Designing serological surveillance programmes to document freedom from disease with special reference to exotic viral diseases of pigs in Denmark

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Summary
Surveillance programmes based on laboratory screening tests are increasingly used to document freedom from disease in order to facilitate trade. The following aspects must be considered when designing such programmes: diseases to be selected; epidemiology of the diseases; unit of analysis (animal or herd); target age group (or target farm type); test characteristics and sample size. Issues related to these aspects are discussed and illustrated using the example of serological surveillance for exotic viral diseases in the pig population of Denmark. Sampling designs based on individual animal samples are compared with herd-based sampling (two-stage sampling). While the latter is likely to require a larger sample size, the increased level of information and the reliability of the results obtained are considered to be worth the expense. Issues related to the development of international standards for declaring freedom from disease are discussed. The authors conclude that international standards are desirable, providing that these standards represent scientifically valid principles.

Keywords

Introduction
In 1995, the World Trade Organization (WTO) was established and the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) was reached (23). The majority of countries actively trading animals and animal products are members of the WTO. The essential principle of the SPS Agreement is that preventive measures related to a trade event are only justifiable if negative health implications are expected for human, animal or plant populations in the importing country (23). Decisions regarding the measures taken need to be based on international standards or a scientific assessment of the risk. In the case of trade in animals and animal products, a risk assessment includes the assessment of the animal health status of both the importing and exporting country (1), with the emphasis on any differences between the two. Of particular interest is the situation where the animal health status of the importing country is higher than that of the exporting country.

To be able to assess the health status of an animal population, surveillance data are required. Surveillance is defined as the continuous investigation of a given population to detect the occurrence of disease or infection for control purposes (19). Therefore, surveillance is always part of a disease control programme. For exotic diseases, the threshold value is
Designing a serological surveillance system

Selection of diseases
As serological surveillance requires considerable resources, the selection of diseases to be surveyed must be based on economic and risk considerations. Sabirovic et al. suggested using a decision tree for selecting diseases to be considered in a risk analysis context (20). A similar tree can also be applied when selecting diseases for surveillance programmes (Fig. 1). The principle of this method is that the need for surveillance depends on a series of characteristics of the diseases under consideration. Risk is defined as the likelihood of the occurrence of an adverse event and the magnitude of the consequences of this event (1, 19). Therefore, the characteristics considered should include the following:

a) the probability of introduction of an exotic disease into the country (e.g. occurrence in neighbouring countries, occurrence in countries that are trade partners)

b) the consequences of the introduction (e.g. impact on trade, impact on production).

The decision criteria can be arranged in a decision tree to guide the decision process. The advantage of this method is that the decision is made transparent and consistent. In Figure 1, the decision regarding surveillance is based on the occurrence of the disease agent, the economic implications regarding trade and domestic production, the clinical disease picture and serological test availability. If a disease is identified to be of significance, but no eradication strategy is officially in place, the decision regarding surveillance ends with the outcome 'inconclusive', as surveillance needs to be part of a strategic plan. In this case, further discussions to define the control status of the disease are recommended. The decision tree drafted in Figure 1 represents a risk-based approach to identify diseases for surveillance programmes.

Unit of analysis
As testing every individual animal in a population is usually unfeasible, a sampling procedure is typically applied for surveillance purposes. As livestock populations often occur in clusters (i.e. individuals are gathered in flocks or herds), the sampling unit can either be the individual animal or the next higher unit, e.g. the herd.

Traditionally, individual animal sampling has been widely used. This approach assumes that each animal in a region or country has the same probability of being exposed to the exotic agent after a new introduction of disease. The appeal of this approach may be partly due to practical considerations. For example, sampling a fixed proportion of slaughtered animals at the abattoir, regardless of the herds of origin, is convenient. In addition, a sampling frame for herds (complete herd register) may not be available in some countries. A disadvantage of using the individual animal as the unit of analysis is that, after the survey, no statement can be made regarding the status of individual herds. The survey will reveal the status of the region or country as a whole, for which the tested individuals are representative, but the clustered occurrence of disease within a population is not taken into account. Sampling of individual animals is nevertheless popular because a relatively small sample size is required.
The alternative unit of analysis is the herd (or flock). If using this approach, the following three sampling designs are possible:

a) some individual animals are sampled from all herds

b) a sample of herds is initially selected at random, then some individuals within the selected herds are sampled (two-stage sampling)

c) a sample of herds is selected at random and all animals within these herds are tested.

