Risk Assessment for *Vibrio vulnificus*

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History of FAO/WHO Risk Assessments for Vibrio spp. in Seafood

- March 2001 – Initial meeting of drafting group
- CCFH requested Vp and Vv in raw shellfish
- Vp in raw finfish (Japan) & Cholera in warm water shrimp for export
- 4 drafting group meetings and 2 expert consultations
- Peer review and publication in 2004

Risk Assessment

- Hazard identification
- Exposure assessment
- Hazard characterization
- Risk characterization

Vv Hazard Identification

- Naturally occurring estuarine bacterium
- Warm moderately saline waters
- Three biotypes (1,2 &3)
- Wound, gastroenteritis, primary septicemia
- Preexisting chronic illness
- 50% fatality rate
- Raw Gulf Coast oysters

V. vulnificus in Gulf Coast Oysters Factors supporting risk assessment

- Consistent high reporting for septicemia
- Seasonal relationship with exposure & cases
- Dominant vehicle of transmission
- Shell storage prevents cross contamination
- Raw consumption eliminates cook variability and uncertainty

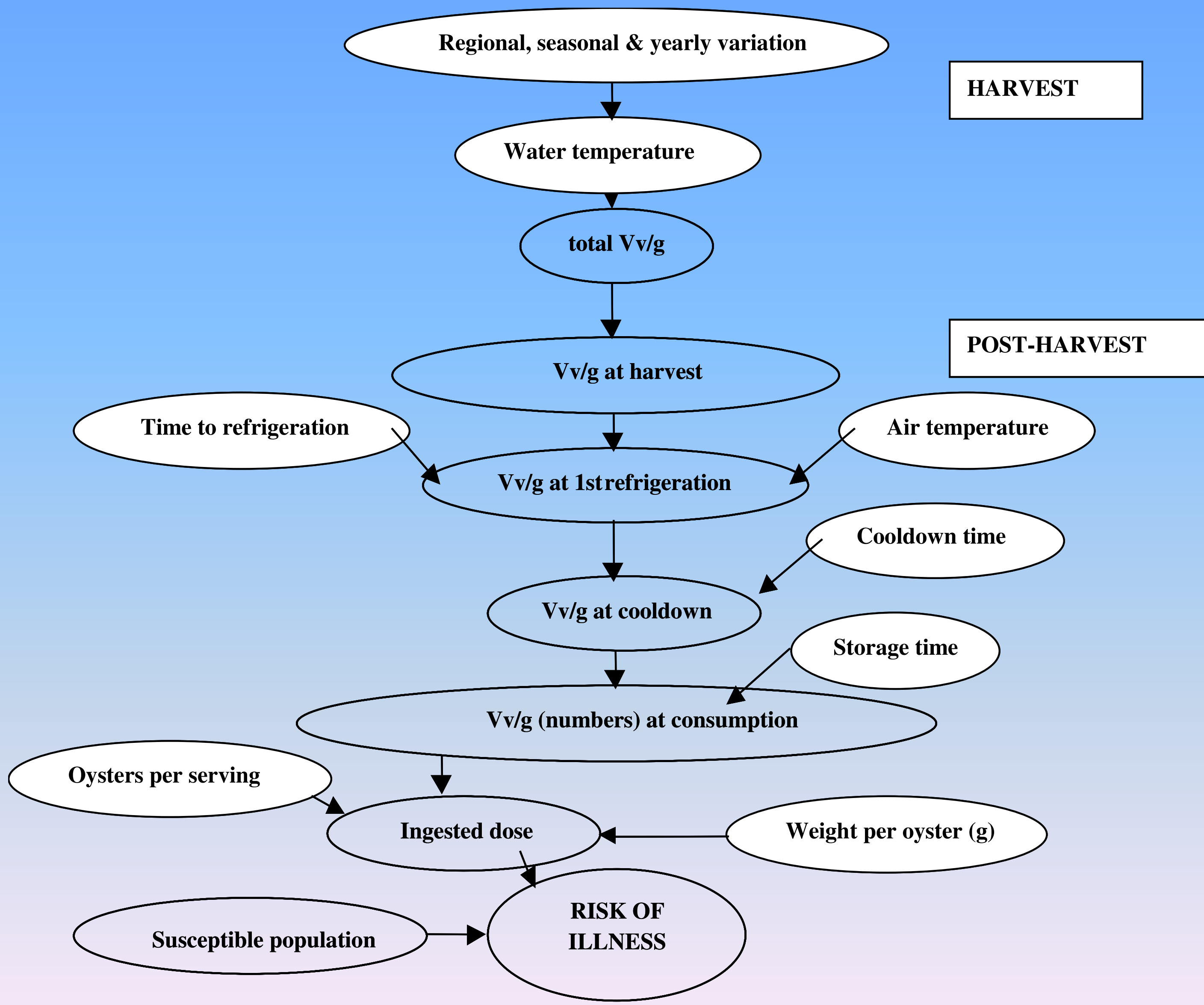
V. vulnificus in Gulf Coast Oysters Factors supporting risk assessment

- Quantitative data on *V. vulnificus* levels at harvest and consumption
- Growth and survival of natural populations in oysters
- Availability of *V. parahaemolyticus* Risk Assessment on raw oysters

Objectives

- Adapt FDA-VPRA model to assess risk of Vv in raw oysters
- Identify most appropriate data/data gaps and limitations for modeling Vv in raw oysters
- Assumptions – grounded by related data
- Conduct risk characterization of Vv in raw oysters
- Evaluate targeted mitigation levels for risk reduction for Vv illness

