The Impact of Commercial Testing for West Nile Virus

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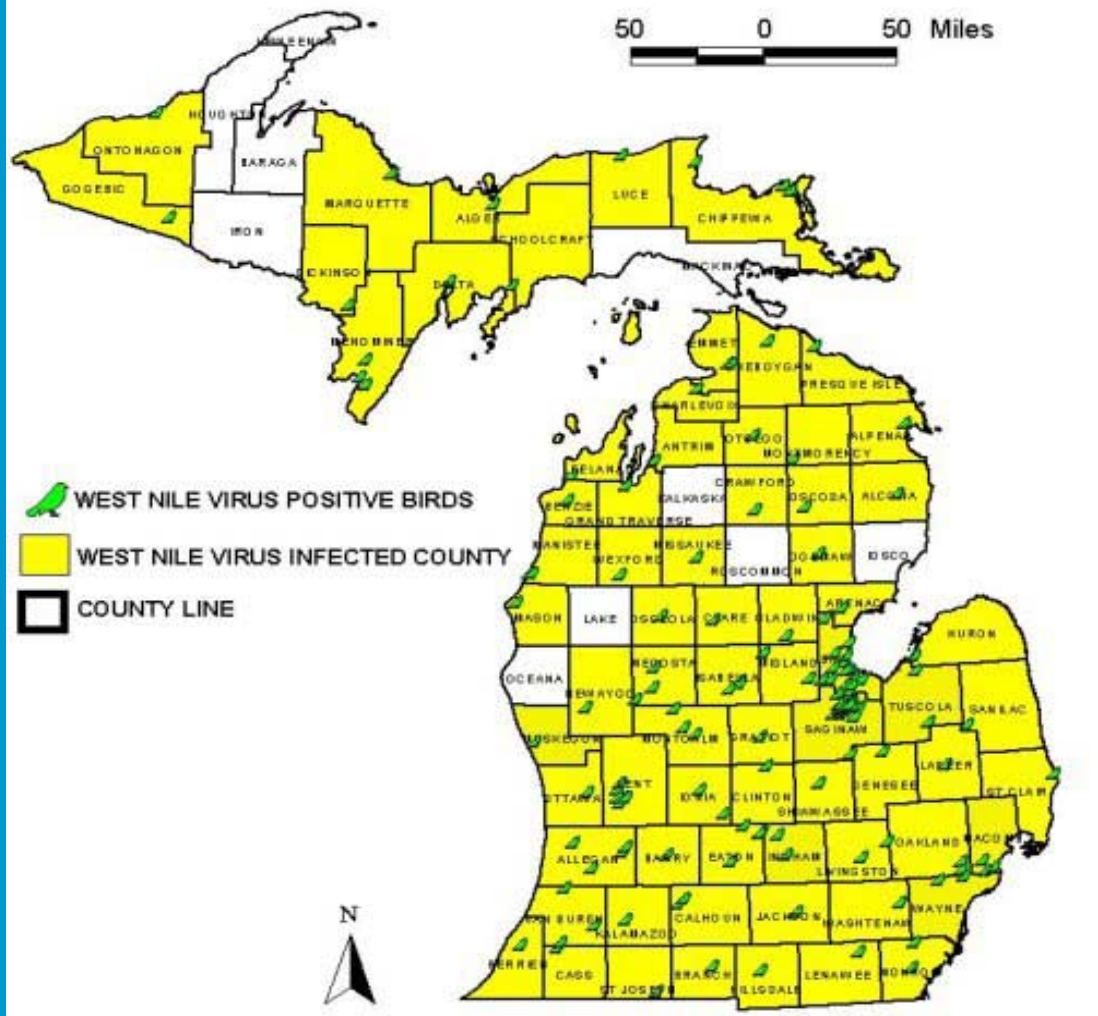
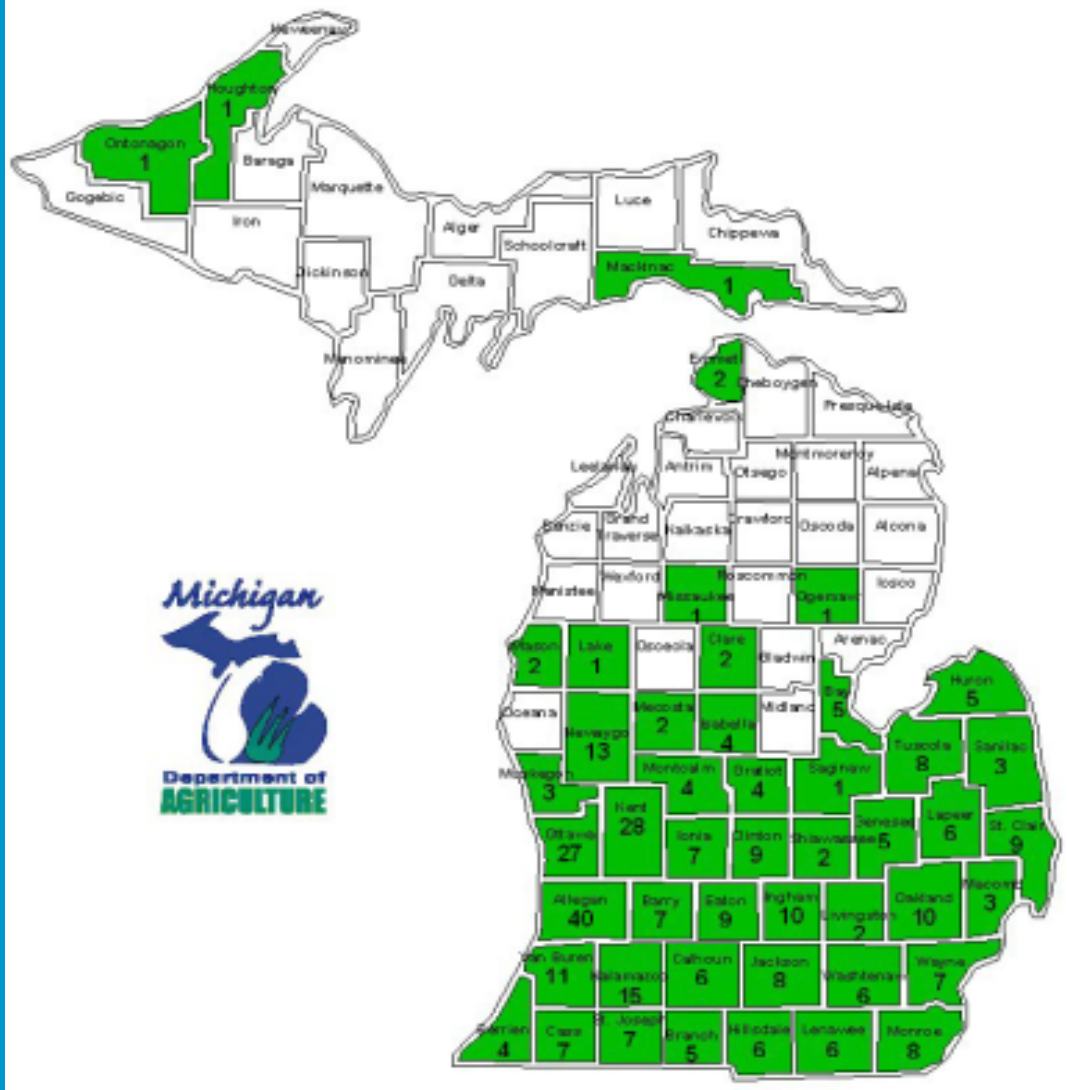
2002 WEST NILE VIRUS SURVEY RESULTS



