
 United States Department of Agriculture
 Animal and Plant Health Inspection Service




Licensing of Veterinary Diagnostic Test Kits

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Safeguarding Animal Health


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



Prelicense Validation

- ▶ 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
 - Within laboratory
 - Between laboratories
 - Suitability of test kit & instructions



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



Sensitivity/Specificity Formula

Test\Gold STD	Infected Animals	Uninfected Animals
Test Positive	True Positive (TP)	False Positive (FP)
Test Negative	False Negative (FN)	True Negative (TN)

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: $PV(-) = TN / (TN + FN)$

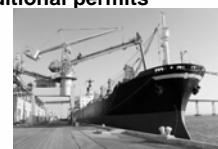
Intended uses impact requirements

- ▶ 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?