Conceptual *V. vulnificus* Model



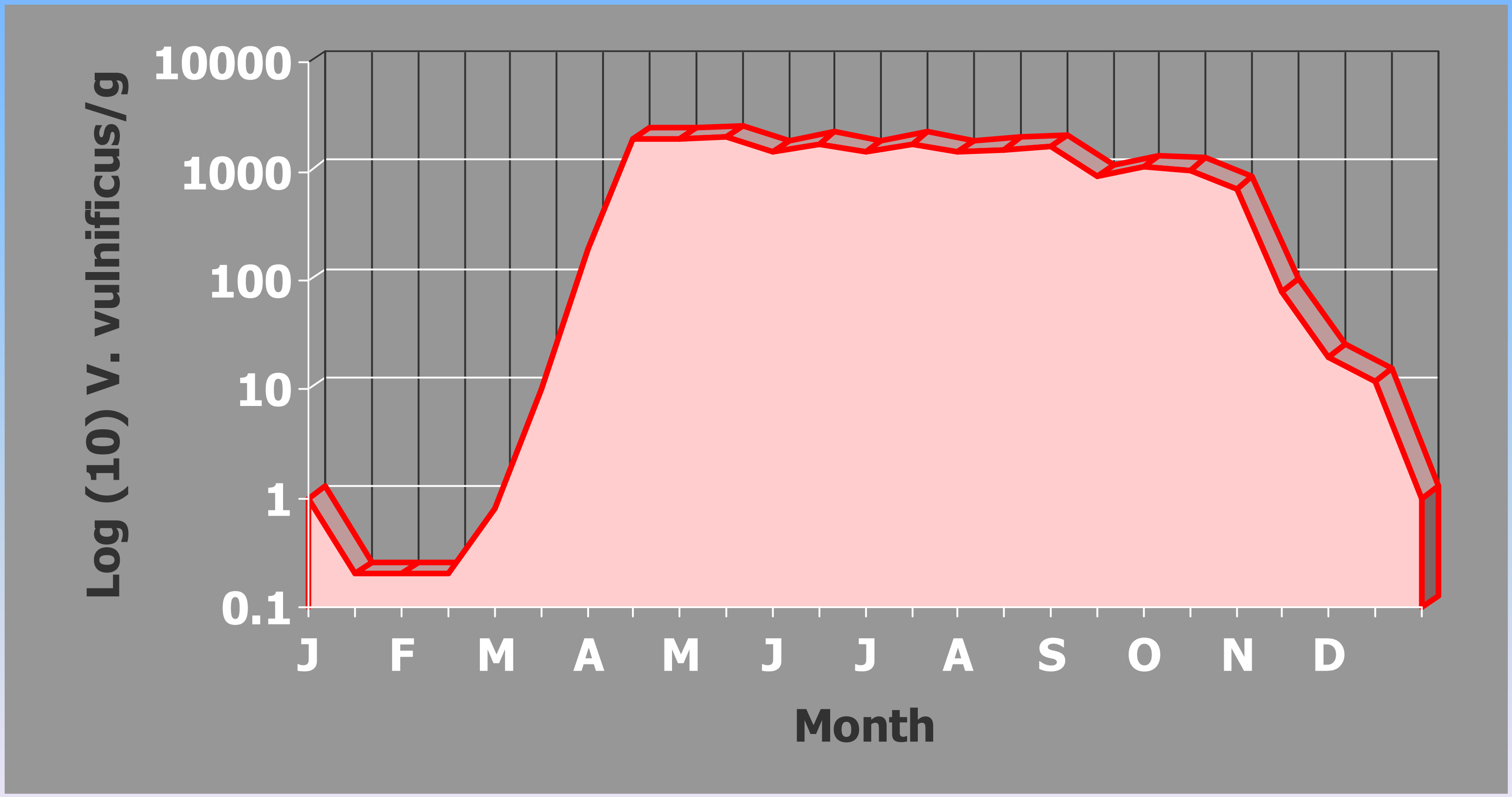
Needed Inputs

- *Exposure assessment*
  - *Vv* levels at harvest
  - % pathogenic
  - *Vv* growth rates
  - *Vv* survival rates
- Hazard characterization
  - Susceptible population
  - Dose response

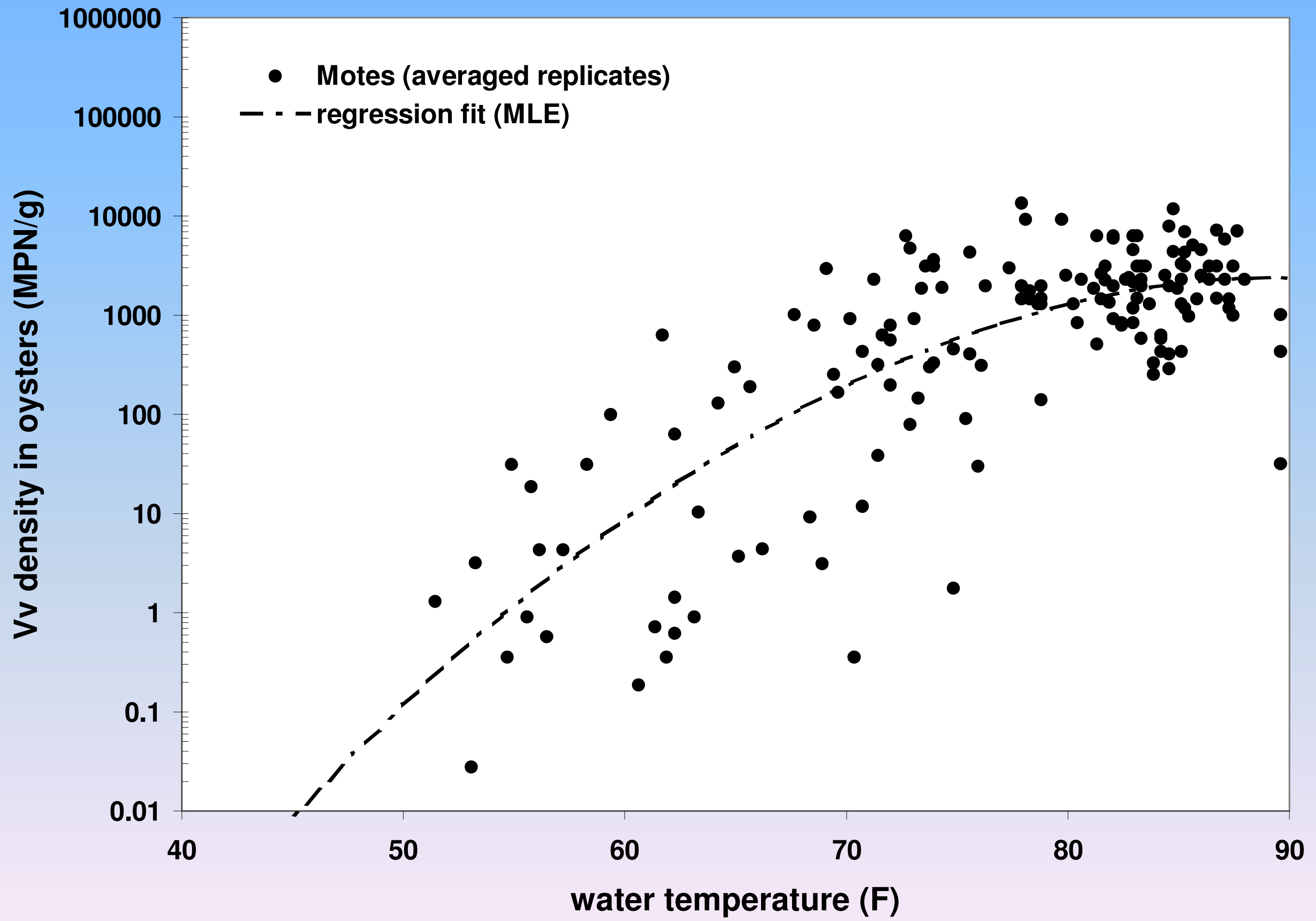
Vv at harvest

- Motes et al. 1998
  - Weekly samples (July 1994-Sept. 1995)
  - FL, AL, LA, TX
  - MPN duplicate oyster (12) samples
- Temperature
- Salinity