Positive Equine WNV Counties 2002

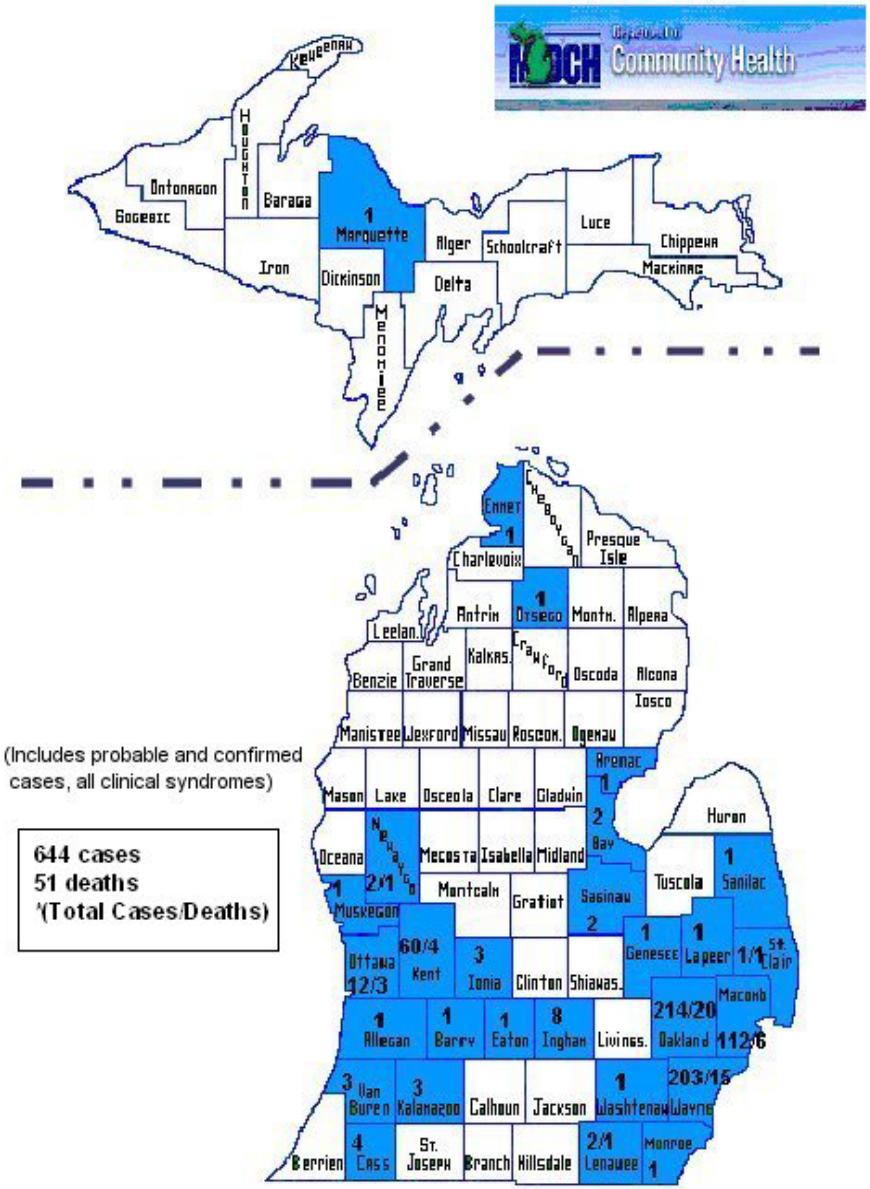
Last Updated 5 Feb 2003



■ = Counties with a positive WNV horse or other equine species (number of positive cases)

Please Note: Locations have not been verified for all of the equine cases and therefore 7 cases are not shown on the map. The total number of positive cases is 341.

