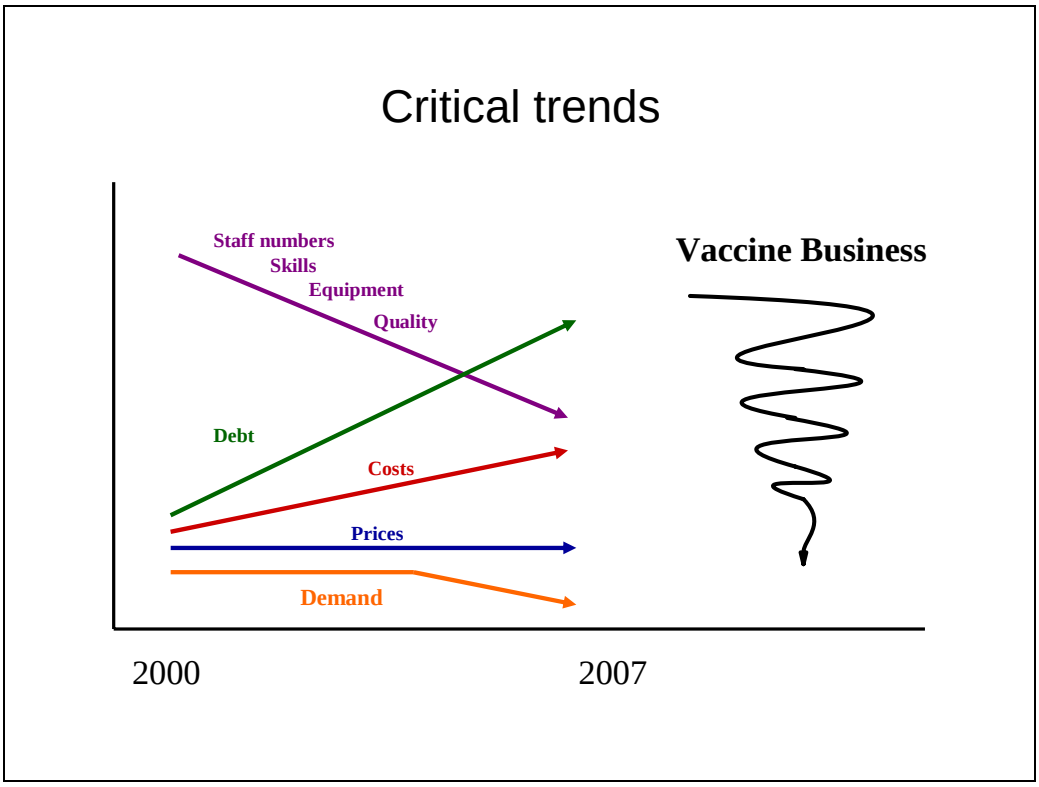
Lao PDR established the Vaccine Production Centre (VPC) thirty years ago to manufacture high quality vaccines for the most important animal diseases in the country, and at one stage it even exported vaccine to a number of neighbouring countries. More recently, DLF set up the Veterinary Supply Unit (VSU) as a single distributor for animal vaccines and medicines within Lao PDR. Unfortunately, over 90% of animals in Lao PDR are not vaccinated and so remain susceptible to these important diseases. During recent years the VPC has been in decline and recent reviews of the vaccine production and distribution business by the European Union and ACIAR have concluded that it needed major changes to survive. In fact, if it had not been for donor projects injecting funds, equipment and training it is very likely that the VPC would have already ceased operating.

11.8.2 Critical issues

This current ACIAR project, in collaboration with counterparts in the Department of Livestock and Fisheries (DLF), aims to help develop a new business model for the supply and delivery of animal vaccines in Lao PDR. The research and analysis conducted by the project team and DLF counterparts in 2007 has found that the current Lao vaccine production and supply business conducted by the VPC and VSU is in a downward spiral towards collapse (see Figure 1) because of the following critical trends:

- Demand for and sales of vaccine are falling.
- Despite some cost-cutting, costs for raw materials (which are imported) are gradually increasing.
- Prices charged for vaccines have been held at artificially low levels and do not cover the true cost of production.
- The VSU has a very large debt owed to it by customers and mostly by provincial governments.
- Staff numbers at the VPC are decreasing.
- Skills at the VPC have declined to a point where they are inadequate.
- Much of the donated equipment at the VPC is old, not operating and is not being repaired.
- The quality and effectiveness of some vaccines is declining.

. Figure 1. The Lao animal vaccine business is spiralling towards collapse.



11.8.3 Future options

Senior officers of the DLF and a representative of the Ministry of Agriculture and Forestry (MAF) planning department (see Attachment 1) met with members of the ACIAR research team in Vientiane on 25 July 2005, to review the progress of the project, *Vaccine Business Development in the Lao PDR.* The meeting analysed the findings of the research (Attachment 3) through an analysis of strengths, weaknesses, opportunities and threats (SWOT) that is presented as Attachment 2.

The ACIAR team presented five options for a new business model that spanned the range of approaches that could be taken for future supply of livestock vaccines (and medicines) in Lao. Each of the options included a 'package' of suggested changes. The group was invited to consider the various options and, if desirable, to combine features from more than one of the options into a new package'. Following consideration and critical review, the senior officers of DLF agreed to recommend a new business model to the Lao Government for endorsement by September 2007.

The five options considered by the group can be summarised as follows:

Option 1: Status quo (nothing changes)

In this option, the VPC and VSU would continue to operate as they do currently, with no changes made. The consultants argued that this option would simply continue the downward business spiral described above in which the VPC's equipment continues to deteriorate, quality declines, there is progressively reduced demand for product, cash flow is reduced, and so on.

Option 2: Status quo with modifications

Option 2 would retain the VPC and VSU but introduce a number of improvements to their operation, notably:

- Bookkeeping and performance monitoring would be improved at VPC by capturing actual (rather than just budgeted) costs of raw materials and wastage would be measured (instead of simply being estimated at a fixed rate)
- The current VPC product range would be reviewed and unprofitable lines would be dropped in favour of imports
- Prices would be gradually increased to a level that the market would bear and these prices would be reviewed regularly
- A code of Good Manufacturing Practice (GMP) appropriate to the conditions in Lao PDR would be developed and implemented to maximise quality
- Promotion of VPC product, and training of resellers and customers, would be progressively undertaken as funds allow
- The existing computerised accounting system at VSU would be implemented, freeing up time for the Director and his assistants to focus on other parts of the business such as inventory management, client relations and promotion
- Debtor management would be tightened and serious efforts would be made by government to recover long-standing debts.

Option 3: Partnership

This option envisages the VPC entering into an arrangement with a significant vaccine manufacturer to run the VPC and/or to import vaccines (and animal medicines) required by Lao PDR. The partner might be a multinational company, or perhaps a regional company (even if State-run) of some size and with a suitable product range. In consultation with the Lao Government, the partner company would manage manufacturing of certain product lines at the VPC and import other lines. (Alternatively, the partner would be concerned only with manufacturing of selected products at VPC while VSU retained control over importation decisions.) This model includes all of the changes described for model (2) but matters such as management of VPC accounts, pricing and promotion would be largely determined by the partner company.

In addition, Lao PDR would establish a regulatory authority similar to that of other countries and possibly modelled on the human medical equivalent in Lao PDR. The regulatory authority would be responsible for establishing that all vaccines (and other animal health products) meet acceptable standards of quality before they could be marketed in Lao PDR.

Option 4: Active importation

In this option, the VPC would cease to exist in its current form and the Lao Government would stop being a manufacturer of vaccines, even in partnership, instead leaving this function to any foreign supplier meeting acceptable standards of quality as determined by the regulatory body. VSU would continue to be the national wholesaler and distributor for vaccines and animal medicines imported into Lao PDR and would take an active stance in identifying the best products (highest quality / lowest price) for the Lao market.

Option 5: Free market

Option 5 would see the complete removal of the Lao Government from manufacturing and distribution of animal vaccines and medicines, leaving these functions to any veterinary vaccine/medicine company, provided its product gained the approval of the regulatory authority. The VPC and VSU would cease to exist and current staff would be redeployed

to the regulatory body or to other animal health functions. The major advantage of this model over options 3 and 4 would be to maximise competition in the Lao vaccine and animal medicines market.

Principles underpinning the selection of a preferred option

Three key principles influencing the choice of a new business model were discussed at the meeting:

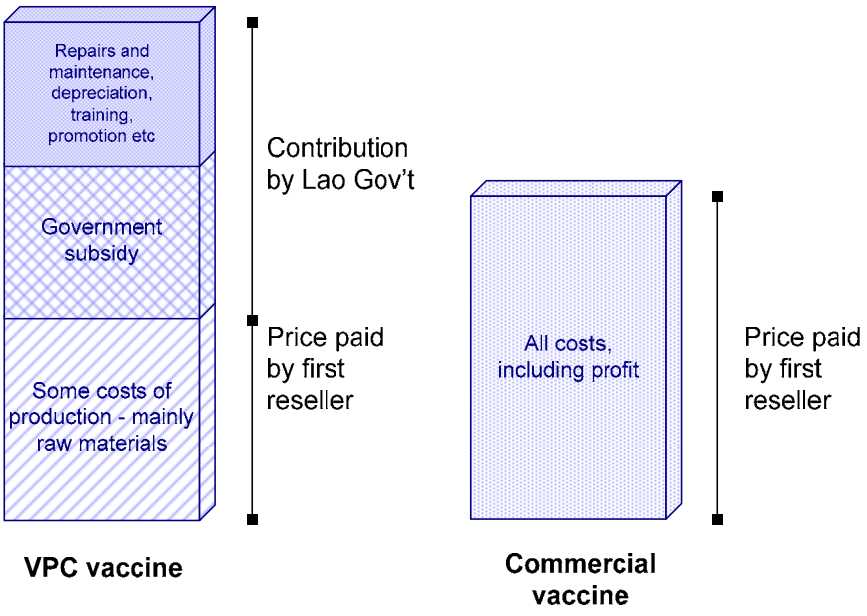
1. The 'true' cost of producing VPC vaccine should be recognised

At present it is difficult to determine precisely what it costs to produce each dose of VPC vaccine, for several reasons:

- Currently available figures on raw material costs are based on a standard 'recipe' rather than actual expenditure to produce each batch
- There is an allowance for 10% wastage of materials and finished product, but this is an estimate
- A number of 'administration' cost items are not included: notably repairs and maintenance, depreciation of equipment, staff training, and product promotion
- Government contributes some of the administration costs (although these costs are known).