V. vulnificus *Densities in Gulf Coast (LA, AL, FL) Oysters at Harvest*



Effect of Temperature on Vv densities in Gulf Coast oysters



Effects of high salinity on exposure and risk

- Salinity not included in VVRA
- Effects minimal for typical Gulf Coast salinities (10-30 ppt)
- Vv levels low or nondetectable in NC & SC sites with high salinity (>30 ppt) & temp.
- High salinity areas typical in Europe, Asia, Australia and New Zealand

Effect of salinty >30 ppt in US oysters

Temperature range	Number of samples	% Vv detectable	Vv/g
<20°C (68°F)	22	41	2.8
20-25°C (68-77°F)	33	30	19.5
25-30°C (77-86°F)	30	23	2.7
>30°C (86°F)	14	36	4.2
All	99	31	8.5

Vv growth and survival in oysters

Study	Holding temperature (Celsius)	Growth rate (log10 per hr)	Assumptions/Limitations
Cook, 1997	28	0.175	Ambient air temperature varied from 24 -33, assumed average of 28 °C
Cook, 1994	18	0.025	Rate per hour assumed constant with observed average 0.75 log increase (n=5) over period of 30 hours
Kaspar and Tamplin, 1993	13		Presumed no growth temperature
Cook et al. 2002	5.7	-0.002	Range 0-16°C representative of oyster industry cooler temperatures

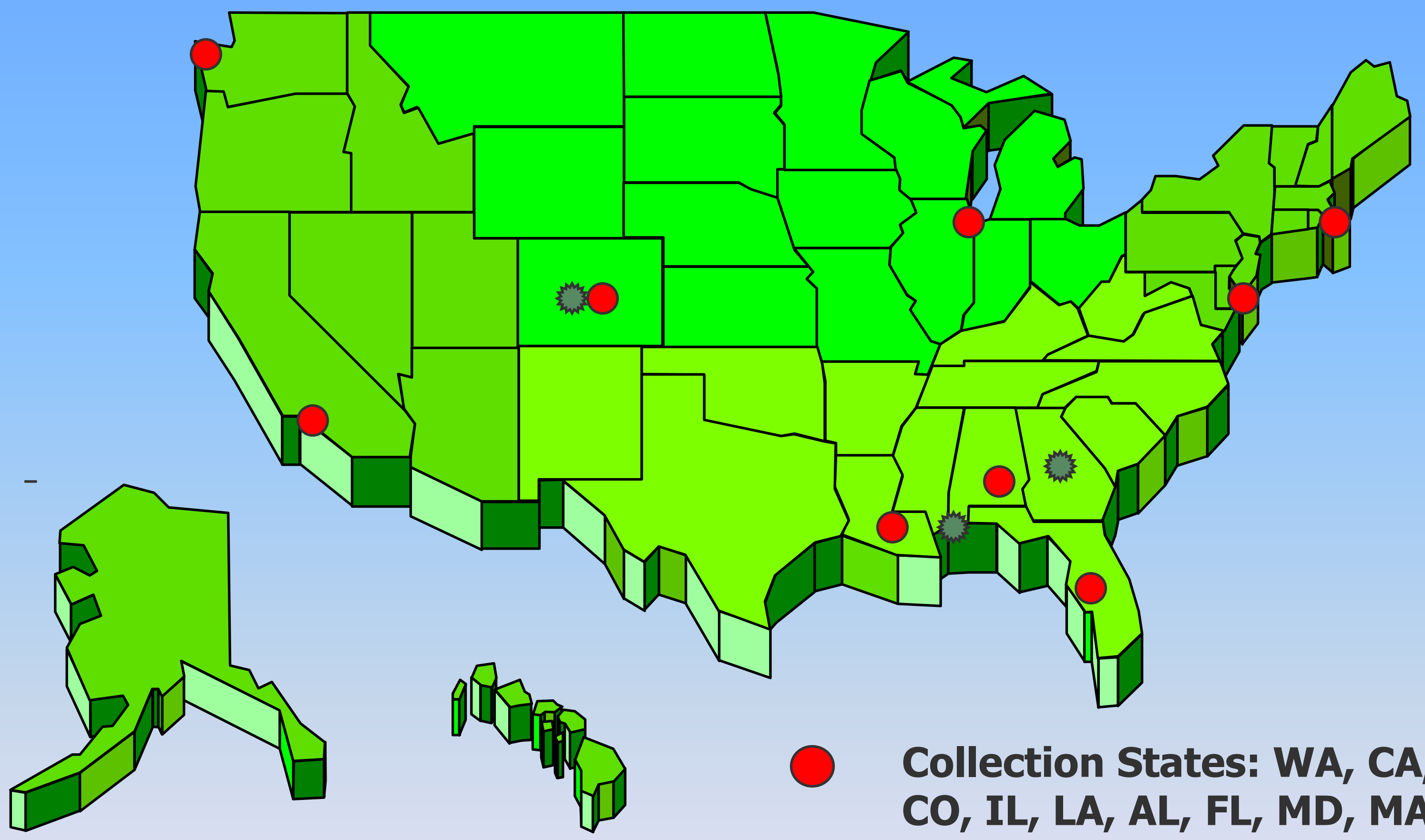
Vv/g exposure predictions

- **Summer**
- log Vv/g at harvest:
  3.27 (0.64)
- log Vv/g at 1st refrigeration:
  4.00 (0.74)
- log Vv/g after cooldown:
  4.46 (0.77)
- log Vv/g at consumption:
  4.15 (0.78)

- **Winter**
- log Vv/g at harvest:
  0.47 (1.09)
- log Vv/g at 1st refrigeration:
  0.57 (1.16)
- log Vv/g after cooldown:
  0.63 (1.21)
- log Vv/g at consumption:
  0.30 (1.22)

