Australian and New Zealand College of Veterinary Scientists

Fellowship Examination

June 2012

Veterinary Epidemiology

Paper 1

Perusal time: **Twenty (20)** minutes

Time allowed: **Four (4)** hours after perusal

Answer **ALL <u>FOUR (4)</u>** questions

Each question is worth 50 marks (total 200 marks)

Paper 1: Veterinary Epidemiology

Answer all four (4) questions

1. Lack of statistical independence, correlated data and "clustering" are related issues having a pervasive influence on the design, analysis and interpretation of epidemiological studies. Describe these phenomena, explaining when they may be encountered, and why they are so important. Describe the main methods for dealing with them at each stage of an investigation. Use examples to support points where necessary. *(50 marks)*

2. Much of modern epidemiology is founded on a theoretical understanding of cause and effect relationships that evolved from the field of philosophy. Describe how theoretical concepts of causation, multiple causation and "causal criteria" are used for explaining the occurrence of disease in animals. In your response use diagrams and prominent examples from veterinary medicine to illustrate major points. *(50 marks)*

3. Simulation modelling is a popular tool for studying the behaviour of infectious diseases in populations. Describe the types of simulation modelling methods currently in use in epidemiology by arranging them according to the underlying mathematical, statistical or logical processes that they are based on. Include advantages and disadvantages of each approach and the typical goals and applications they are suited to. *(50 marks)*

4. Bernard Vallat, director general of the OIE, made the statement, "As a result of globalisation and climate change, we are currently facing an unprecedented worldwide impact of emerging and re-emerging animal diseases and zoonoses". Discuss this statement, including what aspects you agree with and what aspects you disagree with in each case justifying your position. In your discussion, cite some historical examples of disease outbreaks and the factors that played a role in their emergence and how they compare with factors playing a role in recent emerging disease outbreaks. Briefly discuss the challenges that face livestock producers and decision makers today as they grapple with emerging diseases. *(50 marks)*

End of paper

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Paper 2

Perusal time: **Twenty (20)** minutes

Time allowed: **Four (4)** hours after perusal

Answer **ALL <u>FOUR (4)</u>** questions

Each question should take approximately **one (1)** hour to complete.
Marks within questions are given to help you apportion your time more efficiently.
Show all steps in calculations.
A formula sheet is provided at the end of the paper for your assistance.
All questions are of equal value.

Answer **<u>FOUR</u>** questions each worth 50 marks .....total 200 marks.

Paper 2: Veterinary Epidemiology

Answer <u>all</u> four (4) questions

1. Veterinary epidemiologists are often consulted on the disease risks involved when importing animals into a country. A knowledge of the Office Internationale des Epizootes (OIE) approach to import risk analysis is necessary **(Part A)** and an application of a quantitative risk analysis process is often required **(Part B).** Stochastic modelling and the use of distribution functions is often used as part of the quantitative risk analysis process and these can also be applied in a number of risk assessment scenarios **(Part C).**

PART A – *(15 marks)*

Outline the OIE Risk Analysis process used for import risk analysis and show how it compares to the food safety risk assessment approach outlined by the Food and Agriculture Organisation and World Health Organisation.

PART B – *(25 marks)*

The Malaysian government wishes to import beef cattle from Northern Queensland, which is not free from leptospirosis, into leptospira free stud farms. The Malaysian government needs to decide whether or not to allow imports of cattle from Northern Queensland.

You have an initial meeting with the government officials and at this meeting are given the following information:

a) The annual risk of importing leptospirosis is thought to be the most appropriate time span for the risk estimate.

b) In a very recent seroprevalence survey in Queensland (QLD), 1500 cattle were randomly selected and tested for leptospira. Of these 5 were found to be positive.

c) The sensitivity of the test used in the leptospira seroprevalence study is thought to be between 85% and 95% and the specificity is 100%.

d) Should imports be allowed, all cattle coming from QLD would require a pre-export test prior to export. The same test would be used as was used in the seroprevalence study.

e) The expected number of cattle that would be imported each year is uncertain. However, discussions suggest that the most likely number is 1,200. This figure could however, be as low as 200 or as high as 3,000.

Question 1, part B continued over page

Design a scenario tree and corresponding quantitative risk assessment model based on the information given above to help this government make this decision. Briefly explain the objective of the model and what the output would tell you. (Note: you do not have time to do an overly complicated risk assessment so keep it simple and logical.)