The average price at which the VSU sells VPC vaccines is too low because it does not cover all of the costs. Comparisons of price with those of commercial vaccines can therefore be misleading, as shown in Figure 2. In this example, the VPC vaccine seems to be cheaper to the first reseller – but this is only because the Government is actually paying some of the cost of production, and many of the expenses that are important in a sustainable vaccine business are not being incurred (eg repairs, training, etc).

Figure 2. Comparison of prices between Lao VPC and a commercial vaccine manufacturer.



2. Keeping the price of VPC vaccine low does not mean cheap vaccine to farmers

The VPC is expected to keep the price of its vaccine low so that Lao farmers can buy it cheaply. However, field research for this project has shown that vaccine resellers – the 'middle men' in government offices and private shops – are, in many cases, applying large mark-ups to the price of the vaccine.

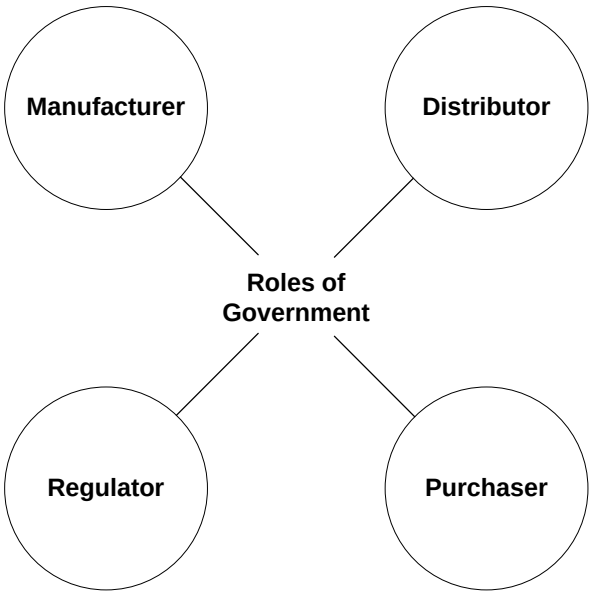
In one example, VPC fowl cholera vaccine sold in Xieng Khouang Province is purchased by resellers for 6,000 kip from the VSU and then sold for 12,000 or even 15,000 kip (100% and 150% mark-ups respectively) to smallholders or village veterinary workers.

Resellers can apply large mark-ups because their customers are prepared to pay those prices. By keeping their own prices low, the VPC and VSU are not covering their own costs while allowing resellers to make good profits.

3. Government should recognise that it is a customer of the VPC

Government currently plays various roles in the animal vaccine business of Lao PDR, as shown in Figure 3. These are quite distinct roles and can be separated, with Government choosing not to continue in one or more roles if it wishes to.

Figure 3. Roles of the Lao Government in vaccine supply.



In most developed countries, governments assume the role of 'regulator': that is, they provide assurance of product quality, efficacy and safety. Some governments are also 'purchasers' because they buy vaccines for disease control programs, particularly when owners cannot afford the vaccine. They are less likely to be 'manufacturers' or 'distributors'.

It is possible for the Lao Government to meet its aims of improving the livestock sector without being a 'manufacturer' or 'distributor'. For example, the VPC could be allowed to operate as a non-profit entity that must cover of all of its own costs solely through the revenue it generates. Instead of subsidising the operations of the VPC, the Government could encourage poorer farmers to vaccinate their livestock by subsidising the price of vaccines purchased by them. This would allow:

- The VPC to set a realistic price for its products (i.e. one that provides sufficient revenue to pay all costs)

- The Government to provide selective subsidisation (e.g. to poorer farmers but not to commercial operators), improving the efficiency of its investment.

The recommended model

The meeting agreed that a combination of options 2 and 4 provided the preferred business model. In summary, this preferred model creates a single body that would source Lao vaccine and animal medicine needs from both locally manufactured and imported products, as well as establishing a separate regulatory authority to ensure quality. The model has the benefits and features shown in Table 1.

A note on vaccine demand

The long term success and sustainability of this or any other proposal to enhance the supply of veterinary vaccines in Lao is dependent on simultaneous initiatives to improve demand for vaccines by livestock owners as well as resources to deliver and administer effective vaccines to livestock. The integration and coordination of supply and demand activities is supremely important and the development and implementation of mechanisms to ensure projects share objectives and information will greatly improve the achievement of long lasting benefits.

Table 1. Features and benefits of the preferred model for animal vaccine business in Lao PDR.

	FEATURES	**BENEFITS**
1	The VPC and VSU are combined to form a single supply body – called, for the purposes of this paper, the Animal Vaccine and Medicine Supply Centre (AVMSC).	• Consolidation and better use of resources • Improved accounting • Best mix of local production and importation of vaccines
2	The AVMSC is responsible for supplying the animal vaccine (and animal medicine) needs of Lao PDR. It determines the best way to procure the required vaccines, whether by manufacturing those vaccines itself (in the current VPC facility) or by importing them. An intermediate option not currently exploited by VPC or VSU is for the AVMSC to import bulk quantities of vaccine (for example, 60 litre packs) and re-package it in smaller quantities suitable for Lao conditions.	• Access to global veterinary vaccine and pharmaceutical market • Access to products not currently available to Lao livestock • Ability to identify and select high quality product • Buying power of single purchaser
3	Decisions to 'make or buy' are reviewed regularly (say, every 6 months) and are determined by relative cost, quality, security of supply and other factors. Accurate cost comparisons are made possible by a modern computerised accounting system for the recording and monitoring of manufacturing activity, quality, inventory and accounts. Costs of repairs and maintenance, depreciation, wastage, staff training and any other costs, including those currently met by Government, are all captured and included in the calculation of cost of production.	• Improved monitoring of cost of production • Increased efficiency of vaccine production and purchasing • Ability to forecast raw material requirements • Ability to monitor finished product inventory • Improved ability to manage debt

4	To improve cash flow in the early stages of the new business, there is an initial review of prices and, where possible, price increase of 10-20% for products currently manufactured by VPC. There is also a review of the range of products manufactured by VPC, with unprofitable lines (mainly poultry vaccines) discontinued and instead imported.	• Revenue matches or exceeds costs • Rationalisation of product lines to ensure that the sale of each product covers its cost of production
5	Initial cash flow is also improved by the Lao Government seeking to recover long-standing debts owed to the VSU primarily by provincial government. This cash is critical for repairs and maintenance of equipment, staff training and recruitment, and a quality overhaul.	• Reduction in debt and stimulus to cash flow • Improved revenue to support self-sufficiency
6	There is a quality overhaul of the manufacturing division of the AVMSC (the former VPC). The overhaul includes the introduction of a system of Good Manufacturing Practice (GMP) specifically developed for the AVMSC by an independent expert. It also includes the repair or replacement of non-functioning equipment.	• Production of reliable and reproducibly high quality vaccines achieved through quality management • Vaccines better match requirements of end users through continuous improvements • End-users benefit from improved immunity in vaccinated livestock • Enhanced disease control • Continuous improvement guided by monitoring and investigation of product complaints and adverse reactions
7	The AVMSC establishes a brand identity and promotes its products throughout Lao PDR with product labels, posters, brochures and other materials. Vaccine manufactured by AVMSC has its own branding (e.g. ‘Laovax’ with associated logo). Every product, whether made in Lao or imported, may carry an additional label showing that the AVMSC stands behind its quality (e.g. ‘AVMSC approved’).	• Increased confidence of end-users in vaccination • Greater awareness of vaccine availability • Greater demand for vaccine

8	Management of the AVMSC is guided by an Advisory Board. The Advisory Board, similar to those operating in the non-profit sector of developed countries, provides the AVMSC with access to high-level business skills at low cost. The Advisory Board comprises 8-12 individuals not selected to represent Government Departments or other bodies but rather for the skills they offer – especially vaccine manufacture, livestock production, finance, marketing, and importing. The Board meets 3-4 times per year and provides high-level advice to the Director and senior staff of the AVMSC.	• Enhanced decision making and business planning • Input of business expertise to strategic directions • Access to global pool of current knowledge and accumulated experience • Improved efficiency of manufacturing and importing operations • Greater returns on investment
9	Separate to the AVMSC, Lao PDR also establishes a Veterinary Medicine Regulatory Authority (VMRA). Essentially, the VMRA is responsible for ensuring that all animal vaccines and medicines marketed in Lao PDR meet acceptable standards of quality and safety, including those manufactured by the AVMSC.	• Consistently high quality of all animal medicines available in Lao PDR ensured by independent authority • Harmonisation of requirements within ASEAN • Improved control of product availability to Lao livestock producers

Reasons for rejecting other options

Option 1: Status quo (nothing changes)

This option was unanimously rejected by the group because it would inevitably lead to the collapse of the VPC. Lao representatives at the meeting acknowledged that the VPC had only been saved from collapse in recent years because of the support provided by various projects. It is unlikely that any donor groups (such as ACIAR or the EU) would participate in further projects involving the VPC without changes to the way the business is managed, as this current project is attempting to do.

Option 3: Partnership

This option was not preferred because it would see the Lao Government lose much of its control over product and pricing decisions to a body with possibly conflicting objectives (i.e. to maximise profit). The group also noted that there had been attempts in the past to privatise the VPC or to develop partnerships with other countries and that these attempts had failed.

Option 5: Free market

This option was also not preferred because of the loss of control by the Lao Government over the supply of animal vaccine to the country. Matters of security of supply, foreign exchange and national pride were noted as reasons for Lao PDR to retain some level of manufacturing capability.

Option 2: Status quo with modifications

Option 4: Active importation

These two options form the basis for the preferred model described above. The group agreed that the hybrid model provided the advantages of access to cheaper (and possibly higher quality) vaccines from other countries with the security of continued manufacture in Lao PDR, combined with measures to improve quality and efficiency of production, distribution and marketing. The group also believed that the new model would provide a

more attractive workplace with the scope to attract and provide further training for qualified people.

Planned activities to complete of the ACIAR Project

Pending endorsement of a new business model by the Lao Government in September, the project team will develop a two-day training course for VPC and VSU managers and senior national staff to assist them to implement the new business model. This training will be run in November 2007 in Vientiane.

Immediately following the training course, it is planned that the Lao Government will run and fund a meeting for stakeholders in Vientiane at which the Lao managers will present the new operational plan to national and provincial government and commercial clients. This may involve other suppliers of vaccines and animal medicines. The ACIAR project will pay a day's per diems to support the meeting.

The project will write and provide all documents in English and translation will be undertaken by the Lao DLF as required.