Option a) is often used during an eradication process when the disease under consideration still occurs in some herds and targeted interventions are applied. Options b) and c) are used in cases where a disease has never occurred in the country or has been eradicated for a considerable time and confidence in the absence of the disease is high. For example, Switzerland switched from the use of a whole population survey to a two-stage sampling approach regarding infectious bovine rhinotracheitis and enzootic bovine leucosis, after the diseases were considered to be eradicated (21). All herd-based sampling designs require a complete sampling frame for herds (i.e. a complete herd register). Additionally, if the samples are not all collected simultaneously, a data management system is necessary to record the number of samples already collected from each herd and to store the test results.

**Target age group and type of farm**

When considering serological surveillance, certain epidemiological characteristics of the disease may justify targeting a particular age group. In principle, older animals are the unit of choice for diseases with persisting antibody titres, because older animals have a higher chance of having been exposed to the agent. However, in livestock industries with a high degree of specialisation, such as the pig industry, some farm types may never be sampled, for example, if only breeding animals are targeted. In this case, a disease could, in principle, still be circulating in farms that house only other age groups (e.g. finishing pigs).

Another approach is to apply risk-based sampling for certain farm types. The rationale behind this method is that certain
farm types represent a higher risk, either in terms of risk of exposure after a new introduction (e.g. farms that import animals) or due to a higher impact of the consequences of infection (e.g. farms at the top of the production pyramid). Therefore, greater economic benefit is gained by spending resources on these farms. This approach is also called disproportionate stratified sampling or sampling with optimal allocation (15). However, a gain can only be achieved if a large difference exists in the risk for disease occurrence between the farm strata (15). In a situation where the assumed prevalence in one stratum (low-risk stratum) is zero and in the other stratum (high-risk stratum) very low, this condition may not be fulfilled. Therefore, difficulties may arise in documenting the benefit from selecting high-risk farms, such as those located near a border.

**Sample size**

Calculations to determine the necessary sample size must be conducted using the appropriate mathematical formulae. Depending on the chosen sampling design, the formula may be more or less complex, but software is now generally available to perform the calculation (e.g. FreeCalc [http://www.ausvet.com.au/surveillance/freecalc.htm; 8, 9]; HerdTest [14]). Sample size is dependent on the prevalence of disease to be detected and the desired confidence level. Additionally, the sample size is influenced by the serological test characteristics, and if herd-based sampling is conducted, by the expected within-herd prevalence (8, 10, 16). In particular, sub-optimal test characteristics (e.g. sensitivity and/or specificity of less than 100%) have often not been adequately considered in the past.

The level of disease to be detected is a subjective value that is set according to international guidelines or requirements of trade partners. For example, the European Union (EU) has used a threshold prevalence of 0.2% of herds with respect to bovine diseases (11). The confidence level is typically set to 95%. Information on the serological test to be applied is very influential in the calculation of the sample size, but is not always readily available. At the herd level, sensitivity and specificity are not absolute measures, as they are determined by the cut-off value. The latter specifies how many positive samples are acceptable for a herd to maintain a disease-free status. Traditionally, a cut-off value of zero was used in most programmes. This means that a single positive sample is sufficient to classify a herd as 'infected'. In a situation where the prevalence is very low (or zero) and a test with a specificity of less than 100% is applied (i.e. in most cases), most positive samples will be false-positive. In practice, this problem is handled by either re-testing the sample or by initiating a detailed follow-up investigation within the herd. To avoid expensive follow-up investigations and the legally difficult consequences of misclassification of farms, a higher cut-off value may be used (7, 9, 13).

### Serological surveillance for exotic viral diseases in pigs in Denmark

#### Current serological surveillance programme

At present, the serological surveillance programme for exotic viral diseases in pigs in Denmark is based on samples of culled sows and boars. The samples are collected at slaughter. The legal target is to collect samples of 10% of culled boars and 5% of culled sows (2). A high-risk area for air-borne transmission of diseases from the south was identified in the past in South-Jutland, where samples are collected from all culled boars and 10% of culled sows. The annual number of samples is approximately 40,000. The sampling programme is currently primarily targeted at the surveillance of Aujeszky’s disease (AD), but a sub-sample of all samples is also tested for other disease agents (Table I). Approximately 18,000 pig farms operated in Denmark in 1998, with a total of about 11.5 million pigs (5).

