Can cELISAs be used with Different Animal Species?

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cELISAs sold by VMRD are licensed for use in defined species. For instance, the test for antibody to Anaplasma is approved for use with bovine serum samples. The cELISA will detect antibody to Anaplasma in serum from other animals including sheep and goats[1]. Further, the test should detect antibody to Anaplasma in serum from any animal species because sufficient quantities of antibody of the appropriate specificity will inhibit the binding of labeled mouse monoclonal antibody in the test and cause a positive result. The reason that the Anaplasma cELISA is not approved for use with sera from sheep and goats and other animals such as wild ruminants is that the available data is insufficient to determine the appropriate cutoff value in order to resolve positives and negatives. The cutoff for the bovine serum cELISA is 30% inhibition (i.e. samples inhibiting the binding of the labeled monoclonal antibody greater than or equal to 30% are positive; samples with less than 30% inhibition are negative).

A group of bovine samples defined as Anaplasma positive or negative by nested PCR followed by hybridization[2] were used to define a 30% inhibition cut-off which resulted in a sensitivity of 95% and a specificity of 98% (see data at www.vmrd.com). Why not use the 30% inhibition cutoff for the other animal species? It is not used because it might not be correct. Sera from defined negative cattle inhibit the binding of labeled monoclonal antibody used in the Anaplasma cELISA to some extent (from 0% to <30%). Whether sera from other animals with no antibody to Anaplasma (negative sera) always inhibit <30% is not known; they may or may not, but it is an empirical question that has not been examined in sufficient detail. Further, a determination of the ability of each infected animal species to make sufficient amounts of antibody with the appropriate specificity needs to be made in order to evaluate the sensitivity of the cELISA for that species.

The cELISA to detect serum antibody to caprine arthritis-encephalitis virus (CAEV) is licensed for use only for goats. However, in research to see if the CAEV cELISA could detect cross-reacting antibodies in sheep infected with a related virus, ovine progressive pneumonia virus (OPPV), it seemed clear that sera from CAEV negative goats inhibited binding of the labeled CAEV monoclonal antibody more than did than serum from OPPV negative sheep[3,4]. The % inhibition cutoff for the VMRD CAEV cELISA for goats is 35% to obtain high sensitivity and specificity, whereas in a research study a cutoff of 20.9% inhibition could be used in the CAEV cELISA with sheep sera to detect cross-reacting antibodies to OPPV[4]. However, more data is needed to further evaluate the sensitivity for the CAEV cELISA for use in detecting antibody to OPPV in sheep from various geographic regions.

Therefore, cutoff data needs to be obtained with serum from each animal species before using a particular cELISA. On the surface, it appears that obtaining data for determining a cutoff is easy. In fact, it requires considerable effort because a “gold standard” is needed to determine true negative and true positive status for a relatively large number of sera from different locations for use in obtaining a cutoff which results in high specificity and sensitivity.

References

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