END
31 August 2007

11.9 Appendix 9 Implementation Training Visit to Lao PDR, 25-30 November 2007

Team

David Kennedy, Scott Williams, Stephen Page, Richard Bevan & Nancy Bourgeois- Luthi.

Date	Activity
Sun 25 Nov	Team members flew to Vientiane
Mon 26 Nov	Implementation Framework Meeting, Lao Plaza Hotel
Tue 27 – Wed 28 Nov	Quality workshop, VPC
Wed 28 – Thurs 29 Nov	Finance workshop, National Animal Health Centre/VSU
Fri 30 Nov am pm	 Marketing workshop, National Animal Health Centre/VSU Implementation meeting.
Fri 30 Nov - Sun 1 Dec	Australian team return to Australia

Details of the program, expected outcomes and participants follow.

Implementation Framework Meeting	
Monday 26 November, Lao Plaza Hotel	
Outcome Understanding the new regulatory and business environment in which vaccine manufacture, distribution and sales will be undertaken in Lao PDR.	
1	Welcome
2	Situation Review
3	New Business Model for an *Animal Vaccine and Medicine Supply Centre (AVMSC)*
4	Opportunities and support in Asia and beyond- AAHA, IFAH
5	Introduction to Quality Management / Quality Production – GMP concepts and models.
6	Setting and maintaining national standards - *Veterinary Medicine Regulatory Authority (VMRA).*
7	Advisory Board - function, structure and membership: discussion and recommendations
8	Discussion and agreement on details of training agenda

Apologies

- Dr Bounlome Duangngun, Director, National Animal Health Centre

Participants

- Dr.Somphanh Champengxay, Deputy DG of Livestock and Fisheries Department
- Mr Inthadome Akkharath, Deputy Director, Division of International Cooperation, Department of Planning, MAF
- Dr.Syseng Khounsy, Deputy Director, National Animal Health Centre
- Dr.Sithong Phiphakhavong, Director, VPC
- Mr.Sengpheth Somsanith, Deputy Director, VPC
- Mr.Signa Kittiphone, Director, VSU
- Miss Onekham Insomvilay, Information systems, National Animal Health Centre
- Peter Rolfe
- Stephen Page
- Scott Williams
- Richard Bevan
- Nancy Bourgeois Luthi
- David Kennedy

WORKSHOP 1: QUALITY ASSURANCE/QUALITY CONTROL/GOOD MANUFACTURING PRACTICE
Tuesday 27 November (and Wednesday 28 November), Vaccine Production Centre
Outcomes
1. Improvements recommended to the current vaccine production procedures and processes, quality assurance and control procedures for vaccine manufacture and storage at and distribution from the Lao Vaccine Production Centre (VPC)
2. Improvements recommended for vaccine manufacturing practices, QA and control procedures, and storage and distribution from the VPC that enable them to become consistent with an appropriate code or standard of GMP (good manufacturing practices)
3. A draft quality plan developed for ongoing quality management at the VPC, including job description for Quality Manager.

Leaders

- Richard Bevan
- Stephen Page

Participants

- Dr. Sithong, DG of VPC
- Mr. Sengpheth, Deputy DG of VPC
- Dr. Somphone, Technical staff of VPC
- Mr. Viengsay, Technical staff of VPC
- Mrs. Khambieng, Technical staff of VPC

- Mr. Saykham, Technical staff of VPC
- Mrs Khantavan, Technical staff Virology.

WORKSHOP 2: PLANNING, FORECASTING AND FINANCE
Wednesday 28 and Thursday 29 November, Veterinary Supply Unit
Outcomes
1. Efficient processes for handling receivals, sales, inventory and procurement are defined and documented.
2. Skills are developed in costing and planning vaccine production and distribution.
3. Skills are developed in using computerised financial management package and standard accounting reports and debtor management.

Leaders

- Scott Williams
- David Kennedy

Participants

- Dr. Sithong, DG of VPC
- Mr. Signa, Head of VSU
- Mr. Phouxay, Adm. staff of NAHD
- Mr. Phonsay, Adm. staff of NAHD
- Mrs. Vilyaphet, Technical staff of NAHD
- Ms. Soukphaphone, Accountant of VSU
- Ms. Sakouna, Cashier of VSU
- Ms. Moone, Administration and Cashier of VPC
- Ms. Kanthaly, Accountant of VPC
- Mrs Khantavan, Technical staff Virology

WORKSHOP 3: MARKETING QUALITY PRODUCTS
Friday 30 November – morning, DLF Conference Room
Outcomes
1. Principles and elements of marketing (customers, product, price, promotion, place) understood
2. Draft marketing plan developed.

Leaders

- Scott Williams
- David Kennedy

- Nancy Bourgeois Luthi

Participants

- Mr. Sengpheth, Deputy DG of VPC
- Dr. Somphone, Technical staff of VPC
- Mr. Phonsay, Adm.staff of NAHD
- Mrs. Vilyaphet, Technical staff of NAHD
- Mr. Signa, Head of VSU
- Ms. Soukphaphone, Accountant of VSU
- Ms Kanthaly
- Ms Soukuna

IMPLEMENTATION MEETING	
Friday 30 November – afternoon, DLF Conference Room	
Outcomes	
Lao plan for implementation of the new business model.	
1	Presentations of outcomes and lessons from the training workshops.
2	GMP Summary Report
3	Implementing the new business model

Participants

- Dr. Somphanh, Deputy DG of Livestock and Fisheries Department
- Mr. Chanthaboune Sirimanotham, Head of Planning Division, DLF
- Dr. Sithong, DG of VPC
- Mr. Sengpheth, Deputy DG of VPC
- Mr. Signa, Head of VSU
- Ms Kanthaly
- Ms Soukuna
- Ms Soukphaphone
- Stephen Page
- Scott Williams
- Richard Bevan
- Nancy Bourgeois Luthi
- David Kennedy

11.10 Appendix 10 Initial Audit and Quality Plan, Vaccine Production Centre, Vientiane, Lao PDR

Vaccine Business Development in the Lao PDR

ACIAR Project AH 2006/155

Initial Audit and Quality Plan

Vaccine Production Centre, Vientiane, Lao PDR

20 December 2007

11.10.1 Executive Summary

The Vaccine Production Centre (VPC) is old and run down, with an immediate need for upgrading.

All production units should be re-painted with epoxy paint to facilitate the maintenance of cleanliness and sterile processes. Critical equipment such as autoclaves need to be refurbished or replaced, and a minus 400C freezer, pH meters and a moisture meter (to determine percentage of water in freeze dried products) need to be purchased. As well as these critical requirements all other current equipment and services [air, water and electricity included] must be critically appraised as to their serviceability now and into the future.

VPC is not competitive with the major vaccine suppliers because of deficiencies in product range, quality and scale of economy. The products produced at VPC most probably meet the needs of current use, however, with the progression of agriculture reform in Lao PDR to more intensive animal husbandry practices, these vaccines will not have the quality profiles required for such use.

The VPC is generally understaffed. The current staff are technically orientated, very enthusiastic and, with training in good manufacturing practices (GMP), will become more competent in their ability to produce and test quality vaccines. However, there are currently no skills in the engineering aspects of vaccine production and this must be addressed.

Development and implementation of a quality plan that addresses each of the following subjects is recommended in order to introduce a Quality Assurance Controlled Production System that satisfies the requirements of GMP. Development of the quality plan will require considerable commitment of time and staff but significant capital investment will only become necessary during implementation.

1. Training
Needs to be undertaken by all the staff of VPC in the business of vaccine manufacture, emphasising the need for accountability and hence traceability as required under GMP and normal accounting principles.

2. Documentation
Training in correct and accurate documentation needs to be undertaken by all the staff of the VPC for without accurate documentation no repeatability or traceability is possible in vaccine manufacture.

3. Premises
A quality plan must be instituted for the ongoing refurbishment of the premises.

4. Equipment
A quality plan must be instituted for the ongoing refurbishment and replacement of equipment.

5. Maintenance and Repairs
Maintenance and repairs are an integral aspect of GMP, often costing as much of a third of any budgeted period of time. A new division, Repairs and Maintenance, must be created at VPC with an engineer in control and a Quality Plan guiding activities.

6. Product Improvements
There are many product improvements identified in this audit which should be undertaken by

the staff of VPC, both in Production and Quality Control, A Quality Plan must be drawn up to capture all the costs and timings of these improvements.

Many of these improvements (and future improvements) would be financed by the business itself after implementation of the improved financial management of the new Animal Vaccine and Medicines Supply Centre.

External sources of finance may be required for major capital expenditure in the short-term.

11.10.2 Introduction

The Vaccine Production Centre (VPC) was audited over a three-day period in November 2007 by Dr Stephen Page and Mr Richard Bevan as part of the ACIAR project team. This combined report has been compiled by Richard Bevan and is based upon visual and verbal observations made during the visit. The report is designed to point out those factors pertinent to a Code of Good Manufacturing Practice [cGMP] as applied to this facility in such a manner that the production process can be made obvious and improved by the application of basic rules pertinent to any production process.

We wish to thank Dr Sithong Phiphakhavong and Dr Sengpheth Somsanith and their staff of VPC for their open, frank and friendly discussions on their capabilities and the products produced at VPC.

11.10.3 Premises

The premises are old and run down and in much need of refurbishing. All unserviceable or unrepairable equipment should be removed from production areas, leaving only usable equipment used in the production process, to result in less cluttering and ease of cleaning.

The outside of the building needs painting and the window timber/metal frames need sealing and re-painting. However, if the facility is going to continue to produce vaccines then the whole of the production unit must undergo a total repair, repaint and refurbishing.

The initial step would be to employ two local cleaners who would systematically clean and strip the floors in the production areas and corridors so as to enable sealing epoxy paint to be applied. These cleaners would then be permanently employed on a full-time basis to systematically clean rooms with suitable detergents, followed by disinfection and subsequent fumigation prior to use in production. These workers would form part of the maintenance team.

Each of the production rooms and the corridors should have their floors stripped, cleaned and sealed with epoxy heavy duty paint to allow for easy cleaning and disinfection. The walls and ceilings should be painted with high quality vinyl paint. Ideally the walls should be coved (corners converted to a smooth concave profile) to the floor, prior to painting, so no sharp corners are evident and difficult to clean.

It is not known if epoxy paint is available in Lao PDR, however a good link would be: http://www.no-slip-safety-protective-floor.com which demonstrates good applications of this technology in clean plants. An Australian epoxy paint expert is a Mr Hans Feldon at Hans@SprayTech.net.au . Wattyl, Taubmans and Eversafe are Australian and international suppliers.