#### Table I

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of samples analysed within the routine surveillance programme for exotic diseases in Denmark, 1998 (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aujeszky’s disease</td>
<td>42,545</td>
</tr>
<tr>
<td>Classical swine fever</td>
<td>28,073</td>
</tr>
<tr>
<td>Porcine epidemic diarrhoea</td>
<td>3,250</td>
</tr>
<tr>
<td>Swine vesicular disease</td>
<td>3,210</td>
</tr>
<tr>
<td>Transmissible gastro-enteritis</td>
<td>43</td>
</tr>
</tbody>
</table>

*sub-sample of samples collected for Aujeszky’s disease surveillance

### Alternative serological surveillance designs

All viral diseases on the OIE Lists A and B were considered (19). Additionally, some emerging diseases with a potential animal or public health impact were included (Table II). Using the approach suggested in Figure 1, the following diseases were selected as candidates for serological surveillance in the pig population in Denmark (only viral diseases are considered here): CSF, AD, transmissible gastro-enteritis (TGE) and porcine epidemic diarrhoea (PED), assuming that an eradication strategy would be adopted for the latter. These are the diseases which are included in the current programme, except for swine vesicular disease (SVD), for which the outcome ‘clinical surveillance’ was reached. Due to the possible weakness of clinical signs and the trade significance of SVD, this disease was nevertheless included in the following calculations.

Porcine reproductive and respiratory syndrome also qualified for serological surveillance according to this scheme. A
Table II
Outcome of disease classification using decision tree

<table>
<thead>
<tr>
<th>Agent/disease</th>
<th>Endemic</th>
<th>Strain difference</th>
<th>Susceptible population</th>
<th>Wildlife reservoir, vector</th>
<th>Impact on trade</th>
<th>Impact on production</th>
<th>Disease present in Europe</th>
<th>Disease present in non-European trade partners</th>
<th>Eradication strategy</th>
<th>Acute clinical disease picture</th>
<th>Detectable at slaughter</th>
<th>Serological test system available</th>
<th>Control programme for endemic disease</th>
<th>Method of surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>African swine fever (a)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Clinical surveillance</td>
<td>Serological surveillance</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Aujeszky’s disease (b)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blue eye (paravipervirus) (c)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Classical swine fever (a)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foot and mouth disease (c)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Getah (togavirus) (c)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis E virus (c)</td>
<td>?</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Porcine epidemic diarrhoea (c)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Porcine enteric calicivirus (c)</td>
<td>?</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Porcine reproductive and respiratory syndrome (c)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Inconclusive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabies (c)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No surveillance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swine retrovirus (c)</td>
<td>?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No surveillance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swine vesicular disease (c)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No surveillance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teschen disease (enterovirus) (c)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No surveillance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmissible gastro-enteritis (c)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No surveillance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vesicular stomatitis (c)</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No surveillance</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a) OIE List A disease
b) OIE List B disease
c) Emerging disease
d) ? = unknown
e) Serological surveillance is always in addition to clinical surveillance
f) At present, no official eradication strategy is in place for porcine epidemic diarrhoea. However, the pork industry would be likely to adopt an eradication strategy, should the disease be diagnosed.
serological surveillance programme that is run by the pork industry is currently in place in Denmark. The disease is not exotic and is therefore not discussed further in this paper.

For each selected disease, a calculation of sample size was conducted for both individual-based and herd-based sampling.

**Individual-based sampling**
Assuming a threshold prevalence of 1% at individual animal level as the target prevalence of disease to be detected, and using estimates of test sensitivity and specificity obtained from laboratory experts and the literature, the number of individual animals to be tested was calculated using FreeCalc (8, 9) (Table III).

**Herd-based sampling**
Assuming a threshold between-herd prevalence of 1% as the target level of disease to be detected, and requesting a herd-level sensitivity and specificity of 0.95 and 0.99, respectively, the number of herds to be sampled was estimated to be 1,735 with a cut-off of 24 (type 1 error = 0.05; type 2 error = 0.05; number of farms = 18,000 [5]; FreeCalc software).