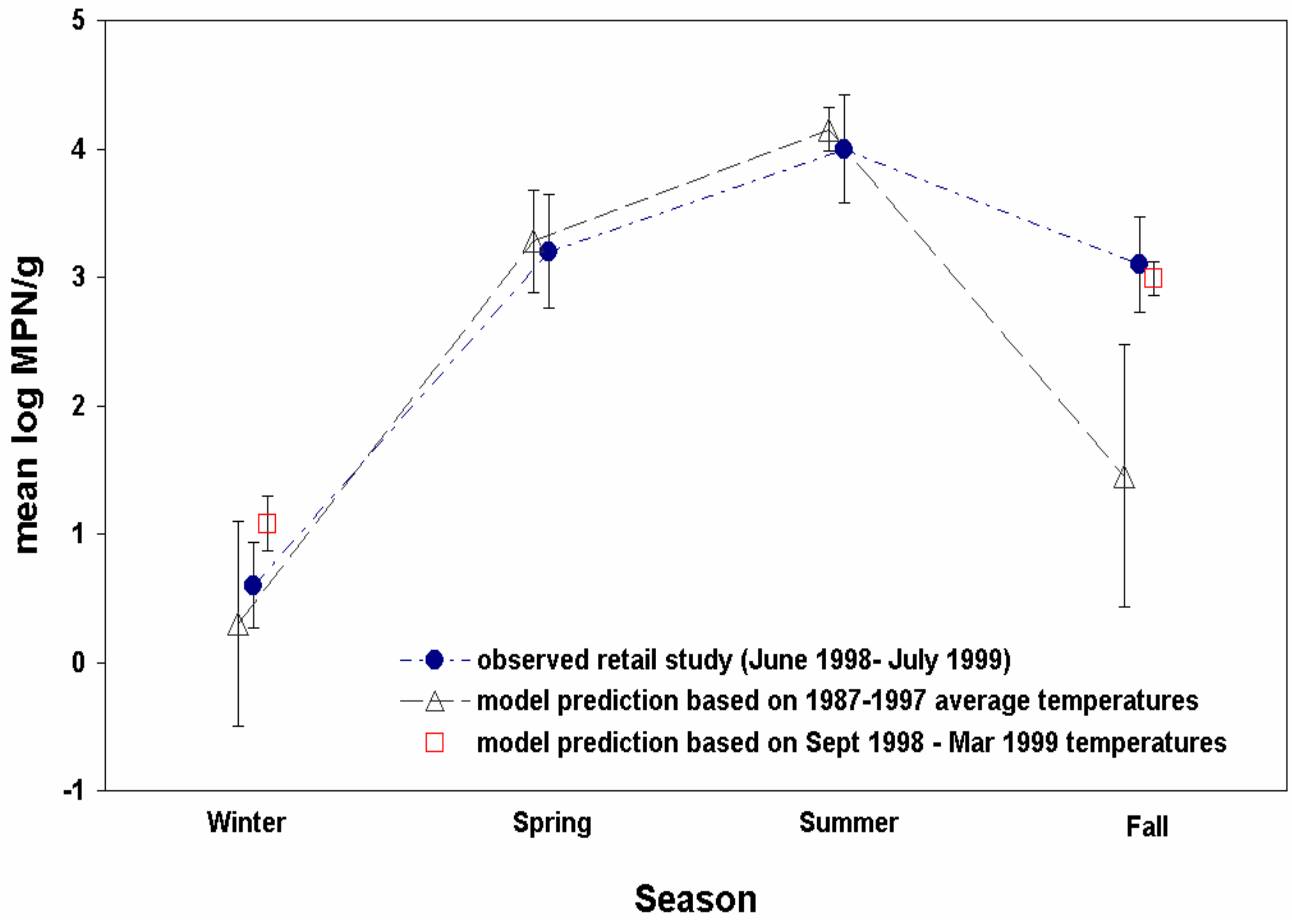
Model Validation

- Validation of model predictions against data not used in model construction
- Data available for this is Vv at consumption (retail study)



May '99

Predicted and observed levels of Vv



Hazard characterization parameters

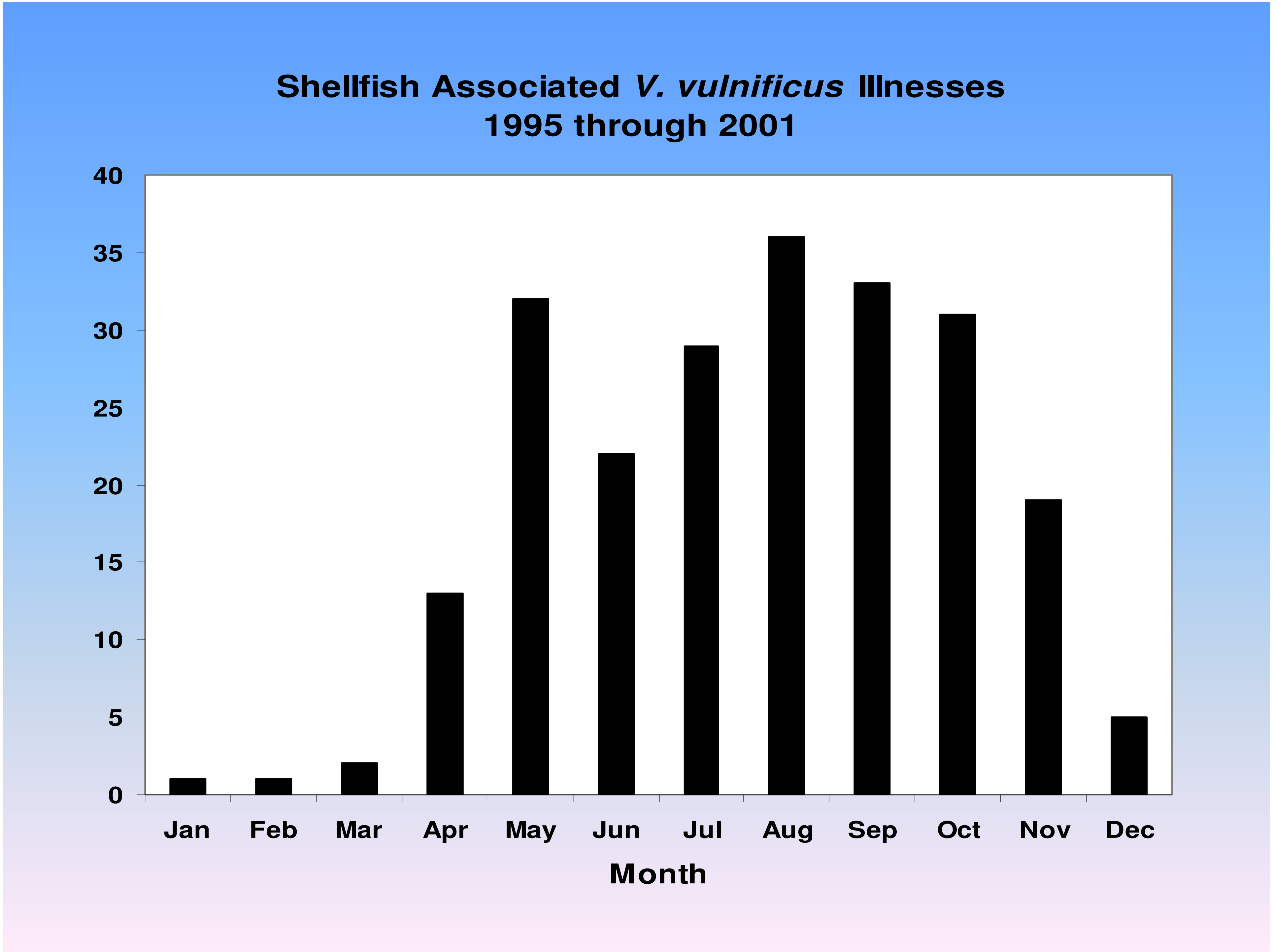
- Mean water temperature
  - DI buoy 1987-97 monthly avg.
- Servings for at risk individuals
  - 50% NMFS landings consumed raw
  - 7% of population at risk
- Mean Vv/serving
  - Model prediction based on water & air temp.
  - Mean serving size of 196g
- Vv cases
  - Reported primary septicemia cases

Vv risk factors in U.S.