This epoxy painting and carpentry would require a local carpenter/painter to be employed either on contract or full-time. Preferably, a carpenter/painter would be employed full-time on the maintenance team

The staff toilet facilities should also be repaired.

11.10.4 People

Without sufficiently trained personnel the vaccine facility will fail, because there will be insufficient staff to carry out the required tasks and as a result of increased workloads staff will ignore or overlook what can be critical procedures. Such process failures can occur for no apparent reason. A good example of this would be a freezer unit thought to run at -20^{0}C but in reality running at -5^{0}C, resulting in poor virus titres in stored live antigens. Another example would be an autoclave thought to run at 121^{0}C, but only running at 105^{0}C, resulting in unexplained contamination.

How should a vaccine manufacturing facility be staffed?

A typical organisation chart should include the following functions:

Organisational Chart for Vaccine Production Facility

Laboratory Director												
↓		↓		↓	↑↓	↓		↓		↓		↓
Bacterial Vaccine Production Manager		Viral Vaccine Production Manager		Quality Control Manager	↑↓ ↓ ↑	Animal House and Animal Testing Manager		Label & Pack Manager		Engineering & Maintenance Manager		Administration Manager
↑		↑		↑	↑	↑		↑		↑		
Quality Assurance Manager												

The usual responsibilities for facility staff are as follows (specific responsibilities may vary depending upon local issues at particular facilities):

Laboratory Director has:

1. Direct responsibility for all staff on site.
2. Direct responsibility for all production.
3. Direct responsibility for budgeting.
4. Direct responsibility for all logistic planning along with all managers on site.

5. Direct responsibility for all administration matters pertaining to the production facility.

Quality Assurance Manager has:

1. Direct responsibility for release of all products, only after they meet VPC standards. If the product does not meet VPC standards, then, with the Laboratory Director, a decision is made as to the fate of the product.
2. Responsibility for assigning all expiry dating to product produced at VPC.
3. Responsibility, with the Laboratory Director, the Bacterial Vaccine Production Manager and the Viral Vaccine Production Manager, for determining raw material specifications for vaccine production.
4. Direct responsibility for raw material receipt and release [or rejection] on its meeting [or not meeting] VPC specifications.
5. Responsibility, with the Laboratory Director, the Bacterial Vaccine Production Manager, the Viral Vaccine Production Manager and the Quality Control Manager, for the determination of quality specifications of all procedures and vaccines produced at the VPC.
6. Responsibility, with the Bacterial Vaccine Production Manager, the Viral Vaccine Production Manager and the Quality Control Manager, for the production of vaccines meeting VPC Standards.
7. Direct responsibility to the Laboratory Director for the maintenance of the quality specifications of procedures and vaccines produced by VPC.
8. Direct responsibility for the accumulation [collection] of all data [batch records] applicable to the production of vaccines at VPC in a centralised system.
9. Direct responsibility for the trending analysis of vaccines [the consistency of the production process] produced by VPC and instituting corrective actions as required.
10. Responsibility for investigations into product complaints as received by VPC and maintaining records of those complaints for reference purposes.

Bacterial Production Manager has:

1. Direct responsibility for the production and filling of bacterial vaccines to the agreed standards and specifications for VPC.
2. Direct responsibility for the reconciliation of all bacterial products produced by VPC.
3. Direct responsibility for the maintenance of cGMP of VPC as it applies to the production of bacterial vaccines [that is, the cleanliness and sterile procedures as they apply to vaccine production].
4. Direct responsibility for monitoring all recordable equipment and processes under his or her control and instituting corrective actions as required [examples of this are incubator temperatures logs and autoclave logs, etc].

5. Direct responsibility for the correct recording of all paperwork pertinent to the production of bacterial vaccines.

Viral Production Manager has:

1. Direct responsibility for the production, filling and freeze drying of viral vaccines to the agreed standards and specifications for VPC.
2. Direct responsibility for the reconciliation of all viral products produced by VPC.
3. Direct responsibility for the maintenance of cGMP of VPC as it applies to the production of viral vaccines [that is, the cleanliness and sterile procedures as they apply to vaccine production].
4. Direct responsibility for monitoring all recordable equipment and processes under his or her control and instituting corrective actions as required [examples of this are incubator temperatures logs and autoclave logs, etc].
5. Direct responsibility for the correct recording of all paperwork pertinent to the production of viral vaccines.

Quality Control Manager has:

1. Direct responsibility for the testing of vaccines produced at VPC and verifying that that they meet agreed standards and specifications of VPC.
2. Direct responsibility for the maintenance of cGMP of VPC as it applies to the testing of bacterial and viral vaccines [that is, the cleanliness and sterile procedures as they apply to vaccine production].
3. Direct responsibility for monitoring all recordable equipment and processes under his or her control and instituting corrective actions as required [examples of this are incubator temperatures logs and autoclave logs, etc].
4. Direct responsibility for the correct recording of all paperwork pertinent to the production of viral and bacterial vaccines.

Animal House and Animal Testing Manager has:

1. Direct responsibility for the in-animal testing of vaccines produced at VPC to the agreed standards of VPC.
2. Direct responsibility for the breeding and production of laboratory animals to the agreed standards and specifications of VPC, including rabbits, poultry, mice and any other required livestock of VPC.
3. Direct responsibility for the maintenance of cGMP of VPC as it applies to the testing of bacterial and viral vaccines [that is, the cleanliness and sterile procedures as they apply to vaccine production].
4. Direct responsibility for monitoring all recordable equipment and processes under their control and instituting corrective actions as required [examples of this are incubator temperatures logs and autoclave logs, etc].
5. Direct responsibility for the correct recording of all paperwork pertinent to the production of viral and bacterial vaccines.

Label and Pack Manager has:

1. Responsibility for the labelling and packaging of all products produced at VPC to the agreed standards and specifications of VPC.
2. Responsibility for the timely labelling of all products produced at VPC to meet current orders for distribution.
3. Responsibility to the Quality Assurance Manager for the correct assigning of expiry dating to all products produced by VPC.
4. Responsibility for all cGMP principles that apply to the labelling of products produced by VPC.
5. Direct responsibility for the correct recording of all paperwork pertinent to the production of viral and bacterial vaccines.
6. Direct responsibility for the reconciliation of all unlabelled and labelled product produced at VPC.

Engineering and Maintenance Manager has:

1. Direct responsibility for the engineering and maintenance of all aspects pertaining to the facility at VPC [including the water systems, air systems, refrigeration, and maintenance and repair of the facility].
2. Direct responsibility for routine cleanliness and maintenance of the facility, employing dedicated cleaning staff, cleaning all facilities including change rooms and toilets.
3. Responsibility for the determination and implementation of preventative maintenance that should occur at the VPC facility.
4. Responsibility, with the Laboratory Director and other managers, for budgeting for preventative maintenance and the purchasing of replacement equipment for continuation of production of vaccines at VPC.

Administration Manager has:

1. Responsibility for the purchasing of budgeted raw materials complying with VPC written and approved specifications.
2. Responsibility to VPC in respect to all normal administrative functions that occur in any production facility and pertinent to Lao custom.

The need to train people in the art and science of vaccine production cannot be over-emphasised. It was clear from the audit appraisals that the basic knowledge was present; however there is currently no comprehensive training in the requirements of GMP, which covers all aspects of the production process. This can be readily achieved with appropriate training.

11.10.5 Production Equipment

The production equipment at VPC can generally be described as old and in need of maintenance.

The electricity supply at the VPC is maintained with the use of questionable connections, especially in wet areas such as the distilled water and the autoclave areas. A contract qualified electrician should be retained to repair this questionable supply as it is a safety issue.

Critical equipment is described below**:**

The Standby Generator

The starter battery for the generator cannot start the generator. A battery must be transferred from a car for use in starting the generator.

Recommendation

Buy a new battery to start the generator and run the generator for a period of time at an interval no greater than a four-week period.

The Distilled Water System

Potable water is only supplied to VPC on a three day a week system. Potable water is held in a reserve tank adjacent to the main building. This water serves as water supply for the distilled water, distilled by heating using electricity to create boiling water and cooling by recycling cooling water back to the reserve tank. The actual still is old and is a replacement from a previous still. Mineral encrustations building up in the distillation plant should be checked, and a maintenance routine introduced if applicable.

The distilled water is collected into two plastic 200-litre tanks. The water is piped to where required by plastic pipes or carried in carboys from a tap adjacent to the plastic tanks. Plastic tanks and plastic pipes cannot be properly cleaned and often a build up of slimy bacteria is the result.

Once distilled, water should be kept hot [it is recommended to store the water at not less than 65^0C and preferably closer to 80^0C] to prevent bacterial growth contaminating the water.

Recommendation

Collect distilled water into a stainless steel tank with heater installed to keep the water hot. The tanks could be local tanks and a simple coil heater placed inside the heater should be sufficient to keep the water hot and to keep adventitious contamination to a very low level. Plastic pipes should be avoided if possible.

Distilled water used for manufacture should be collected when hot and filled and sterilised on the same day as to avoid build up of pyrogens in the distilled water.

Autoclaves

This is the highest priority

Autoclaves are the critical hub of any vaccine unit and must work properly to reliably and reproducibly sterilise all media, clothing and equipment needed for manufacture.

A number of autoclaves, both vertical and horizontal were evident during the audit. All autoclaves were self-steam generating using electrical power units of varying vintages. Some of the autoclaves were not used and may not be repairable. There are two 1x1x3 meter horizontal autoclaves, one of which is being stripped to supply parts for the other, while the one in use leaks steam when in use due to an ill-fitting door gasket. The autoclaves are of 1982 vintage of Indian origin. There was one vertical autoclave of small volume that still in use. If either autoclave irreversibly fails then VPC is finished.

Recommendation

To buy a new autoclave with a vacuum cycle to sterilise gowns and other materials requiring a drying cycle could cost anywhere from $USD250,000 – 500,000 as a delivered unit.

An alternative would be to buy second-hand autoclaves at a far cheaper rate, bearing in mind that a second-hand autoclave will cost almost as much to refurbish as the cost of the autoclave, but even so will be a lot cheaper than buying a new autoclave. There are a large number of second-hand dealers on the Internet selling a large number of second hand autoclaves world-wide. See http:///www.directindustry.com/industrial-manufacturer/autoclaves-62736.html.

The third option would be to contact local hospitals, which must have autoclaves, and have their engineers visit VPC to determine what must be done to service the autoclaves. If the engineers are not available then there would certainly be suitable people in Thailand to carry out this required process.