The estimates for serological test sensitivity and specificity were as described above. Additionally, estimates for the within-herd prevalence were obtained from experts and from the literature. With these input values, the sample size and cut-off values at herd level were calculated (Table III, FreeCalc software). The total number of samples to be analysed was obtained by multiplying the number of samples required per herd by the number of herds to be tested.

Risk-based sampling of certain herd types was also considered. For example, a surveillance programme including all farms that sell breeding stock and semen was discussed. However, this argument was based on availability of sample material, rather than statistical calculations, because serum samples are already collected on a regular basis from these farms for surveillance of other diseases (e.g. porcine respiratory and reproductive syndrome, respiratory diseases, *Salmonella enterica*). Risk-based sampling with respect to other farm characteristics, such as location or pig density in the area, would require a herd register that included these factors. This is currently not available in Denmark, as the herd register used is based on more simple data. This option was therefore not considered further.

**Comparison of sampling designs**
The number of individual samples analysed under the current surveillance programme allows the detection of a prevalence as low as 1%, with 95% confidence, for all diseases listed in Table 1, except TGE. This was concluded by comparing the actual number of samples analysed with the sample size calculated in Table III for individual-based sampling. However, the relative weighting of the diseases, in terms of the number of samples analysed, differed significantly between Table I and Table III for individual-based sampling. The diseases that require smaller sample sizes (AD and CSF), because of higher test specificity, were sampled more intensively than the diseases that required larger sample sizes (PED, SVD).

The comparison indicated further that the number of samples analysed could be reduced considerably if individual-based sampling was selected as the method of choice in the future. However, this assumes that the animals sampled are representative of the total population and that these animals have an equal probability of being infected, should the agent be present. An attempt was made to assess the coverage of the current sampling strategy. As only sows and boars are targeted, no farms that have only slaughter pigs are covered. These farms account for approximately 30% of all herds in Denmark (5). With regard to the farms with sows and boars, the sample also appeared to be biased towards larger herds and herds selling breeding animals (data not shown).

### Table III
**Input parameters and results of sample size calculations for serological surveillance of five exotic viral pig diseases in Denmark**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Sensitivity of serological test</th>
<th>Specificity of serological test</th>
<th>Individual-based sampling</th>
<th>Herd-based sampling</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of samples to be tested (a,b)</td>
<td>Cut-off (c)</td>
<td>Within-herd prevalence</td>
<td>Samples per herd (a,d)</td>
</tr>
<tr>
<td>Aujeszky's disease</td>
<td>0.99</td>
<td>1.00</td>
<td>301</td>
<td>0</td>
</tr>
<tr>
<td>Classical swine fever</td>
<td>0.99</td>
<td>1.00</td>
<td>301</td>
<td>0</td>
</tr>
<tr>
<td>Porcine epidemic diarrhoea</td>
<td>0.99</td>
<td>0.99</td>
<td>1,841</td>
<td>23</td>
</tr>
<tr>
<td>Swine vesicular disease</td>
<td>0.99</td>
<td>0.99</td>
<td>1,841</td>
<td>23</td>
</tr>
<tr>
<td>Transmissible gastro-enteritis</td>
<td>0.70-0.80</td>
<td>0.95-0.90</td>
<td>20,496-46,300</td>
<td>2,119-7,070</td>
</tr>
</tbody>
</table>

b) assumptions: target threshold prevalence of disease to be detected = 1%; population size = 11,560,000; type 1 error = 0.05; type 2 error = 0.05
c) cut-off = maximum number of positive samples allowed for the country to maintain non-infected status
d) assumptions: herd size n = 1,000; type 1 error = 0.05 (herd-level sensitivity); type 2 error = 0.01 (herd-level specificity)
e) cut-off = maximum number of positive samples allowed for a herd to maintain non-infected status
f) assumptions: target threshold herd prevalence = 1%; population size = 18,000; type 1 error = 0.05; type 2 error = 0.05; number of herds to be tested = 1,735
Comparison of the individual-based sampling with the herd-based sampling design (Table III) demonstrated that the number of samples required for individual-based sampling was approximately ten times smaller than that required for herd-based sampling, as long as the test sensitivity and specificity was high. However, if test performance was sub-optimal (see data for TGE in Table III), the number of samples required for individual-based sampling increased rapidly. Furthermore, Table III shows that the within-herd prevalence was highly influential on the number of samples required per farm when using herd-based sampling. For example, the serological tests for AD and CSF perform equally well. However, the within-herd prevalence of CSF may be low and therefore, the number of samples required per farm increased from two to eleven. Furthermore, the estimates for within-herd prevalence are relatively uncertain as the estimates may be influenced by factors such as the housing system or time after infection (10).