Risk factor	**Prevalence per 100,000 individuals**
Diabetes (insulin-dependent)	540.5
Liver disease (cirrhosis)	2000.0 (range: 1600 - 9900)
Gastric acidity	38.9
Cancer	1420.0
Hepatitis (B and C)	(range: 400 - 1600)
Kidney disease	108.0
Haemochromatosis	1081.1
AIDS	540.5
Immune-compromised due to treatment/surgery	
Asthma	25.7
Rheumatoid arthritis	51.4
Psoriatic arthritis	37.9
Lupus	(range: 4 - 250)
Polymylagia rheumatica	53.0
Giant cell arthritis	12.0
Transplant recipients	59.5

Dose response obstacles

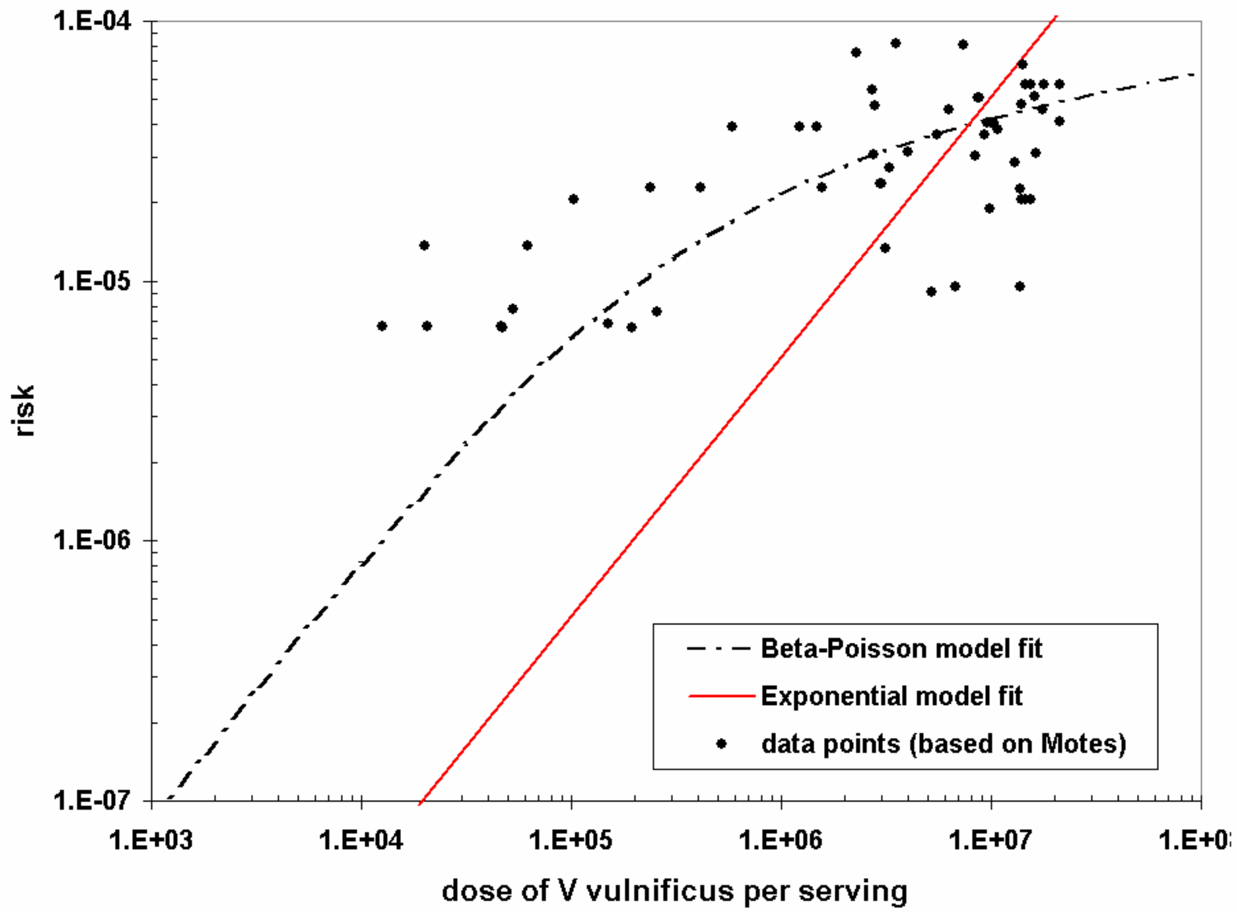
- Cases rare among at risk population
  - variability in strain virulence
  - variability in susceptibility of population
- Animal models not reliable
  - Lack of agreement between studies
  - Route of administration (oyster consumption)
- Controlled human volunteer studies unethical


Shellfish Associated *V. vulnificus* Illnesses
1995 through 2001
40
35
30
25
20
15
10
5
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Month

Model inputs and Vv cases

Month	Mean and Std dev of water temperature	Servings for at risk individuals	Mean V. vulnificus per serving (dose)	Average # Cases
Jan	12.9 (2.9)	128,000	14,000	0.14
Feb	15.1 (2.8)	132,000	70,000	0.14
Mar	17.4 (2.0)	151,000	109,000	0.29
Apr	21.7 (1.7)	131,000	675,000	1.86
May	25.8 (1.9)	110,000	5,025,000	4.57
Jun	28.8 (1.4)	105,000	11,561,000	3.14
Jul	30.0 (1.2)	97,000	15,598,000	4.14
Aug	30.3 (1.0)	88,000	16,536,000	5.14
Sep	28.2 (1.7)	99,000	9,008,000	4.71
Oct	22.7 (2.7)	127,000	1,943,000	4.43
Nov	18.4 (2.8)	146,000	257,000	2.71
Dec	15.4 (2.5)	149,000	39,000	0.71

Beta Poissson vs Exponential



Predicted Cases by Beta Poisson and Exponential vs Observed Cases

Season	Beta Poisson cases	Exponential cases	Observed cases
Winter	0.52	0.03	0.57
Spring	11.86	7.59	9.57
Summer	12.28	16.60	13.99
Fall	8.03	1.60	7.85