If the electrical system/boiler system of the autoclaves is unrepairable then the purchase of a second hand boiler [eg 30 Horse Power Electrical Siemens boiler at $USD 20-30,000] may be another option. The autoclaves would need to be re-designed with an outside source of steam and vacuum cycle installed into one of the large autoclaves. This would be the cheapest option. See http://www.sbt.siemens.com.

Any option will cost money, and money needs to be spent now on these vital pieces of equipment.

Minus 70^{0}C Freezer

There is one only -70^{0}C freezer on site containing all master and working seeds of VPC as well as the challenge cultures used to validate the vaccines. This is not only contrary to GMP [i.e. storing virulent and vaccine cultures together], it is also very dangerous in respect to VPC's continued operation, for if this freezer breaks down, then VPC loses its sole source of seeds and ability to manufacture vaccines.

Recommendation

The purchase of a new -70^{0}C freezer is advisable as a back-up for this one freezer. Immediate transfer of some master and working seeds and some challenge cultures to an off-site -70^{0}C freezer is strongly recommended.

In the meantime, isolate the challenge cultures into lockable containers [a metal box], with the key held by the site Director [not the Production Managers] so that the Production Managers do not accidentally choose a challenge culture to produce vaccines [this has happened before with disastrous results].

When the new -70^{0}C freezer is obtained transfer the production cultures to the new freezer and leave the challenge cultures in the old freezer.

See http://www.industrialfreezersales.com.

Consider purchasing an independent temperature recorder to record the temperature of this freezer. A data logger could be used to monitor these temperatures. For information on data loggers see http://www.hdi.com.au**.**

Minus 35 to 40^{0}C freezer

This is the 2nd highest priority

The current freezer used to hold all the produced but not finished live viral antigens is simply not cold enough. If temperatures were recorded for this freezer then the temperature would be in the range -5 to -20^{0}C which is at the eutectic point for products frozen in that freezer. This means constant ice crystal movement in the stored antigens, reducing stability to weeks. This is inconsistent with GMP and with good production practices.

Recommendation

Buy a -35 to -40^{0}C freezer as a priority. At this temperature the products are below eutectic point and are hence stable for years, rather than weeks or less. Cost to purchase this freezer would be in the vicinity of $USD15,000 or less for a second hand freezer. See http://www.Med1Online.com and http://www.thermoline.com.au/products.html.

Consider purchasing an independent temperature recorder to record the temperature of this freezer. A data logger could be used to monitor these temperatures.

The current method of storage of antigens relies upon glass bulbous bottles with long necks and small flat bottoms making safe and economic storage of high value antigen very risky.

Recommendation

Buy sterile PET roller bottle storage units. See http://www.bellcoglass.com/subcat.php?start_limit=0&cat_id=6&subcat_id=204-35k- **.** This will provide a cheap and stable storage system.

Egg Incubator[s]

There are two egg incubators used to incubate embryos and to hatch chickens. One was working when we were present, hatching chickens for QC testing. The incubators were present in a corridor, under less than ideal conditions. The incubators were in need of a good clean as chicken dander and spider webs were obvious in the incubators. The globes used to indicate when the incubators were

delivering required heat for the eggs were not working and required replacing [poor GMP] and the wet and dry bulb thermometers were not serviced and had not been for a considerable length of time. The dry thermometer indicates the incubator temperature and the wet bulb thermometer indicates the humidity. The readings of both thermometers allow the relative humidity to be calculated and ideal incubation conditions for the embryos to be maintained.

Recommendation

Clean the incubators. Move the incubators to the annex of the viral production area, which is relatively clean compared to where the eggs are currently incubated. Clean the thermometers, replace the water wick for the wet bulb thermometer [if you don't have spare wicks, tell me and I will send you a contact where you can obtain same] and using distilled water fill the water receptacle and start to record temperatures. See http://www.ext.vt.edu/pubs/poultry/factsheets/8.html and http://www.msstate.edu/dept/poultry/hatch.htm for conditions ideal for hatching chickens.

Draw up a table and record temperatures and calculate relative humidity twice each day of incubation [see Form No. 1 at end of document].

Standardised Thermometer

No standardised thermometer exists on site.

Recommendation

A mercury thermometer exists in the incubator in the bacterial vaccine production area which reads from -20^{0}C to +200^{0}C. This thermometer could be standardised using ice and boiling point calibration and become the VPC standardised thermometer against which all thermometers are standardised on site. See http://www.oznet.ksu.edu/library/fntr2/mf2440.pdf.

8. Bench Incubators

There are a number of bench incubators used to incubate inoculated eggs, for sterility tests, or for bacterial cultures in various different areas of the VPC facility. They are all set at their recommended temperatures [most probably 37^{0}C] but the temperatures have not been calibrated, nor recorded on a daily basis when in use.

Recommendation

Using calibrated maximum-minimum thermometers record temperatures twice daily [see Form No. 2] so a record is available for the recording of correct temperatures and corrective actions can be implemented if necessary.
Maximum-minimum thermometers cost approximately $USD15.00 each. See http://www.brannan.co.uk/products/env_maxmin.html.

9. pH Meters

These are 3rd highest priority

No pH meters exist at VPC. pH paper is used to determine pH. This is poor GMP and can lead to product failure and could result in safety issues with vaccines in the field.

Recommendation

In the past pH meters were very sensitive pieces of equipment liable to breakage. Today, rugged hand held pH meters are available. Four () should be purchased: one for media production, one for bacterial production, one for viral production and one for quality control. They are readily available. See http://www.globalw.com/products/**ph**100.html .

Moisture Meter

This is the 4th highest priority

No moisture meter exists at VPC to measure residual moisture [water] in freeze dried [lyophilised] vaccines. The moisture meter is the basic tool that determines the residual water left in the product after freeze drying and is the primary indication that the product is stable if the residual water is between 1-5%v/w of the final product. In the past this could have been carried out using a vacuum oven followed by weighing of the freeze dried plug, and later by the Karl Fischer Method, but this is now superseded by equipment which will carry out the recordings electronically and print out the results in a couple of minutes.

Recommendation

Buy a moisture meter for the determination of residual water in freeze dried vaccines. See http://www.fda.gov/cber/gdlns/moisture.htm and http://www.Mettler-Toledo.com.

Balances

There is one top-pan balance and one analytical balance at VPC to weigh out raw materials for use in vaccine production. No calibration or validation studies have been carried out on these balances since they were purchased.

Recommendation

Is there any Weights and Measurement Laboratory in Lao that could carry out a calibration check on the balances? If not the calibration should be carried out by purchasing a set of standard weights for regular calibration checks on both balances. Suggest you need 50 and 100g weights for checking the top pan balance and 50mg, 100mg, 500mg and 1000mg weights for the analytical balance. See http://www.**balances.**com/sartorius/calibration+weights.html.

Domestic Fridge / Freezers

There are three domestic fridge / freezers at VPC in the viral production area, the bacterial production area and the quality control area. All three are very old, with doors which do not close properly, and doubtful performance. All contain materials which are labile and needed for production [including bacterial seeds] or quality control purposes. These fridge/freezers should be retired and replaced.

Recommendation

Purchase three local domestic fridge/freezers to replace these old units. Add maximum/minimum thermometers to each section and record temperatures. These will provide a cool or frozen environment more suitable for their purpose without a

great deal of expense and with temperature monitoring greater confidence in product performance can be achieved.

Telstar Freeze Dryer Chart Recorder

The current chart recorder at VPC is broken and for product efficacy needs to be replaced with a new chart recorder.

Recommendation

Contact Telstar re the availability of a replacement chart recorder. See http://www.Telstar.eu.

Laminar Flow Work Stations

There are HEPA laminar flow work stations situated in critical production and quality control areas. Since installation there would have been no integrity testing done on this equipment and it was noticed that at least one had considerable spillage of material onto the filter [bacterial filling laminar flow]. It is recommended that these cabinets should be tested annually.

Recommendations

1. Is any testing of HEPA laminar flow cabinets undertaken in Lao? If not then this testing would have been undertaken by people from Thailand. See http://www.gmpua.com/CleanRoom/Design/CleanroomQualification.pdf. It would appear that the company M+W Zander does this work in Thailand.
2. To test the laminar flows locally, turn the laminar flows on and after 15 minutes, expose TSB petri plates in the cabinets for 3 hours and then incubate the plates for 3 days and note the degree of contamination. This will give a general indication to see if the laminar flows are working.

11.10.6 Documentation

Under any Code of Good Manufacturing Practice the documentation/labelling of any procedure or process is mandatory. Under any accountancy or costing system accurate accounting or recording is also mandatory. Recording and labelling systems at VPC are either non-existent or very poor. As VPC is about to embark on a business venture a lot of time and work, although little cost, must be devoted to correcting the documentation system.

As this documentation is enhanced it is very important to train all staff who use the paper work in the correct manner in which it is intended.

Under any code of GMP the use of pencils to record transactions is prohibited.

Under any code of GMP the use of indelible pens is mandatory.

No correction fluid (e.g. ‘White-out’) is to be used to alter a figure – rather, cross it out and put in the correct figure and initial and date the correction.

If the Standard Operating Procedure (SOP) is changed as the production process is undertaken then the operator is to write on the back of the SOP and have the alteration approved by his/her superior.

Records should be original, rather than copying from work books or scraps of paper.

Recommendation

VPC staff need to review the type of documentation required in the form of Standard Operating Procedures. This can be achieved by writing SOPs and laminating them, and separately having Operating Instructions that are filled in on a batch basis. This system has the benefit that the original SOP is always present and less overall paper is required.

Specific Documentation Required:

Batch and Bulk Number Allocations

- It should be a QA function to allocate batch numbers.
- All batch numbers should be unique so they can be easily recognised. The batch number may be preceded by product name
- Batch numbers should be recorded in a central location.
- Bulk [antigen] should have a different batch number allocation to finished product.
- Do we need to review the batch numbering system at VPC?

Seed Stocks

- See Form No. 3. It is most important that VPC knows the stocks of seeds. The seed register should be held by the QA Manager and must be filled in and updated whenever seed is removed. This task should be carried out as soon as possible so there is a continuous record of seeds held by VPC. Two registers need to be kept as follows:
  - Master Seed Production and Reconciliation
  - Working Seed Production and Reconciliation
- An inventory must also be kept for all challenge cultures as well.

Frozen Antigen Storage [Pre-Freeze Dried]

Inventory must be maintained for all antigens held frozen waiting for freeze drying. This could be in the form of some accounting data, but must be available to production and accounting staff [see Form No. 4].