2002 Lab Positive Human West Nile Virus Cases



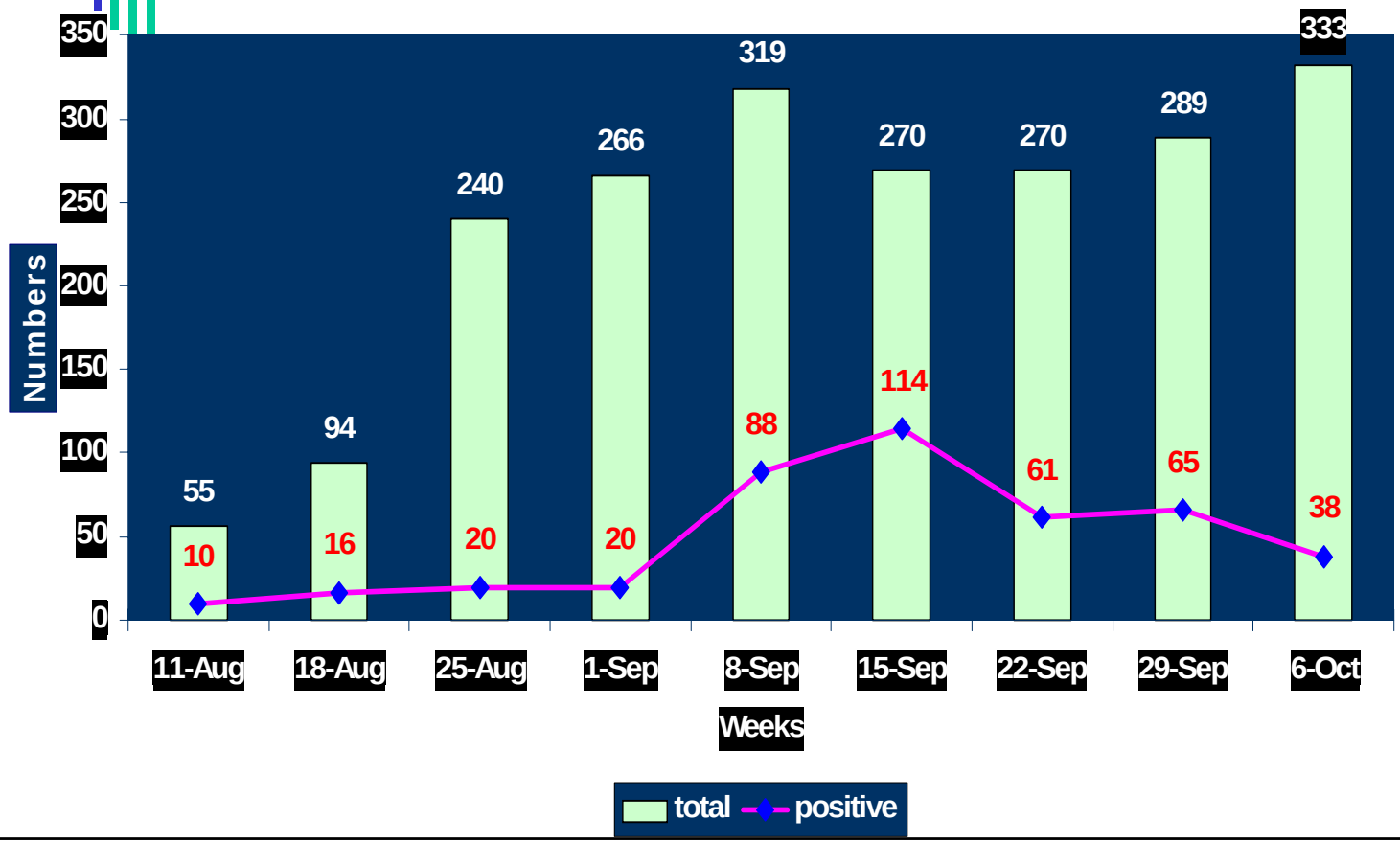
(Includes probable and confirmed cases, all clinical syndromes)

644 cases
51 deaths
*(Total Cases/Deaths)

2002 MDCH Interactions with Clinical Labs

- Blast Fax communication network heavily utilized to request:
  - 1) send CSF/sera to MDCH or
  - 2) split and retain a portion if going to commercial labs or
  - 3) ask commercial labs to forward positive samples to MDCH

Weekly WNV Testing (Aug-Oct)