Post Harvest Processing

- Approved or proposed technologies
  - mild heat treatment
  - freezing
  - irradiation
  - hydrostatic pressure
- Reduce V.v. to non-detectable (<3 MPN/g)
- HACCP plan
- Label: "Processed to reduce V.v. to non-detectable levels"

Annual Vv illnesses at targeted levels of mitigation

Target	Risk per serving (mean and 95% uncertainty interval)	Annual number of cases (mean and 95% uncertainty interval) [a]
3/g	1.09×10^{-7} (4.10×10^{-8}, 2.73×10^{-7})	0.16 (0.06, 0.4)
30/g	8.20×10^{-7} (3.42×10^{-7}, 2.12×10^{-6})	1.2 (0.5, 3.1)
300/g	5.26×10^{-6} (2.60×10^{-6}, 1.05×10^{-6})	7.7 (3.8, 15.3)

Scenario analysis by RA

- Time/temperature controls
  - ISSC time/temperature matrix for Vv 1997
  - Canadian immediate cooling for Vp 2000
- Regions or countries: different ecology or practices than Gulf Coast
  - High salinities for Vp & Vv (New Zealand)
  - Intertidal harvest in Pacific NW
- Mitigations for other pathogens
  - Warm temperature depuration of Norwalk in UK

Effect of time unrefrigerated on numbers of Vv cases

Season	Time unrefrigerated	Expected # cases (90% uncertainty range)
Winter	0 hr	0.19 (0.06, 0.68)
	5 hr	0.40 (0.09, 1.96)
	10 hr	1.08 (0.23, 4.45)
	20 hr	5.12 (1.29, 11.05)
Spring	0 hr	6.77 (5.27, 8.45)
	5 hr	11.59 (9.78, 14.08)
	10 hr	15.48 (13.49, 18.82)
	20 hr	19.28 (16.11, 24.06)

Season	Time unrefrigerated	Expected # cases (90% uncertainty range)
Summe r	0 hr	7.65 (6.57, 8,82)
	5 hr	12.16 (10.46, 14.04)
	10 hr	15.31 (12.93, 18.34)
	20 hr	17.55 (15.51, 21.66)
Fall	0 hr	3.06 (1.64, 5.46)
	5 hr	7.37 (4.66, 10.62)
	10 hr	11.64 (8.91, 15.72)
	20 hr	17.30 (13.72, 21.98)

1996 ISSC Time/Temperature Matrix Effect on Vv Illness Reduction

Season	Time unrefrigerated	Mean and std dev of time unrefrigerated	Mean and std dev of Log Vv/g at consumption	Expected # cases
Spring	Pre 1996 change	5.27 (2.81)	3.36 (1.11)	12.6 (10.7, 15.2)
Spring	Post 1996 change	5.13 (2.77)	3.27 (1.08)	11.7 (9.8, 14.0)
Summer	Pre 1996 change	5.27 (2.81)	4.25 (0.81)	12.9 (11.1, 15.0)
Summer	Post 1996 change	5.13 (2.77)	4.12 (0.78)	12.2 (10.5, 14.1)

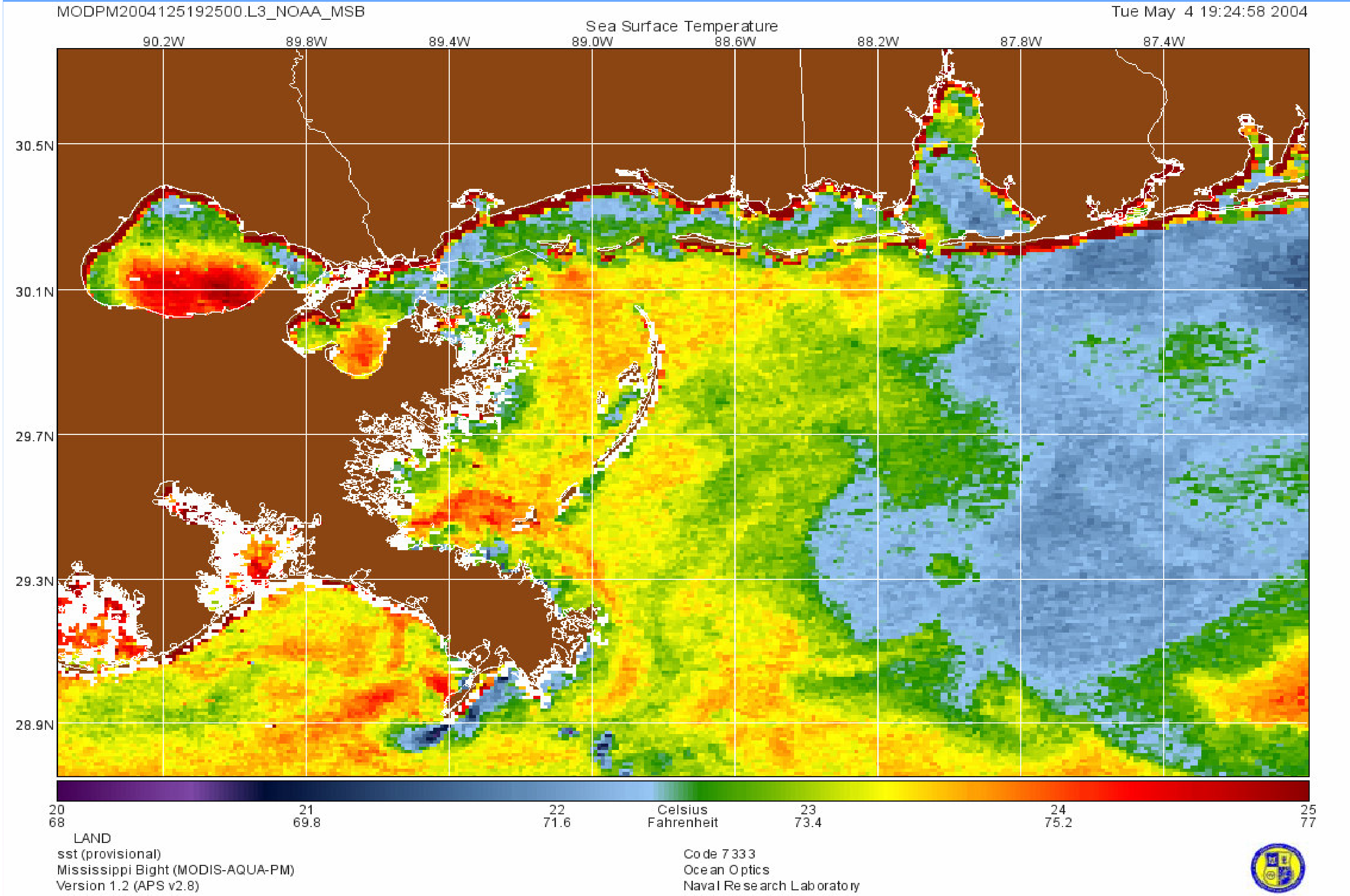
Effect of salinty >30 ppt on Vv level and risk