PART C – *(total of 10 marks)*

Risk can be described using various probability functions such as Beta, Hypergeometric, Binomial, Negative Binomial, Poisson, etc. For each of the following problems, select the appropriate function that could be used to solve the problem and insert the appropriate inputs for that function.

a) 600 Kangaroos were randomly selected from Iron Range National Park, 15 were carrying antibiotic resistant *E. Coli* (AREC). Assume the sensitivity and specificity of the diagnostic method are 100%. Use this information to describe the function and its inputs in order to model the true prevalence of Kangaroos with AREC in the park. *(2 marks)*

b) If in problem a) above, none of the kangaroo sampled had tested positive for AREC, what function and inputs could you use to model the true prevalence of AREC in kangaroos in the Park given these results? *(2 marks)*

c) The poultry industry wishes to test for avian influenza antibodies in wild waterfowl (birds). Similar studies in China have shown that one in every 1000 waterfowl in the population has avian influenza antibodies.

   i. Give an appropriate function and inputs to model how many waterfowl will have to be examined before one bird is found with antibodies. *(2 marks)*

   ii. Give an appropriate function and inputs to model how many will have to be examined before 10 birds are found with the antibodies. *(2 marks)*

d) Veterinary services estimate that the prevalence of leptospira in feral pigs in northern QLD is now 2%. A farmer in the area estimates he has 100 of these pigs on his property. Give an appropriate probability distribution and parameters that could be used to estimate how many of these pigs are likely to be carrying leptospira. *(2 marks)*

Continued over page

2. Clinical bovine leucosis produces economic losses in the form of impaired reproduction, decreased meat and milk production and condemnation at slaughter. Bovine Leukaemia Virus (BLV) can be transmitted horizontally from animal to animal, vertically from infected cows to approximately 10 percent of their foetuses *in utero*, and experimentally via milk.

The following problem is adapted from a serological study to determine the prevalence of Bovine Leukaemia Virus (BLV) infection in cattle in Florida, USA.

PART A – *(total of 35 marks)*

Eighteen dairy herds (with 7,679 cows over 18 months of age) in Florida were selected for the prevalence study, using a stratified (by breed) random sampling procedure. Each of the 7,679 serum samples was tested for BLV antibodies, using the agar gel immunodiffusion test with a glucoprotein antigen (AGID-G). The results of the serological tests are shown in Table 1.

Table 1: Prevalence of antibodies by breed to BLV in Florida dairy cattle, by breed

Breed	**% Prevalence (No. Positive/No. Tested)**
Jersey	63.1 (159/252)
Holstein	47.4 (3,234/6,826)
Guernsey	46.1 (178/386)
Brown Swiss	42.8 (92/215)

Answer the following questions:

a) Discuss your interpretation of the results in Table 1. *(5 marks)*

b) Let us assume that the true prevalence of BLV (determined by a non-serological method) in the dairy population from which the sample (7,679 cows) was drawn is 20%. Let us also assume that after a follow-up study, 1,459 of the AGID-G positive cows were shown to be infected with BLV.

Question 2, part A continued over page

Use this information to calculate parameters that may help you evaluate the AGID-G test. Discuss the results of your calculations and what they are telling you about how the test is likely to perform in the field and how this will influence your interpretation of the results.

Given the limitations of using the existing AGID-G test include in your discussion how you think the test could be improved to better meet the objectives of the study. *(10 marks)*

c) The same test (AGID-G) was used in western France to screen 10,336 dairy cows for possible BLV infection. Let us assume the same sensitivity and specificity as before, but that the true prevalence of BLV infection in dairy cattle in western France is only 1%. Evaluate the usefulness of the test under these circumstances and comment on the likely test results when using the test in western France. *(5 marks)*

d) Describe and discuss some alternative ways by which you could evaluate the AGID-G test if you didn't know the true prevalence of BLV. *(15 marks)*

PART B – *(total of 8 marks)*

You have put forward two strategies A and B to eradicate BLV from cattle in Florida. Costs due to the disease are production losses. The benefits of an eradication programme are the total of expected losses to be avoided. Additional costs are those invested in the programme. We suppose that the costs and benefits occur at the end of each year.

