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'Instructions for authors' were published in the June 1998 issue. They can be found in <http://www.farmwide.com.au/nff/vetasscn/aboutava/instruct.htm>.

'Statistical guidelines for authors' were published in November 1997. They can be found in <http://www.farmwide.com.au/nff/vetasscn/aboutava/statguid.htm>.

What constitutes freedom from disease in livestock?

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The occurrence of livestock disease is a major impediment to the movement of animal commodities both within and between countries. The formation of the World Trade Organisation (WTO) and the signing of the Agreement on the application of sanitary and phytosanitary measures (SPS Agreement) have begun the worldwide process of reduction of tariff barriers to agricultural trade. One notable result has been heightened scientific interest in evaluating and managing the risks of spread of disease between countries through the movement of livestock commodities. Improved analysis of the import risks requires complementary improvements to the quality and quantity of animal health data, on which this analysis is based.

International developments have led to local changes, which have been supported by the worldwide acceptance of disease zoning within a country, as advocated by the International Animal Health Code of the Office International des Épizooties (OIE). With zoning, health status can be established in a defined location within a country, provided that appropriate veterinary infrastructure exists and is capable of maintaining the difference in health status between adjacent areas. As a result, public veterinary services are concentrating on activities, which substantiate the animal health status of both farms and zones. For this purpose, the primary unit of diagnostic interest is usually the entire herd of animals (or flock or some other aggregate which can be assumed to be mixing randomly). However, it is interesting to note that consumers are increasingly demanding assurance of the wholesomeness and safety of individual cuts of meat. To be able to assure this, we would need to know the life history of individual animals. Thus over the longer term, there may be a return to the individual animal as the unit of interest for public veterinary services. This has already happened in some countries, which have developed national systems of identification of individual cattle. The systems include records of parentage, movements among farms, health status and treatments applied. Exporting countries such as Australia are moving to address the issue of identifying individual animals, but face substantial challenges mainly because of extensive grazing systems.

In principle, accreditation of freedom from a particular disease either at the farm, zone, national or regional level is possible when there is no clinical, epidemiological or other evidence of the disease or its agent over a reasonable period of time, consistent with an understanding of its natural history and epidemiological characteristics. To support such accreditation, a credible surveillance system based on a knowledge of the natural history, modes of transmission and spread of the disease as well as the adequacy of diagnostic methods must be in place. Because of its variable quality, a self-reported history is no longer regarded sufficient. Increasingly, other forms of evidence of freedom from disease are being used, such as screening representative samples of animals and herds. If screening gives suspicious results, further investigation usually follows.

A significant problem with screening tests, such as serological assays, is that they are imperfect in their ability to differentiate the animals that have the disease from those that do not. In other words, there is always the possibility of false positive and false negative results. This problem is compounded when a herd is to be classified as diseased or not, based on the results of screening a sample of animals rather than all individuals in the herd.

When testing individual animals, the factors which affect the interpretation of test results are the sensitivity and specificity of the test; and the pre-test likelihood of disease. For screening purposes, whenever an animal is selected at random from a group, the pre-test likelihood of disease is equivalent to the true prevalence of disease in the group. When testing herds, the factors that affect the interpretation of test results are sensitivity and specificity of the test at the individual animal level, the number of animals tested from the herd in question, the prevalence of the disease of interest in the herd, the total number of animals in the herd, and the number of reactors (1, 2, 3 and so on) used to

classify the herd as positive for the presence of the disease.

Consequently, it is worth noting in regard to screening herds:

1. As the number of animals tested from a particular herd increases, herd-level sensitivity increases.
2. As the number of animals used to classify the herd as positive is increased, there is a corresponding increase in specificity.
3. As herd-level sensitivity increases, herd-level specificity decreases and vice versa.
4. Individual and herd level screening test characteristics are not equivalent.
5. If specificity of the test at the individual animal level is perfect (100%), then all non-infected herds will be correctly classified as not diseased, that is, herd-level specificity also equals 100%.
6. However, the converse is not true when only a sample of animals from a herd is tested. Even if a test has perfect sensitivity when an individual animal is tested, some herds containing animals with the disease will be incorrectly classified as free from disease, that is, herd level-sensitivity will be less than 100%.

A diagnostic conundrum arises when imperfect tests are used to examine a sample of individual animals and to make a decision about the herd status:

1. No reactors are found in the animals chosen for testing – is the herd infected or not?
2. A small number of reactors is found – is the herd infected or not?

Traditionally, veterinarians have been comfortable in accepting a herd as not infected in the first instance mentioned above. However, we have been reluctant to accept the probabilistic evidence, that in many cases with imperfect tests, a small number of reactors also provides excellent evidence for lack of infection.

Australian animal health experts provide considerable international leadership in gaining a better understanding of these difficult issues. The tables from Cannon and Roe's¹ booklet on livestock disease surveys are probably still the most common reference used by veterinarians to determine the appropriate number of animals to test when substantiating freedom from disease or detecting disease. However, the formulae used to derive the sample sizes displayed in these tables assume that the screening tests used have perfect sensitivity and specificity. More recently, Jordan² and Cameron and Baldock^{3,4} have developed methods of incorporating both sensitivity and specificity into the calculations. These approaches involve the use of computer

programs and provide probabilistic interpretations of results. The programs have been called 'Herdacc'² and 'FreeCalc'³ and can be used for both single-stage (where the disease status of a herd is to be ascertained by testing a number of animals) and two-stage (where there is the additional requirement of ascertaining the disease status of a zone by investigating a number of herds) sampling. Among other things, these programs can be used to calculate required sample sizes for substantiating freedom when using imperfect tests. In doing this, they provide a 'cut-point' number of reactors (CNR) which is the maximum number of reactors that could be expected in the sample if the herd was not infected given the assumptions made. Where test specificity is 100%, the CNR will always be zero, but where specificity is imperfect, the CNR will be greater than zero.

These evolving methods for substantiating freedom from disease are now being incorporated into the design of surveillance programs for animal health. At present, the Johne's disease market assurance programs for cattle, sheep and alpaca in Australia use sample sizes based on similar formulae but with the assumption of perfect specificity. Unfortunately, the screening tests used for Johne's disease have a poor and variable sensitivity, when individual animals are tested. Consequently, when used to assess herds, large numbers of animals need to be tested to ensure a reasonable confidence in the findings. This is expensive and is a disincentive to participation for many producers.

The concept of using additional information to reduce the number of animals required for testing in any particular herd is being investigated in Australia. For example, if animals in poor condition are chosen for screening, fewer animals may be required to give the same level of confidence regarding the Johne's disease status in a sheep flock.

The challenge ahead is to maintain well-considered and thorough evaluations of the different options, which aim to reduce the cost of assessing the status of herds, but maintain a high level of confidence in the results.

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