Temperature range	Vv/g Harvest	Risk/serving (range-best & worst case for post harvest growth)
<20℃ (68℉)	2.8	($1.0x10^{-8}$, 3.4 10^{-7})
20-25℃ (68-77℉)	19.5	($6.5x10^{-8}$, 2.9 10^{-6})
25-30℃ (77-86℉)	2.7	($8.3x10^{-9}$, 4.6 10^{-7})
>30℃ (86℉)	4.2	($1.3x10^{-8}$, 6.9 10^{-7})

Future Directions

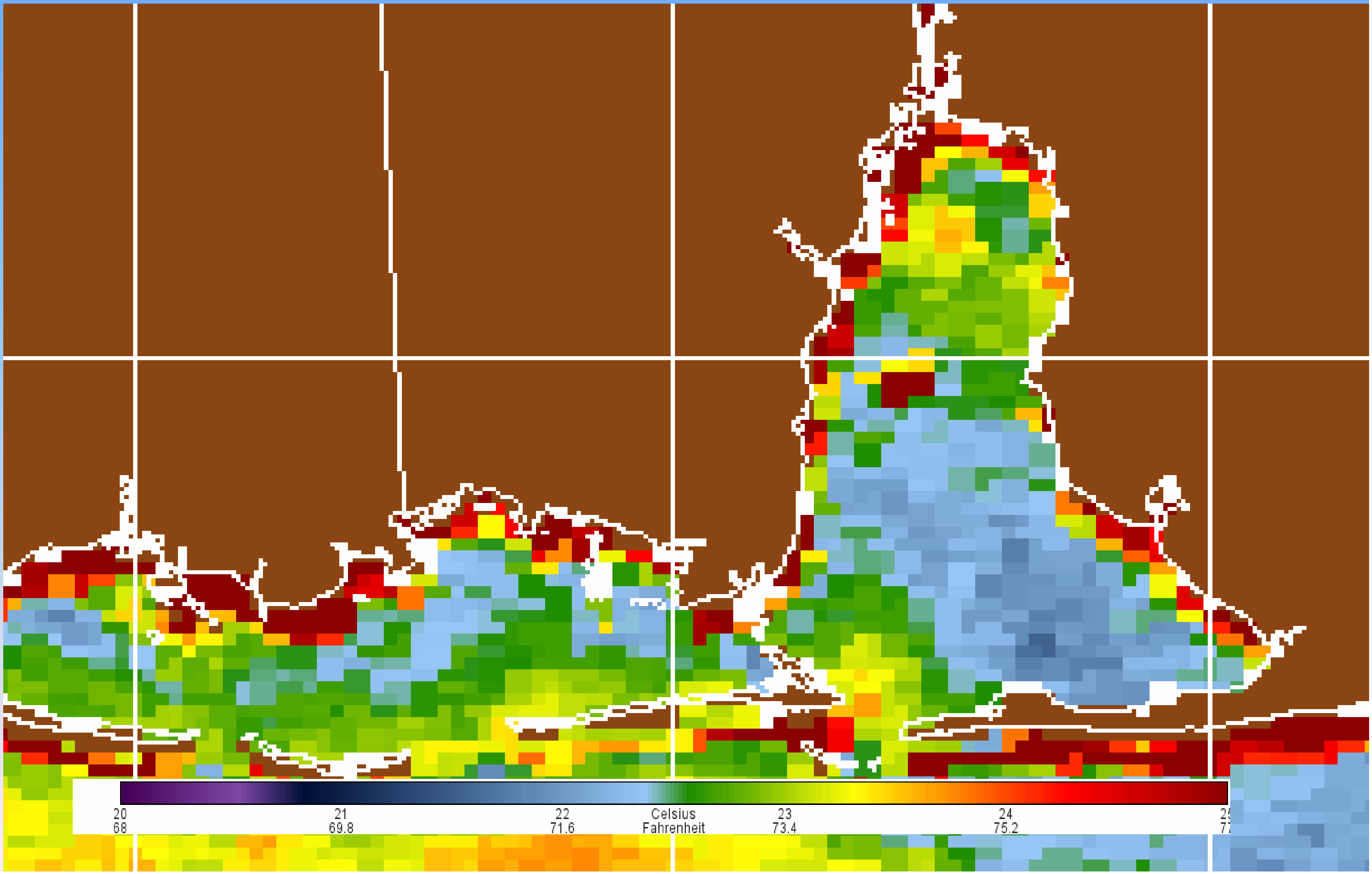
Remote Sensing

May 4, 2004 SST



May 4, 2004 SST

Zoom of MS, AL Coast

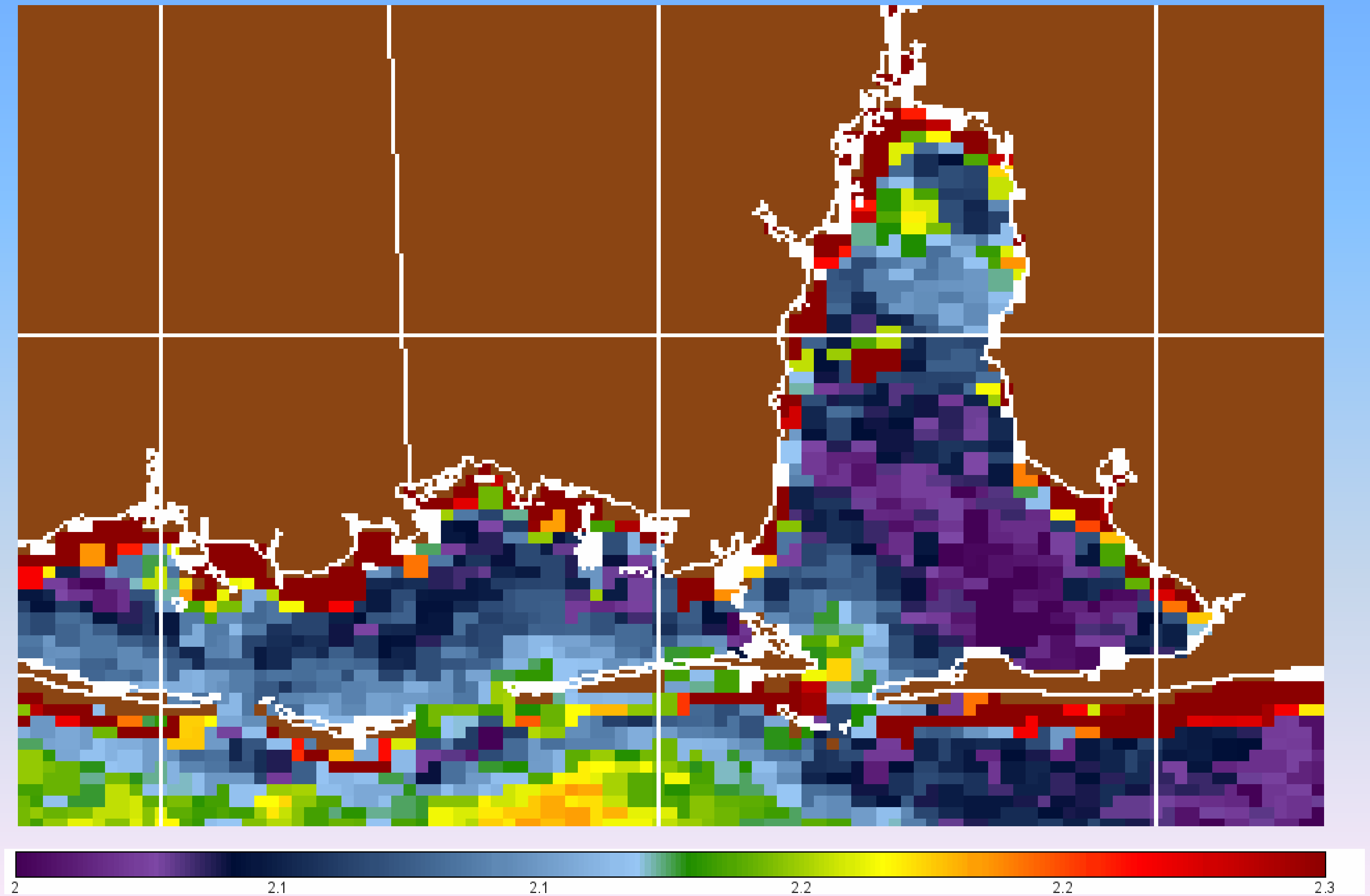


Model Equations for the Gulf

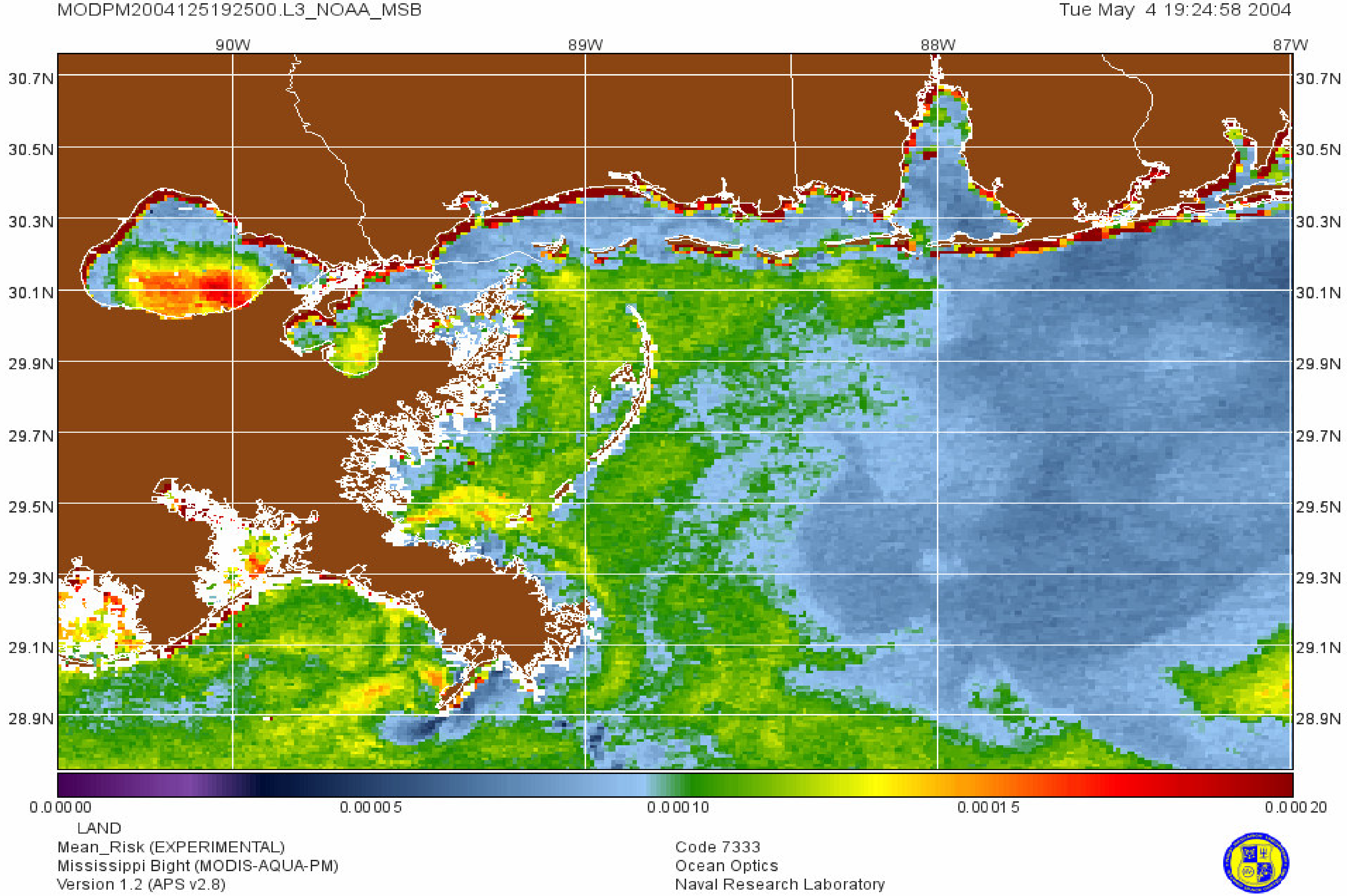
- mean(log(Vp/g)) = -0.63 + 0.12*WTEMP
- mean(log(risk)) = -7.23 + 0.14*WTEMP
- Approximation of VPRA formulas
- Other formulas (i.e. mitigations) possible

May 4, 2004 Mean Log Vp/g

Zoom in of MS, AL coast



May 4, 2004 Mean Risk



Advantages of remote sensing

- Surgical management of risk instead of using sporadic distribution NDBC
- Real time posting of risk on website
- Predictions of mitigation or PHT times
- Potential to refine VPRA or VVRA using remote sensing data other than SST
- Objective measurements for international harmonization

Conclusions

- VPRA provided suitable framework & many parameters transferable to VVRA
- Temperature based predictions of exposure validated by market data
- Beta poisson fit for dose response agrees with seasonality of Vv cases
- Interventions to reduce Vv illnesses can be evaluated with confidence
- Remote sensing may provide real time objective measurements of risk & facilitate international harmonization