Calculations are necessary to identify which strategy is the most favourable from an economic point of view. The current costs and benefits (in millions of dollars) of the two programmes are given in a table:

	Strategy A		**Strategy B**	
Year	Costs	Benefits	Costs	Benefits
1	20	0	2	1
2	10	8	2	3
3	7	14	4	6
4	4	18	5	7
5	0	23	6	14

Real interest rate = 5%, calculated once annually at the end of each year

a) Calculate the discount factors (DF1 to DF5 in the table below) that are necessary to calculate the present value of the costs and benefits over 5 years. Use the given interest rate. *(2 marks)*

Question 2, part B continued over page

The following table gives the net present value of the costs and benefits for years 1 to 5 for both strategies.

Present values

		Strategy A		Strategy B	
Year	**Discount Factor**	**Costs**	**Benefits**	**Costs**	**Benefits**
1	DF1	19.05	0.00	1.90	0.95
2	DF2	9.07	7.26	1.81	2.72
3	DF3	6.05	12.09	3.46	5.18
4	DF4	3.29	14.81	4.11	5.76
5	DF5	0.00	18.02	4.70	10.97
Total		37.46	52.18	15.99	25.58

b) Discuss which strategy would be the most economically sound strategy. Use two appropriate economic measures to quantify and support your answer. *(6 marks)*

PART C – *(7 marks)*

As part of the eradication programme three different treatments (I, II & III) used in a cohort study in a cattle feedlot, resulted in differences in carcass mass at slaughter. Treatment group 0 received no treatment. The following table shows costs and returns (in $) adjusted to a standard pen of 100 cattle.

Calculate the missing numbers for rows beginning with a), b), c) and d) and write the answers in your answer book. Use the information to quantify which treatment is the best from an economic point of view. Justify your answer using the figures you calculated.

	TREATMENT			
Item	**0**	**I**	**II**	**III**
Offal	187	199	227	268
Hides	16	17	18	14
Meat	222	233	263	342
a) Gross Return				
Cost of drugs and labour	9	10	50	180
b) Marginal Cost over Treatment 0				
c) Marginal Return over Treatment 0				
d) Treatment net return				

Continued over page

3. Mackay in central Queensland has recently detected Johne's disease in a few cattle herds. This is an introduced disease into what was considered to be a disease-free area.

The Queensland Government veterinarians are interested in finding out what the true prevalence of the disease currently is in the Mackay shire. They would like to use this information to ultimately decide whether a general control campaign needs to be undertaken or not.

They have the following information for you:

- **Proserpine River catchment**
  Sugar cane growing (164 holdings) and beef cattle grazing (140 holdings) are the main agricultural activities along with some minor horticultural activity.
- **O'Connell River catchment**
  Sugar cane growing (287 holdings) and beef cattle grazing (289 holdings) are the dominant agricultural activities.
- **Pioneer River catchment**
  Sugar cane growing (326 holdings) and beef cattle grazing (186 holdings) are the main agricultural activities.
- **Plane Creek catchment**
  Sugar cane growing (544 holdings) and beef cattle grazing (417 holdings) are the main agricultural activities with limited broadacre cropping and horticultural activity also occurring.

There are approximately 4,500 dairy cattle and 850,000 beef cattle kept on the small holdings of all four catchments.

a) Outline and discuss a practical sampling strategy to determine the prevalence of Johne's disease in cattle in Mackay Shire based on the information given above and using the serological test only. Include in your discussion how you could obtain estimated prevalences for the calculation of sample sizes. *(10 marks)*

b) The ELISA test used as the diagnostic test has a poor sensitivity (40%). Discuss how this will influence your sampling design and the results of your study. *(5 marks)*

Question 3(c) over page

c) Let us consider the problem of estimating the seroprevalence of Johne's disease at individual animal level for the Pioneer River catchment

Assume the following:

i. The total population of cattle in this catchment is 30,000 beef cattle
ii. The proportion of affected holdings is 2%
iii. The estimated prevalence of Johne's disease at individual animal level in Pioneer River catchment is 5 %
iv. The government vets are prepared to work with a 5 percentage point error margin (precision or maximum acceptable difference)

Using simple random sampling, how many holdings would you sample to estimate the prevalence at individual animal level for the Pioneer River catchment? Show your calculations. *(5 marks*)

d) Discuss the importance of sampling frames and some of the pitfalls associated with inadequate sampling frames. *(5 marks)*