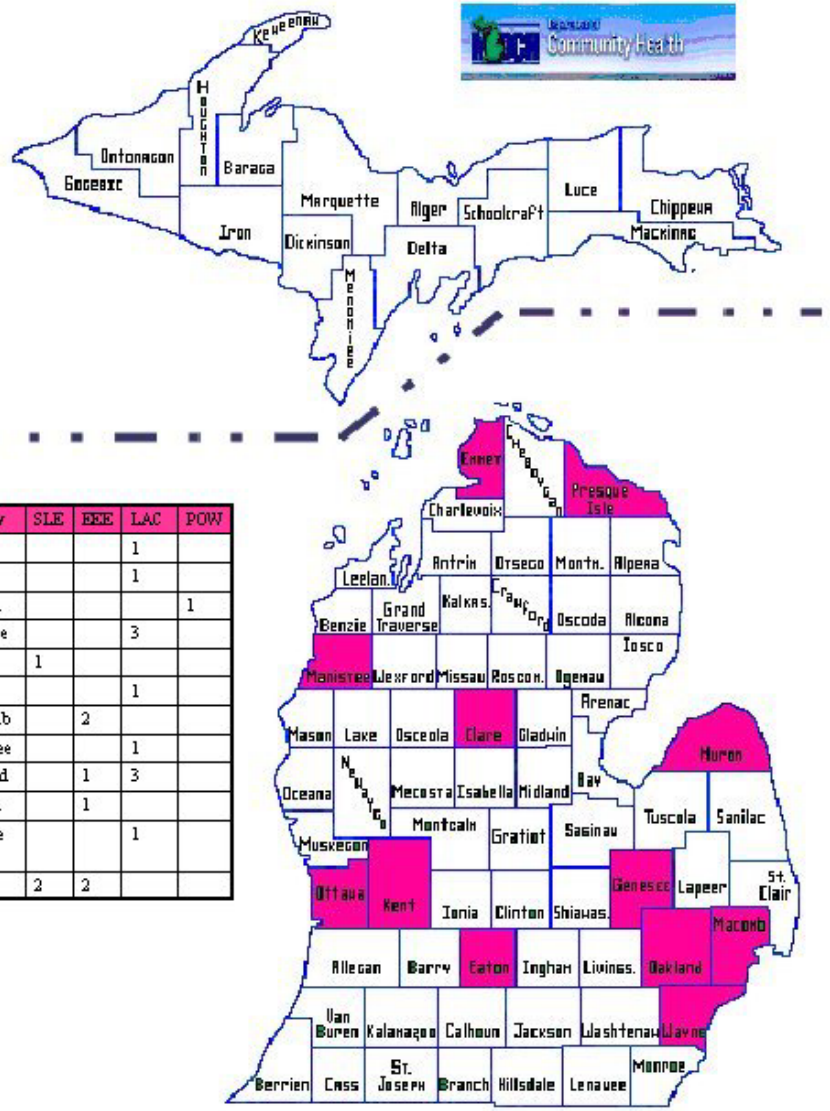
2002 MDCH Interactions with Clinical Labs, cont.

- **Later in the outbreak, because reagents supplies were limited, labs were notified by B-fax that specimen testing would be triaged, based upon patient symptoms:**
  - **CSF samples and sera from those presenting with CNS symptoms suggestive of meningitis/encephalitis would be tested first.**
  - **All other sera would be held and tested as reagent availability confirmed.**
- **This resulted in a large number of sera being sent to commercial laboratories**.

2002 MDCH Interactions with Commercials Labs

- Personal call to each commercial lab testing for WNV, requesting:
  - Forward all samples testing positive for WNV coming from MI
- Problems:
  - Some MI residents tested out-of-state
  - Some samples sent from MI labs lived outside of MI
  - Large volume of samples from many states being tested by commercial labs- a reporting/forwarding challenge