Discussion and conclusions

A number of options are available regarding designing a survey with the objective of documenting freedom from disease. In addition, two situations can be distinguished, the first being how to obtain a disease-free status and the second being how to maintain a disease-free status. Intuitively, more rigorous designs should be applied when a disease-free status is initially declared. After the disease-free status has been confirmed repeatedly, the sampling intensity could be reduced. Audigé et al. suggested a quantitative solution for this approach, where the interpretation of a survey result includes the pre-survey probability of the country being free of the disease (7). Using this method, the reliability of a survey result increases with the number of past negative surveys. This would allow for reduced sampling activities over the years.

One of the key principles of the SPS Agreement is equivalency (23). Equivalency means that alternative risk management measures are acceptable if these measures provide the same level of health protection. In the context of serological surveillance, different sampling designs are equivalent if the designs have the same power to detect infection. Whether individual-based and herd-based programmes are comparable in this respect is arguable. If considering a country or region as a whole, the information provided by both methods seems to be similar. However, individual-based sampling is dependent on the fulfillment of underlying assumptions, which are often not realistic. In contrast, herd-based sampling provides much more detailed information, as a statement can be made at the herd level. As most livestock species are clustered in herds or flocks, using the latter as the unit of analysis appears to be more adequate. Although herd-based systems appear to be superior to individual-based systems, no simple method of quantitatively assessing the equivalence of results is currently available.

For international requirements, the tendency appears to be towards using the herd as the unit of analysis. For example, the EU uses the herd as the unit of analysis when establishing requirements for declaring a region or country free of enzootic bovine leucosis, brucellosis and leucosis (11). Similarly, the OIE defines the sampling unit for rinderpest and contagious bovine pleuropneumonia as 'a group of animals in sufficiently close contact that individuals within the group are at approximately equal risk of coming in contact with the virus if there should be an infectious animal within the group'. The text that follows states that under most circumstances, the sampling unit will be the herd, and that ideally, a unit should contain no less than 50 and no more than 1,000 animals (17, 18).

In the SPS Agreement, countries are encouraged to use international standards or guidelines whenever available. The OIE has been recognised as the relevant international organisation for establishing animal health standards (22). These standards can be published in the International Animal Health Code (19). International standards are desirable, but only if they represent scientifically defensible guidelines. Standards therefore need to be developed in a collaborative effort by epidemiologists, microbiologists and administrators. Recent academic progress in the field of sampling and survey analysis must be translated into practically applicable designs that can be included in international standards.

A few issues related to recent approaches to sample size calculations deserve special attention: for example, the suggestion that the cut-off value for classifying a herd as infected should not necessarily be zero (7, 9, 13). In other words, because of unspecific serological tests, a certain number of positive results are expected and assumed to be false-positive results. In order to avoid expensive follow-up investigations, a certain number of positive test results is thus accepted from the start. Although this suggestion is mathematically valid, Table III demonstrates that the number of (false-)positive results for TGE can be high when using a test with limited specificity. Whether such an approach would be politically acceptable on an international market is not clear. A high number of positive results would require in-depth investigations before being dismissed as false-positives, even in a country with an established disease-free status. The authors suggest that the OIE fosters discussions on such topics among Member Countries.

As a consequence of the review of the surveillance system for exotic viral diseases in pigs in Denmark, the following conclusions were reached. A herd-based surveillance system was demonstrated to have a number of advantages over an individual-based system. Although such a system is not currently available in Denmark, this was identified as a long-term goal. Similar systems are already in use in some countries of Europe. The possible reduction and re-allocation of numbers of samples tested for individual diseases will be

Discussion and conclusions

A number of options are available regarding designing a survey with the objective of documenting freedom from disease. In addition, two situations can be distinguished, the first being how to obtain a disease-free status and the second being how to maintain a disease-free status. Intuitively, more rigorous designs should be applied when a disease-free status is initially declared. After the disease-free status has been confirmed repeatedly, the sampling intensity could be reduced. Audigé et al. suggested a quantitative solution for this approach, where the interpretation of a survey result includes the pre-survey probability of the country being free of the disease (7). Using this method, the reliability of a survey result increases with the number of past negative surveys. This would allow for reduced sampling activities over the years.

