United States Department of Agriculture
Animal and Plant Health Inspection Service

Safeguarding Animal Health

Licensing of Veterinary Diagnostic Test Kits

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Authorities, Regulations, & Guidance

- Virus-Serum-Toxin Act
  - Authorizes the regulation of the manufacture and distribution of biologics including diagnostics (test kits) intended for use in diagnosis of infectious diseases in animals

- Title 9, Code of Federal Regulations (9 CFR)

- Veterinary Services (VS) Memorandum 800.73

What is a regulated test kit?

- Complete diagnostic test kit contains:
  - All unique reagents required to run test
  - Instructions for running test
  - Instructions for interpretation of test results
  - Claims, uses, and limitations
- Used to diagnose existence of or susceptibility to potential disease causing agents in animals
- Reagents alone are not regulated

Licensing Requirements

- Diagnostic test kits should, with reasonable certainty, yield the results intended when used according to label (insert) instructions.
- The architecture, recommendations, claims, disease, animal species, sample type, and intended uses determine specific requirements.
**Prelicense Validation**

- Guidelines in VS Memorandum 800.73
- Sensitivity/Specificity
  - Test large number of known positive & negative animal samples covering a range of reactivity
  - Compare against the “gold” standard assay
- Accuracy
  - Agreement between test kit & “gold” standard
- Determine kit ruggedness
  - Compare known samples results against variations in test parameters e.g. temperature, incubation times

- No claims to quantify the results are allowed
- Evaluate in 3 laboratories
  - Serum panel (repeatability/reproducibility)
    - Precision: degree of scatter
      - Within assay
      - Between plate
      - Between assay
      - Between laboratories
  - Suitability of test kit & instructions

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**Prelicense Requirements**

- Outline of Production for review and approval
  - Master Seed concept
- Inspection of manufacturing facilities
- Manufacture of 3 prelicense serials
  - demonstrate consistency in production
  - requires confirmatory testing by CVB
- Labels and insert for review and approval

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**Sensitivity/Specificity Formula**

<table>
<thead>
<tr>
<th>Test/Gold STD</th>
<th>Infected Animals</th>
<th>Uninfected Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Positive</td>
<td>True Positive (TP)</td>
<td>False Positive (FP)</td>
</tr>
<tr>
<td>Test Negative</td>
<td>False Negative (FN)</td>
<td>True Negative (TN)</td>
</tr>
</tbody>
</table>

Specificity: \( TN/(FP + TN) \)

Sensitivity: \( TP/(TP + FN) \)

Accuracy: \( (TP + TN)/(TP + FP + FN + TN) \)

Prevalence: \( (TP + FN)/(TP + FP + FN + TN) \)

Positive Predictive Value: \( PV(+) = TP/(TP+FP) \)

Negative Predictive Value: \( PV(-) = TN/(TN + FN) \)
Intended uses impact requirements

- Herd/population status vs. individual animal tests (screening vs. confirmatory, etc.)
- APHIS Program needs
  - May have different recommendations, uses, interpretations for different populations, species, and program needs
  - Sale/distribution may be controlled by APHIS

U.S. Veterinary Biologics Permits

- Same requirements as domestic manufacturer
- Must have a U.S. based individual or corporation responsible for the permit
- Inspections of foreign manufacturer and U.S. quarantine sites
- CVB does not issue Conditional permits

Licensure

- Provides controlled production of kit components
  - Minimize variation within and between serials
- USDA evaluation of kit before and after licensure
- U.S. Veterinary Biologics License does not equal an Official test

Questions?