Other Arboviruses in Michigan, 2002

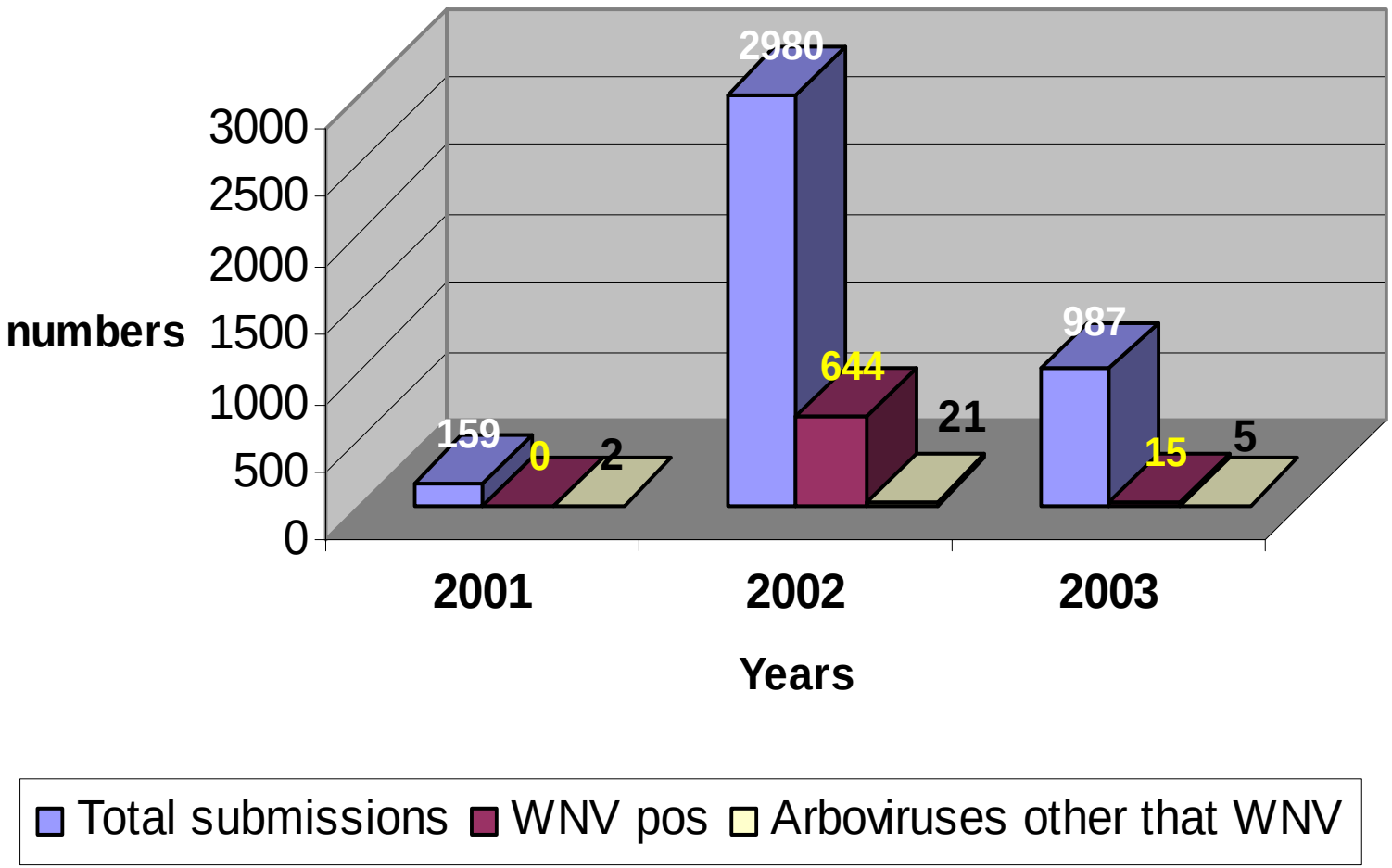


County	SLE	EEE	LAC	POW
Clare			1	
Eaton			1	
Emmet				1
Genesee			3	
Huron	1			
Kent			1	
Macomb		2		
Manistee			1	
Oakland		1	3	
Ottawa		1		
Presque Isle			1	
Wayne	2	2		

2003 MDCH WNV Preparations

- Clinical labs asked to send samples to MDCH or split samples and retain portion for later confirmation at MDCH.
- Commercial labs contacted before season with request to submit positives to MDCH for confirmation testing. Emphasized non-specific nature of screening test and need for confirmation of positive results.

Arbovirus testing 2001-03



Commercial Tests

- Pan Bio FDA Approved, uses purified native WNV Ag
- Focus, not FDA approved in 2003 season, uses CDC licensed Ag
- Both good sensitivity, eliminate negatives
- High volume of test requests cannot be managed in PH System alone; screening tests an appropriate approach, if tests are properly interpreted and appropriate confirmatory testing performed.

CDC IgM Capture ELISA

- Includes negative control for background (heterophile) Ab detection
- Run WNV and SLE Ag together
- P:N >3 = Positive
- Repeatedly reactive
- WNV at least 2x greater than SLE
- PRNT confirmation required if:
  - Newly identified WNV activity state
  - Early in season, low-unknown prevalence
  - Equivocal result

Focus WNV IgM Capture ELISA

- **INTENDED USE**

  The Focus Technologies West Nile Virus IgM Capture ELISA is intended for qualitatively detecting IgM antibodies to West Nile virus in human serum. In conjunction with the Focus Technologies West Nile Virus ELISA IgG, the test is indicated for testing **persons having symptoms of meningioencephalitis**, as an aid in the **presumptive** laboratory diagnosis of West Nile virus infection. **Positive results must be confirmed by neutralization test, or by using the current CDC guidelines for diagnosing West Nile encephalitis**.