Animal House; Labelling of Cages/Identification of Animals

There appeared to be a total lack of labelling used in the animal house. All cages should be labelled to identify the contents of the cages. Animals, particularly chicken

and rabbits should be identified with ear tags or wing tags so identity is assured. See http://www.lopsandcavies.com/Ear_Tag_Cavy.htm for how this can be done.

In animal breeding the breeders and their offspring should be identified so a proper breeding program can be set up and to avoid inbreeding, so that importation of new male rabbits [and hence potential of introducing disease into the rabbit colony] may be avoided.

Labelling of Boxes of Unlabelled Finished Products

The current system of boxing unlabelled finished product with cardboard insert identifying the product is poor GMP but can be fixed with a very simple system which I believe VPC should institute without a great deal of effort. See http://www.avery.com/us/software/index.jsp for simple formatting of these labels. VPC will need a colour printer to do in house.

For products under quarantine [that is, not released for sale] a yellow sticker is applied by the production staff who pack the product. The product, batch number, date of packing and the signature and the numbers of boxes of this product are indicated on this label.

This product cannot be processed / labelled / sold until the product is released by the Quality Assurance Manager.

VETERINARY VACCINE PRODUCTION CENTRE

QUARANTINE – UNDER TEST NOT FOR SALE.

Product:……Batch Number:……

Date of Production:……..

Number of bottles in this box:……..

Signature:……

Number of Boxes:……..of……..for this batch

When the Product is Released by the Quality Assurance Manager a green sticker is placed over the yellow sticker and then the product may be labelled and packed and sold. Note that the Quality Assurance Manager has designated the expiry date of the product.

VETERINARY VACCINE PRODUCTION CENTRE

RELEASED FOR LABELLING AND SALE.

Product:……Batch Number:……

Date of Release:……Expiry date:……...

Number of bottles in this box:……..

Signature:……

Number of Boxes:……..of……..for this batch

If a product is rejected then the Quality Assurance Manager will place a red sticker over the yellow or green sticker and the product will be disposed of by the recommended method.

VETERINARY VACCINE PRODUCTION CENTRE

REJECTED; NOT FOR SALE.

Product:……Batch Number:……

Date of Rejection:……:……..

Number of bottles in this box:……..

Signature:……

Number of Boxes:……..of……..for this batch

11.10.7 Production and Quality Control Testing of Products at VPC

The quality control testing at VPC covers some aspects that will reveal some major problems in product performance in the field. Sterility testing, although not following international norms, will detect gross contamination of products, although contamination of these products may be masked by the use of excessive formalin in killed bacterial products or antibiotics in live viral products.

The safety tests will detect safety issues only if gross problems exist, which is typical of most safety tests.

The potency tests will detect the presence of the antigen that has been produced, however the challenge tests are usually carried out using the homologous [same] organism, thus only demonstrating homologous protection, whereas in reality many different strains may exist in the field.

The following tables demonstrate the substrates or raw materials used and the tests under taken by VPC compared with those which are usual in large vaccine units, highlighting where VPC may wish to go in the future.

Freeze Dried Avian Vaccines			*Indicates concern*
Raw Materials	*VPC*	*Large Vaccine Unit*	*Degree of Concern*
Defined SPF seeds	Supplied as defined seeds; treatment since supplied undefined as passaged on non-SPF substrate	Defined from master to vaccine	Some concern as to the presence of extraneous agents, and to seed identity
SPF eggs	"Clean commercial eggs" untested, small in numbers	SPF eggs used in all production processes Unlimited eggs	Some concern as to the presence of extraneous agents
Bulk antigen	Sterility test only HA test for NDV CAM observation for FP Embryo obs for IB No virus titre done	Sterility test Virus titre	Poor yield of virus and thus vaccine failure on freeze drying
Freeze dryer	Small volume	Large volume	Non competitive
Volume checks	How done?	Would have under control	Need to review
Homogeneity	How done?	Would have under control	Need to review
Reconciliation	How done?	Would have under control	Need to review

Finished Product Testing

Tests	*VPC*	*Large Vaccine Unit*	*Degree of Concern*
Vacuum testing	Done	Done but usually back fill with nitrogen	Leaking caps at VPC, stability profile?
Sterility test	Sterility test, contamination maybe masked by antibiotics	Sterility test	Needs to be validated
In vitro Mycoplasma test	Not done	Done	Mycoplasma major primary cause of chronic respiratory disease in chickens
Virus titre	One test decides	Multiple duplicates	False high titre of

	virus titre of product	of tests with reference preparations used as comparison	VPC vaccine may lead to vaccine failure in field
Chicken safety test	Inoculating same chickens as eggs are sourced from may mask problems	SPF chickens inoculated with 2x100dose of vaccine over 5 weeks	VPC safety test may not reveal problems
Identity	By observation in embryos	By observation in embryos and antibody in safety test chickens	VPC observations may not detect problems, wrong virus grown
Invitro extraneous agent testing	Not done	Done in SPF eggs and tissue culture	VPC vaccine may have problems undetected
Moisture test	Not done	Done	Moisture content should be 1-5% for ideal stability
Stability profile	Not determined	Highly defined parameters tested	Unknown profile means poor product profile

Swine Fever Vaccine			*Indicates concern*
Raw Material	*VPC*	*Large Vaccine Unit*	*Degree of Concern*
Viral seed	Defined lapinised "C" strain. WS to last many years	Tissue culture strain	Concern as to seed identity, consider having seed gene sequenced
Substrate	Local rabbits, few in number, expensive and labour intensive	Cell culture, large volume	Non competitive
Bulk antigen testing	Sterility only No virus titre	Sterility Virus titre	Poor yield of virus and thus vaccine failure on freeze drying?
Freeze dryer	Small in volume	Large volume production	Non-competitive
Volume checks	How done?	Would have under control	Need to review
Homogeneity	How done?	Would have under control	Need to review
Reconciliation	How done?	Would have under control	Need to review

Finished Product Testing

Tests	*VPC*	*Large Vaccine Unit*	*Degree of Concern*
Sterility test	OK, except masking of contamination by antibiotics	OK	Needs to be validated
Virus titre	No duplication of testing, End point testing?	Multiple duplicates of tests with reference preparations used as comparison	False high titre of VPC vaccine may lead to vaccine failure in field
Safety testing	Not done in pigs? I did not ask	Done in pigs	Possible safety problems
Identity testing	Temperature rise in rabbits	Antibody in safety test pigs	Needs reviewing
Invitro extraneous agent testing	Not done	Done and tissue culture	VPC vaccine may have problems undetected
Moisture test	Not done	Done	Moisture content should be 1-5% for ideal stability
Stability profile	Not determined	Highly defined parameters tested	Unknown profile means poor product profile

Haemorrhagic Septicaemia and Fowl Cholera Vaccines		*Indicates concern*	
Raw Materials	*VPC*	*Large Vaccine Unit*	*Degree of Concern*
Seed material	OK, except for long term storage	OK	Seed identity should be confirmed
Substrates	Variable as to quality of supply	Defined and of constant supply	Varying yields
Antigen quantification	Browns tubes and spectrophotometer	Similar	OK
Antigen purity	Spread to plates and gram stain	Similar	OK
Inactivation testing	Residual formalin may mask viable bacteria	Similar	May have to review method
Batch size	40 litres	> 150 litres	Scale of economy, many batches
Formalin inactivation	0.5% + 0.1% added later	0.2 – 0.3% at most	Too high, may affect long term antigenicity of vaccine

Alum precipitate [HS only]	How defined?	Highly defined	Some alums are good adjuvants others not
Oil emulsion [HS only]	Oils expensive, process expensive	Highly defined, high volume	How reactive?
Preservatives	Only formalin	Most probably add thimerosal	Consider use of thimerosal
Homogeneity	How is this done?	Would have under control	Review how done
Reconciliation	How is this done?	Would have under control	Review how done
Fill volume checks	How is this done?	Would have under control	Review how done

Finished Product Testing

Tests	*VPC*	*Large Vaccine Unit*	*Degree of Concern*
Sterility Testing	OK but formalin may mask contamination	OK	Sterility tests need validation
Safety Tests	FC in chickens HS [alum] in mice HS [Oil] in mice	Would use target Species	Consider testing HS [Oil] in target species
Alum quantification	Not done	Done	Consider chemical testing
Formalin assay	Not done	Done	Consider introducing test to VPC, can provide details
Potency test	FC in chickens done HS in mice done	Would do	Consider heterologous challenge tests
Stability testing	Not done	Highly defined	Need to institute

Form No. 1

VPC Document Number	Date of Issue	Date of Expiry	Approved by

VPC Egg Incubation Records

Batch Number of Eggs:……..Date Set:……..Purpose:…….
Numbers of eggs set:…….

Date	Days of Incubation	Dry Bulb Temperature	Wet Bulb Temperature	Relative Humidity	Comments [Filled water reserve, etc]	Sign
	1					
	2					
	3					
	4					
	5					
	6					
	7					
	8					
	9					
	10					
	11					
	12					
	13					
	14					
	15					
	16					
	17					
	18					
	19					
	20					
	21					
	22					
Comments: Include , dead eggs, clear eggs, cracked eggs, hatched eggs, usable eggs and any pertinent information						

Signed:……..Date:……..
Submitted to Quality Assurance by :……..Date:……
Checked by Quality Assurance by:…….Date:……

Written by	Date	Checked by	Date	Valid from
				Valid to

Form No. 2

VPC Document Number	Date of Issue	Date of Expiry	Approved by

VPC Equipment Temperature Records

Equipment Recorded:…….. Maximum-Minimum Thermometer:……

Date	am		pm		Sign
	Maximum	Minimum	Maximum	Minimum	
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					
20					
21					
22					
23					
24					
25					
26					
27					
28					
29					
30					
31					
Comments:					

Signed:……..Date:……..
Submitted to Quality Assurance by :……..Date:…….
Checked by Quality Assurance by:…….Date:…….

Written by	Date	Checked by	Date	Valid from
				Valid to

Form No. 3

VPC Document Number	Date of Issue	Date of Expiry	Approved by

Bacterial and Viral Seed Reconciliation Log
Seed Material: NDF WS001……Date of Production:…12/10/2005…….

How stored: Freeze Dried/~~Frozen~~

Sterility/~~purity~~ Test:…Satisfactory/~~not Satisfactory~~ …Titre or Count: $10^{10.02}$ EID_{50}/mL…….

Storage:…-700C…….. Retest:……20/12/2007……..

Date	Seed Material	Total vials	Used in/No of vials used	Reconciliation	Initials by 2 staff [pick/check]
example 12/12/07	NDF WS 001	150	NDF # 12/07 3 vials	147	SP/SS
example 20/12/07	NDF WS 001	147	NDF # 13/07 4 vials	143	SP/SS
Example 20/12/07	NDF WS 001	143	Retest 2 vials	141	SP/SS
example		141			
Comments					

Signed:……..Date:……..