Question 3(e) over page

e) Assume resource constraints mean you can only randomly select **five (5)** holdings from the 186 in Pioneer River Catchment and you have labelled them A to E. The population of cattle in each holding is given in the table below: *(15 marks)*

Farm	All cattle	No. of 4 years or older
A	610	200
B	910	360
C	2250	650
D	1000	480
E	3000	1065
Total	**7770**	**2755**

i. Ignoring the sensitivity and specificity of the ELISA diagnostic test for Johne's disease, how would you advocate sampling the cattle on these farms to estimate seroprevalence at the animal level with 99% confidence (Z=2.58) and how many cattle would you sample from each holding? Assume the same precision as before of 5%.

ii. What is the problem that arises from ignoring the sensitivity and specify in the calculation of the sample sizes?

iii. What additional information would you need to work out sample sizes for estimating seroprevalence at the animal level based on a cluster sampling strategy and how could you obtain this information?

f) *(10 marks)*

i. After the survey was carried out, for one holding, all 14 animals sampled tested negative for Johne's disease using the ELISA. Discuss this result and advise your client as to what the true animal level prevalence of Johne's disease on this farm could potentially be given the sample size. Comment on how the design of the study could influence this result.

ii. Assume that at the end of the survey, 4 out of 104 cattle sampled in the catchment tested positive using the ELISA. Describe how you would interpret this result.

iii. Discuss a few different methods available for calculating the true prevalence in the catchment.

Continued over page

4. **PART 1 –** *(total of 30 marks)*

A veterinarian was engaged in a program, which included the epidemiological diagnosis of calf mortality on a dairy farm. She suspected there was an association between calf mortality and the calving location, which was either outside in pens or inside in a shed. The outside pens were noted to be in poor condition.

In order to study the relationship between location of calving and calf mortality, she collected the following data over the next two months; recording the birthplace of all the calves as they were born, and observing whether each calf subsequently survived or died during the first month of life.

Of 210 calves born in the outside pens, 84 died. Of 90 calves born in the shed, 9 died.

a) Name the study design used by the veterinarian and give some advantages and disadvantages of this type of study design. *(7 marks)*

b) The veterinarian explained to her student aides that if records about the birth place (outside pens vs. shed) had been kept for a number of calves that had died previously, and for a number of calves that survived, she could have designed a different type of study, instead of spending two months on data collection.

   Identify the alternative study design that she could have implemented and give some advantages and disadvantages of this type of study design. *(7 marks)*

c) Work out some appropriate measures of association given the study design and results above, show how you derived these, and interpret the results of each. *(6 marks)*

d) Suppose that over a one-year period, each of the 2,000 cows on this dairy has one calf. Suppose that 70% of these calves are born in outside pens, and 30% are born in the shed. Combining these figures with those used in your calculations of measures of association in part 4c) above, compute the number of calves born in outside pens that are expected to die, showing how you derived this number. *(2 marks)*

e) Assuming no bias and that the association is causal, how many deaths (number) would have been prevented if all calves had been born in the shed? (Show your calculations). *(2 marks)*

Question 4 (f) over page

f) Suppose that information is now made available describing the date of each calving event. As well, the farmer advises that a decision about where a cow is allowed to calve is affected by the time of year. *(6 marks)*

Assume that if you ignore time of year:

Outside pens have a RR = 6 [RR = relative risk]

i. If you stratify by time of year, you get the following:
Outside pens in Summer: RR = 3.8
Outside pens in Winter:RR = 4.2

What is your conclusion about the relationship between time of year and the risk of disease in calves and what role is time of year playing in the relationship? Justify your answer.

ii. If the results you got after stratifying for time of year were as follows:
Outside pens in Summer RR = 2.4
Outside pens in Winter RR = 5.7

What is your conclusion about the relationship between time of year and the risk of disease in calves and what role is time of year playing in the relationship? Justify your answer.