PanBio WNV IgM Capture ELISA

- **INTENDED USE**

  The West Nile virus IgM Capture ELISA is for the qualitative detection of IgM antibodies to West Nile virus in serum as an aid in the clinical laboratory diagnosis of West Nile virus infection in patients with **clinical symptoms consistent with encephalitis**. **The PANBIO West Nile virus IgM Capture ELISA results are presumptive. Positive results must be confirmed by Plaque Reduction Neutralization Test (PRNT), or by using the current CDC guidelines for diagnosis of this disease.**

Focus & Pan Bio Assays 2003

- No negative patient control for nonspecific Ab in current package insert procedures
- Focus Laboratories did include this step in-house on positives
- PanBio developed a background subtraction procedure late in the season to improve specificity

Test Performance

		DISEASE	
		Present	**Absent**
TEST	**Positive**	True Positive (TP)	False Positive (FP)
	Negative	False Negative (FN)	True Negative (TN)

Sensitivity = TP/TP+FN

Specificity = TN/TN+FP

False Positive Rate = FP/FP+TP

False Positive Rate = FP/Total tests

PVP=TP/TP+FP

NVP=TN/TN+FN

Predictive Value

- The probability of the presence or absence of disease given the results of a test
  - PVP is the probability of disease in a patient with a positive test result.
  - PVN is the probability of not having disease when the test result is negative.
- How predictive is this test result for this particular patient?
- Determined by the **sensitivity and specificity** of the test, ***and*** the **prevalence rate** of disease in the population being tested.
- Early in season, prevalence is low or unknown

Test Performance

2% Prevalence Population 5000

Sens 99% Spec 96%

		DISEASE: Present	DISEASE: Absent
TEST	Positive	99 (TP)	196 (FP)
	Negative	1 (FN)	4704 (TN)

False Positive Rate = 196/196+99=66%

False Positive Rate = 196/5000=9.8%

PVP=99/99+196=33.6%

NVP=4704/4704+1=99.9%

APHL Survey

- # PHLabs requiring specimens be submitted for confirmatory testing 22/40
- # PHlabs that received specimens for confirmatory testing 34/40
- 405 specimens retested at PHLs using CDC ELISA procedure (using CDC or Focus Ag)
  - 201 positive
  - 204 negative
- 50% FP

Focus WNV IgM ELISA in a normal blood donor pool, flavivirus vaccination/infected serum panels and autoimmune sera

Panel	N	Focus IgM ELISA			Focus IgM ELISA with BS		
		Positive	Negative	Equivocal**	Positive	Negative	Equivocal**
Blood Donor	**236**	2 *(0.8%)*	234 *(99.2%)*	0	0	236 *(100%)*	0
Flavivirus							
JE	40	2 *(5%)*	36 *(90%)*	2 *(5%)*	2 *(5%)*	38 *(95%)*	0
Dengue	19	4 *(21%)*	10 *(53%)*	5 *(26%)*	3 *(16%)*	12 *(63%)*	4 *(21%)*
SLE	32	10 *(31%)*	21 *(66%)*	1 *(3%)*	ND	ND	ND
YF	40	0	40 *(100%)*	0	ND	ND	ND
Flavivirus Total	**131**	**16 *(12%)***	**107 *(82%)***	**8 *(6%)***			
Autoimmune							
ANA	20	1 *(5%)*	19 *(95%)*	1 *(5%)*	0	20 *(100%)*	0
RF	21	4 *(19%)*	17 *(81%)*	4 *(19%)*	0	21 *(100%)*	0
Autoimmune Total	**41**	**5 *(12%)***	**36 *(88%)***	**5 *(12%)***	**0**	**41 *(100%)***	**0**

Redesigned Pan Bio IgM ELISA

		Redesigned PANBIO WNV IgM Capture ELISA		
IFA		Negative	Equivocal	Positive
	Negative	275	3	0
	Positive	7	2	65

Relative Specificity = 275/278 = 98.9%
Relative Sensitivity = 65/74 = 87.8%

Questions for PHLs

- What testing needs to be provided by PHLs?
  - PRNT Confirmatory Testing
  - Limitations of commercial/clinical testing
- Why specifically confirm arbovirus positives?
  - Limited knowledge of community physicians
  - Value of specific surveillance to mosquito abatement programs
  - Value of specific surveillance to medical community
    - Disease specific treatment
    - Differential outcome of infections
  - Recognize emergence of new disease
  - Basis for future funding?
- What can PHL afford to do?
    - Limits of funding, staffing
    - Epidemic *vs* endemic setting


MDCH
Bureau of Laboratories