Submitted to Quality Assurance by :……..Date:……

Checked by Quality Assurance by:……Date:……

Written by	Date	Checked by	Date	Valid from
				Valid to

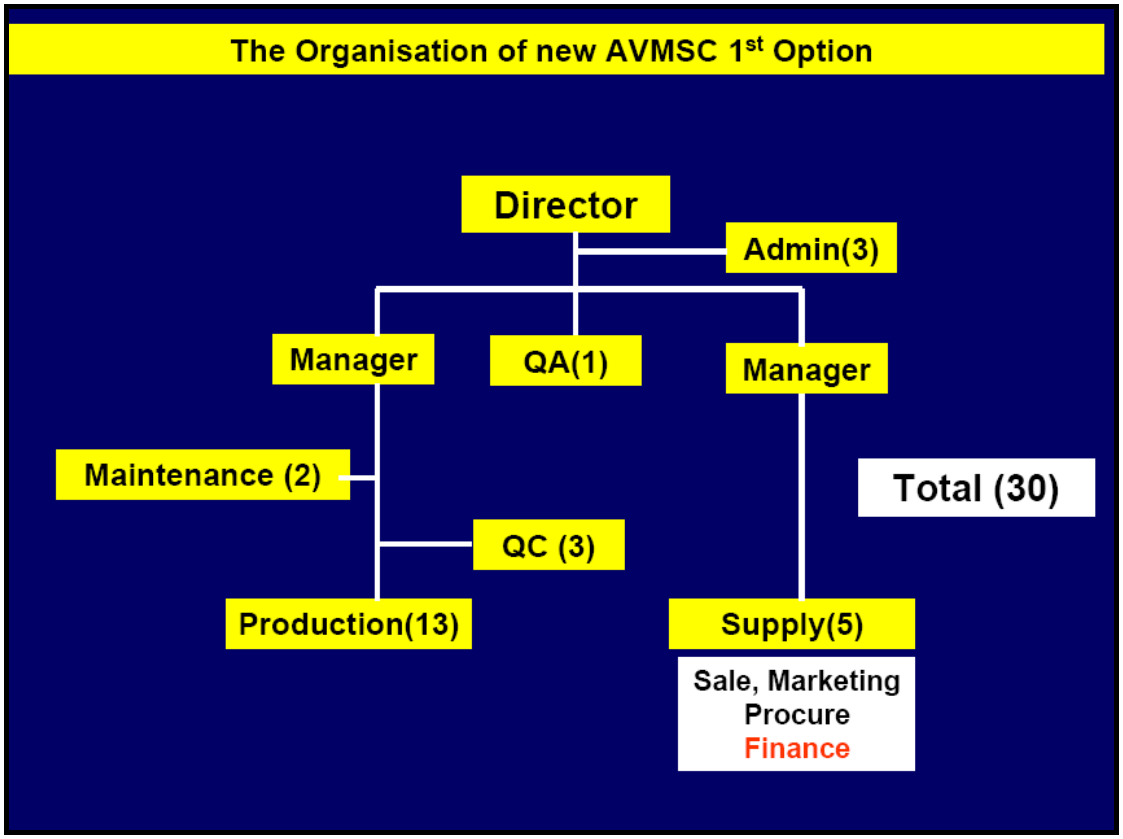
Form No. 4

VPC Document Number	Date of Issue	Date of Expiry	Approved by

Viral Antigen Bulks held Frozen waiting Freeze Drying at VPC
Freezer Number:……..Freezer Temperature:……..

Date of Addition	Bulk Product	Batch Number	Sign Pick/check	Date of Removal	Batch Product	Sign Pick/check
10/10/07	NDF	#07/07	SP/SS	20/12/07	NDF#O67	SP/SS
15/10/07	SF	#06/07	SP/SS			
21/10/07	FP	#01/07	SP/SS	25/12/07	FP#017	SP/SS

11.11 Appendix 11 Draft Organisation Structure & Anticipated Staff Numbers, AVMSC, 30 November 2007



11.12 Appendix 12 AVSMC Advisory Board DRAFT Terms of Reference, 30 November 2007

An Advisory Board will be established to provide independent, high-level business and technical advice on request to the Director of the AVMSC.

Appointment

The Advisory Board will be appointed by the Minister of Agriculture and Forestry on the advice of the Director General of Livestock and Fisheries.

The Minister will appoint a distinguished and respected person as the Chairman of the Advisory Board.

Objective

To provide expert and independent advice to the AVMSC to ensure that AVMSC has access to world best practices and can make high quality decisions for the enduring benefit of livestock and livestock producers throughout Lao PDR.

Operation

The Advisory Board will provide independent advice to the Director of the AVMSC on any aspect of the operation of the AVMSC as requested by the Director.

The Advisory Board will meet as required, approximately 2-4 times per year.

The Director will attend meetings and provide data and reports as requested by the Advisory Board.

The Director will provide a secretariat to record the proceedings and decisions of the Advisory Board.

Minutes and recommendations approved by the Advisory Board will be submitted to the Director and the Minister within 30 days of each meeting.

Deliberations and recommendations of the Advisory Board are commercially sensitive and will be subject to confidentiality arrangements. They will only be disclosed to those authorised by the Director.

Tasks of the Advisory Board

The Advisory Board will review and comment on the annual budget.

The Advisory Board will review and comment on the performance of the AVMSC in the following areas:

- strategic plan
- management structure and operations
- income, expenditure, debt and profitability
- products manufactured/sourced and the respective quantities made/procured and marketed
- equipment purchase and maintenance
- compliance with the AVMSC Quality Plan.
- other matters as requested by the Director

Structure and Membership

The structure, operation and membership of the Advisory Board may change from time to time at the discretion of the Minister, considering the advice of the Director, but is expected to comprise 8-12 individuals who will be selected on the basis of their personal skills and experience and not as representatives of government or other organisations.

Members will be appointed for terms of 3 years and be selected on the basis of their skills and experience in the areas of:

- vaccine manufacture and quality assurance,
- veterinary pharmaceutical product availability, quality and the global veterinary medicine market,
- smallholder livestock production in Lao PDR,
- commercial livestock production in Lao PDR,
- animal health epidemiology & economics,
- accounting and business finance skills,
- marketing and business management,
- importation processes to Lao
- government economic policy and regulation
- similar manufacturing enterprises.