PART 2 – *(total of 12 marks)*

You are asked to advise a horse breeder who wants to buy twenty horses which are tested free of equine infectious anaemia (EIA) with an ELISA diagnostic test. The client wants your advice to buy the animals because they come from a country where equine EIA is present at a rather high level (prevalence = 55%) and he faces the risk of bringing the disease onto his stud. From the literature you find that the sensitivity of the ELISA test was 90.9% and the specificity 100%.

a) Based on the test results (all animals tested negative), recommend whether the client buy these animals or not. Explain the basis for your answer. *(7 marks)*

b) Define the predictive value of a positive test result. Explain why for this example the predictive value for a positive test is high. *(5 marks)*

Question 4, part 3 over page

PART 3 – *(8 marks)*

Suppose a case-control study was performed into the effect of a lighting regime on the presence of intestinal lesions due to coccidiosis in broilers. In total, data from birds of 208 flocks were obtained. Coccidiosis lesions were found in broilers in 99 flocks. Nearly 50% of the flocks with lesions were reared under an intermittent lighting regime, while this figure was 28.4% for the flocks without lesions.

a) Discuss how you would go about calculating a sample size for a case-control study.

b) Calculate and interpret the odds ratio for exposure to intermittent lighting regime.

c) Calculate the attributable fraction (AF) for exposure to intermittent lighting regime. Describe what the AF tells you about the lighting regimes and what are the assumptions when interpreting an AF?

End of Paper

FORMULA SHEET

$$\overline{X} = \sum_{i=1}^{n} \frac{x_i}{n}$$

$$s = \sqrt{\frac{\sum (x_i - \overline{X})^2}{n-1}}$$

$$s = \sqrt{\frac{\sum x_i^2 - \frac{(\sum x_i)^2}{n}}{n-1}}$$

$$CI \approx ID \times \Delta t$$

$$RR = \frac{P(D+ \mid E+)}{P(D+ \mid E-)} = \frac{a/(a+b)}{c/(c+d)}$$

$$AR = [P(D+ \mid E+)] - [P(D+ \mid E-)]$$
$$= [a/a+b] - [c/c+d]$$

$$OR = \frac{ad}{bc}$$

$$Variance\ (\hat{p}) = \frac{\hat{p}(1-\hat{p})}{n}$$

$$SE\ (\hat{p}) = \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$$

$$95\%\ conf.\ interval = \hat{p} \pm 1.96 \times SE_{\hat{p}}$$

$$n = \frac{Z^2 \hat{P}\hat{Q}}{L^2}$$

$$c = c_1 n_1 + c_2 n_1 n_2$$

$$n_2 = \sqrt{\frac{C_1 S_2^2}{C_2 S_1^2}}$$

$$n = [1 - (1-a)^{1/D}]\ [N - \frac{(D-1)}{2}]$$

$$D = [1 - (1-a)^{1/n}]\ [N - \frac{(n-1)}{2}]$$

Sensitivity = p(T+|D+) = a/(a+c)

Specificity= p(T-|D-) = d/(b+d)

Predictive value of a positive test = p(D+|T+) = a/(a+b)

Predictive value of a negative test = p(D-|T-) = d/(c+d)

P = (a+c)/(a+b+c+d)

Accuracy = (a+d)/(a+b+c+d)

$$p(D+) = \frac{p(T+) - p(T+ \mid D-)}{1 - [p(T+ \mid D-) + p(T- \mid D+)]}$$

$$TP = \frac{AP + spec - 1}{sens + spec - 1}$$

$$s^2 = \frac{1}{n-1} \sum_{i=1}^{k} a_i^2\ f_i - \frac{\left(\sum_{i=1}^{k} a_i f_i\right)^2}{n(n-1)}$$

$$Kappa = \frac{P(agreement) - P(agreement\ by\ chance)}{1 - P(agreement\ by\ chance)}$$

$$FV_n = P(1 + I)^n$$

$$PV = Fv_n) (l + r)^n$$

$$PV = \frac{A_1}{(1+r)} + \frac{A_2}{(1+r)^2} + \ldots + \frac{A_n}{(1+r)^2}$$

$$= \sum_{t=1}^{n} \frac{A_t}{(1+r)^t}$$

$$PV = A [(1 + r)^n - 1]/[r(1 + r)^n]$$

$$NPV = \sum_{t=1}^{n} \frac{B_t - C_t}{(1+r)^t}$$

$$\frac{B}{C} = \frac{\sum_{t=1}^{n} B_t / (1+r)^t}{\sum_{t=1}^{n} C / (1+r)^t}$$

$$AF_E = \frac{P(D+|E+) - P(D+|E-)}{P(D+|E+)}$$

$$= \frac{AR}{P(D+|E+)} = \frac{AR}{a/(a+b)}$$

$$AF \approx \frac{OR - 1}{OR}$$

End of paper