One of the key principles of the SPS Agreement is equivalency (23). Equivalency means that alternative risk management measures are acceptable if these measures provide the same level of health protection. In the context of serological surveillance, different sampling designs are equivalent if the designs have the same power to detect infection. Whether individual-based and herd-based programmes are comparable in this respect is arguable. If considering a country or region as a whole, the information provided by both methods seems to be similar. However, individual-based sampling is dependent on the fulfillment of underlying assumptions, which are often not realistic. In contrast, herd-based sampling provides much more detailed information, as a statement can be made at the herd level. As most livestock species are clustered in herds or flocks, using the latter as the unit of analysis appears to be more adequate. Although herd-based systems appear to be superior to individual-based systems, no simple method of quantitatively assessing the equivalence of results is currently available.

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As a consequence of the review of the surveillance system for exotic viral diseases in pigs in Denmark, the following conclusions were reached. A herd-based surveillance system was demonstrated to have a number of advantages over an individual-based system. Although such a system is not currently available in Denmark, this was identified as a long-term goal. Similar systems are already in use in some countries of Europe. The possible reduction and re-allocation of numbers of samples tested for individual diseases will be
discussed further. It was also noted that the current programme does not cover the entire pig population, but only the herds with breeding pigs. Although the high number of samples probably compensates for the limitations of the sampling method, efforts will be directed at improving the coverage of the sample.

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Conception de programmes de surveillance sérologique destinés à démontrer le statut indemne d'une maladie : l'exemple des maladies virales exotiques chez les porcins au Danemark


Résumé
Les programmes de surveillance basés sur des tests de dépistage en laboratoire sont de plus en plus utilisés pour démontrer l'absence d'une maladie et faciliter les échanges. Lors de la conception de tels programmes, il convient de prendre en considération les éléments suivants : les maladies à sélectionner ; l'épidémiologie de ces maladies ; l'unité d'analyse à considérer (animal ou troupeau) ; le groupe d'âge cible (ou type d'élevage cible) ; les caractéristiques du test et la taille de l'échantillon. Les auteurs traitent de ces différents aspects en prenant l'exemple de la surveillance sérologique des maladies virales exotiques dans la population porcine au Danemark. Les schémas d'échantillonnages individuels sont comparés aux échantillonnages par troupeau (échantillonnage à deux degrés). Cette dernière méthode requiert sans doute un échantillon plus large, mais les auteurs estiment que l'information ainsi obtenue est meilleure et que la fiabilité des résultats le justifie. Les questions liées à l'élaboration de normes internationales pour l'établissement d'un statut indemne au regard d'une maladie font l'objet de la discussion. Les auteurs aboutissent à la conclusion que des normes internationales seraient souhaitables, à condition qu'elles reposent sur des principes validés scientifiquement.

Mots-clés
Concepción de programas de serovigilancia destinados a acreditar la ausencia de enfermedad: el ejemplo de las enfermedades víricas exóticas del cerdo en Dinamarca


Resumen

Para acreditar la ausencia de enfermedad y facilitar así los intercambios, se viene recurriendo cada vez más a programas de vigilancia basados en pruebas de criba realizadas en laboratorio. A la hora de concebir este tipo de programas es preciso tener en cuenta los siguientes aspectos: enfermedades que han de vigilarse; epidemiología de esas enfermedades; unidad de análisis (animal o rebaño); grupo de edad considerado (o tipo de explotación considerada); características de la prueba clínica; y tamaño de las muestras. Los autores examinan diversas cuestiones relacionadas con todos estos parámetros, ilustrándolas con el ejemplo de la vigilancia serológica de la presencia de enfermedades víricas exóticas entre la población porcina de Dinamarca. En este sentido, comparan los sistemas de muestreo individual con los sistemas de muestreo por rebaño (muestreo en dos fases). Aunque estos últimos requieren posiblemente muestras de mayor tamaño, los autores consideran justificado el esfuerzo por la mayor cantidad de información y la superior fiabilidad que proporcionan. Los autores abordan asimismo cuestiones ligadas a la elaboración de normas internacionales para declarar un territorio libre de enfermedad, concluyendo que tales normas son deseables siempre y cuando se fundamenten en principios científicamente válidos.

Palabras clave


References