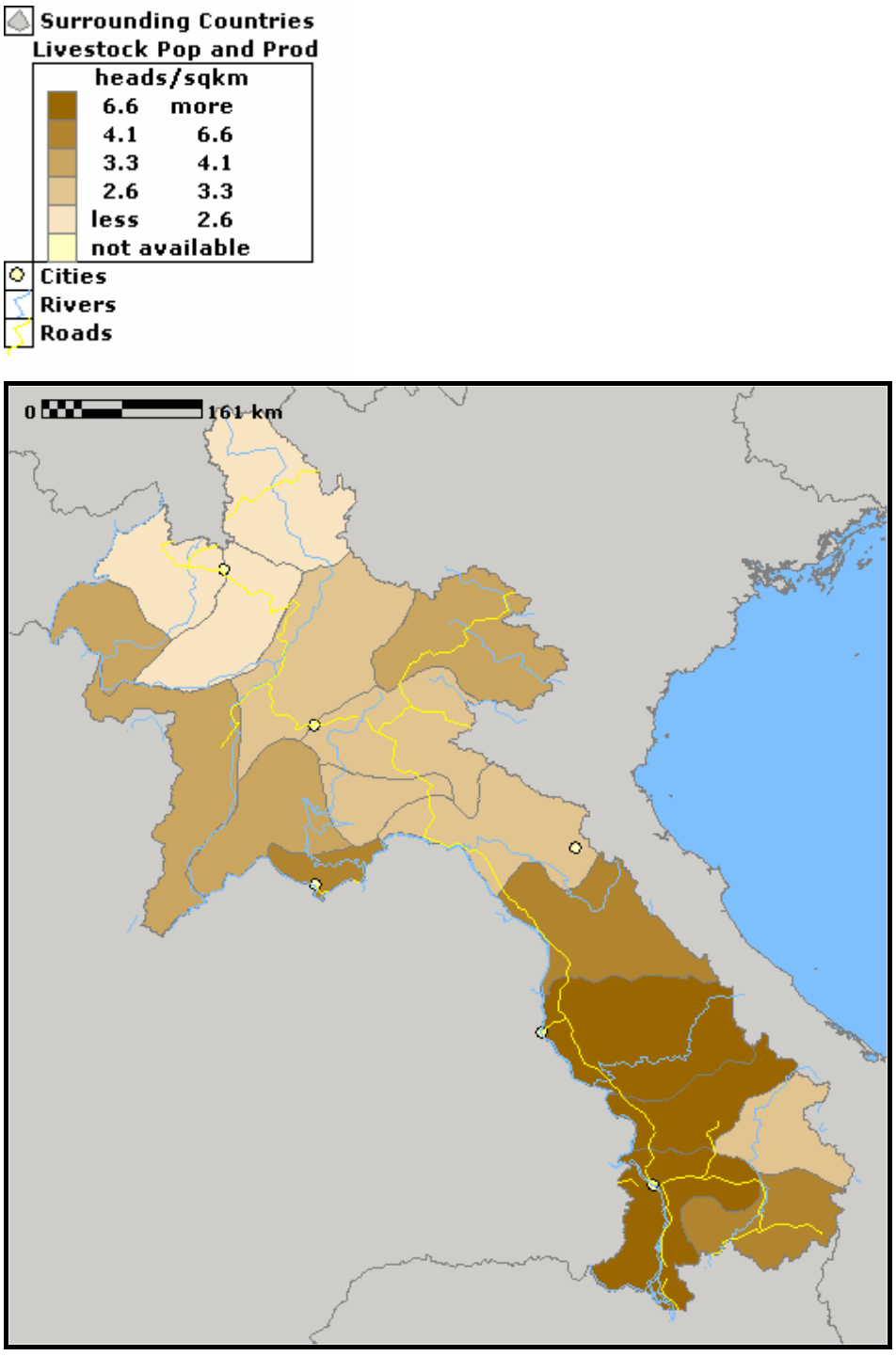
END

11.13 Appendix 12 Livestock Distribution and Densities in Lao PDR

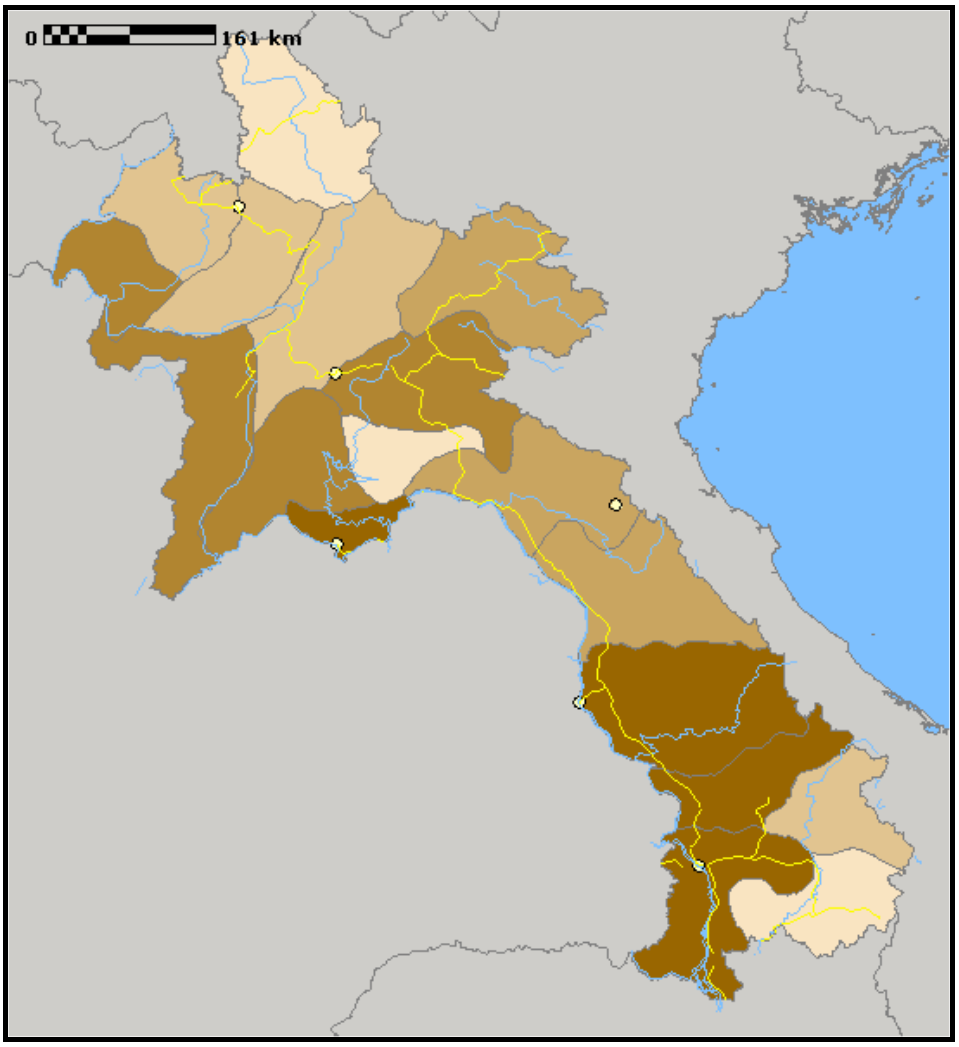
Numbers of animals per square kilometre.

Source: Global Livestock Production and Health Atlas. Animal Production and Health Division. FAO. http://www.fao.org/ag/aga/glipha/index.jsp

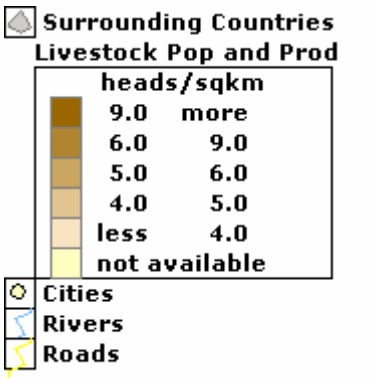
11.13.1 Buffalo 2004

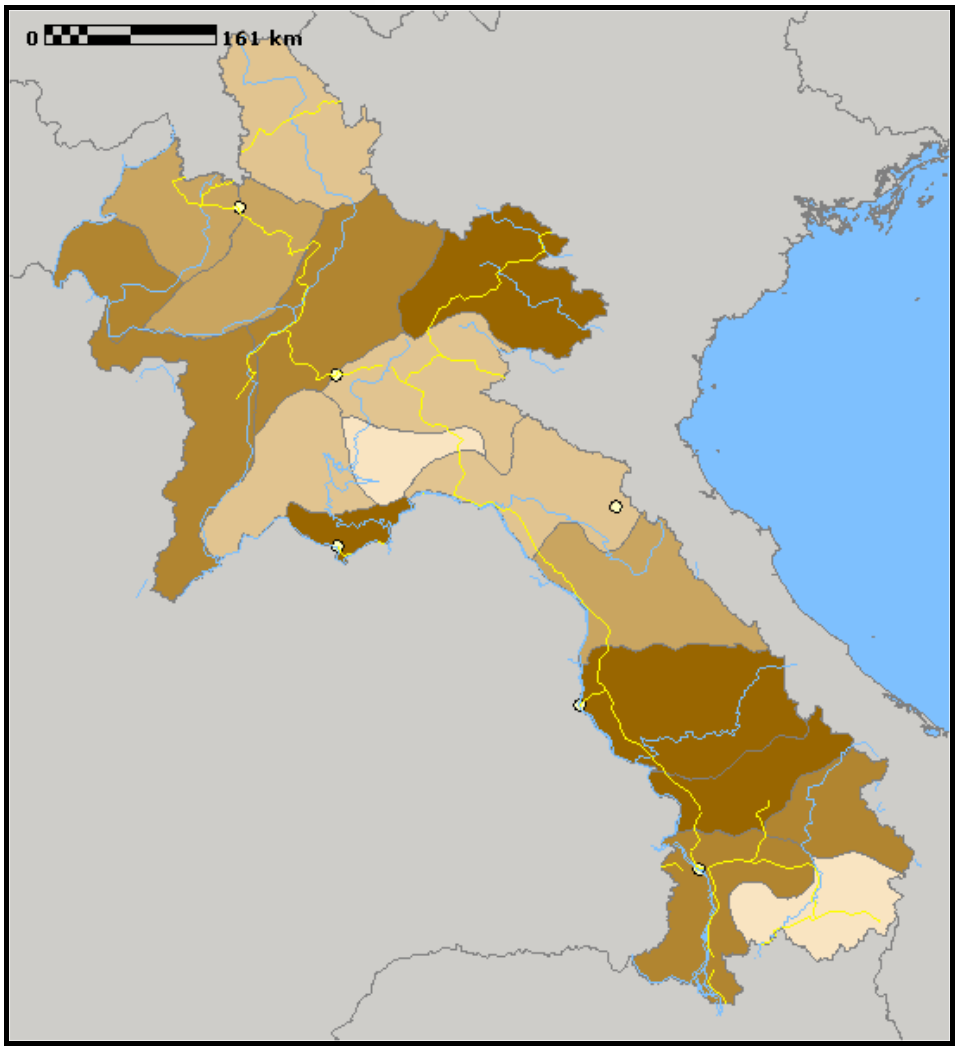


11.13.2 Cattle 2004

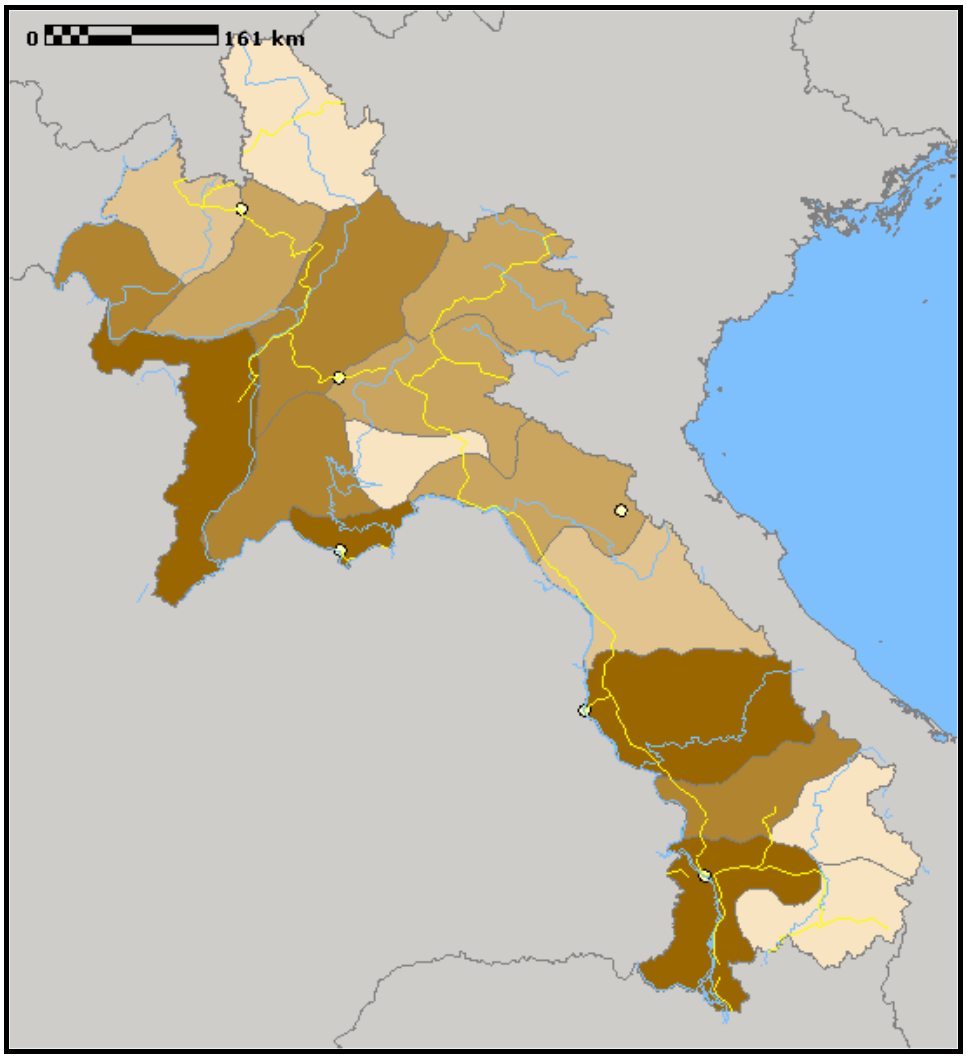


11.13.3 Pigs 2004





11.13.4 Chickens 1999



11.13.5 Ducks 1999