

Biocontainment Casualty Case Studies: 2001-2010



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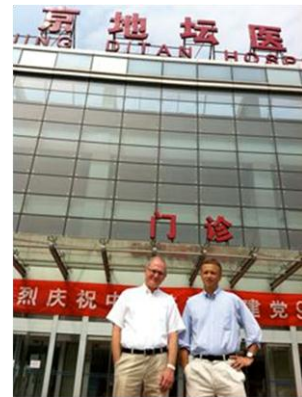
Objectives

Use case studies of laboratory accidents to explore:

The global proliferation of containment facilities for research, clinical laboratory and vaccine manufacture

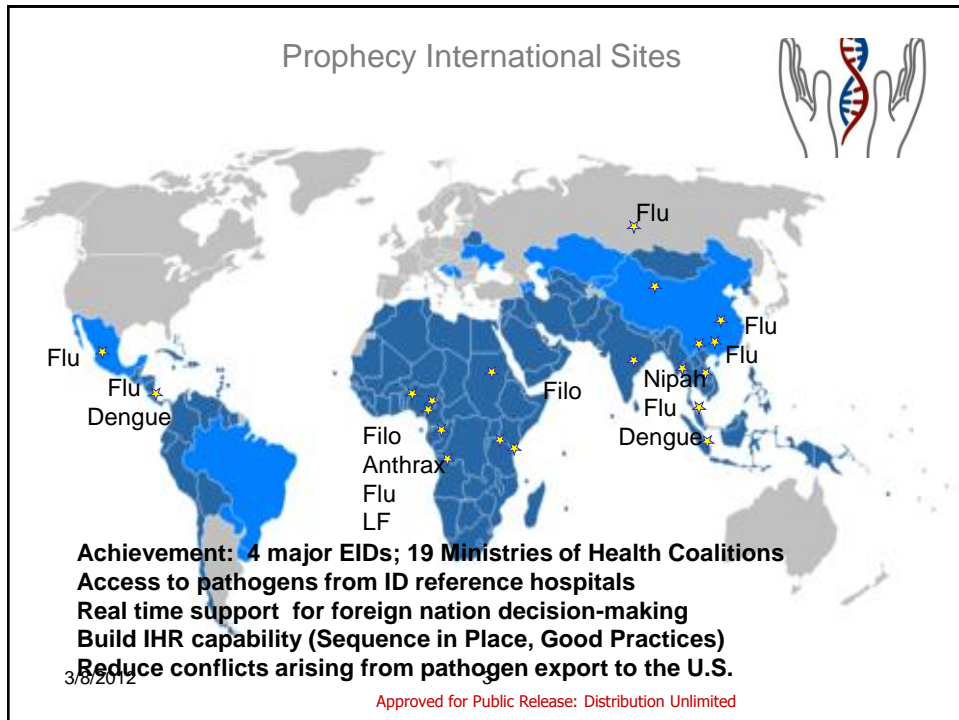
To discuss conflicts in foreign nation sovereign health autonomy and IHR2009 with Western biocontainment policy and practices.

Entice participants to the glamorous, fast-paced, lucrative field of global biocontainment support.



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Problem Statement: Demand for Biocontainment



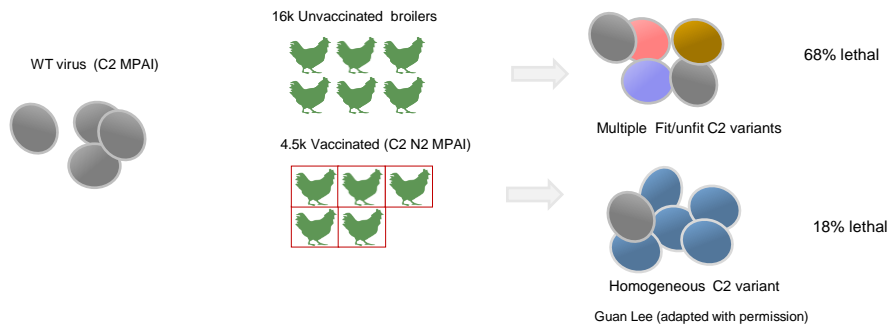
Each nation makes (unilateral) decisions to protect their governments and citizens. This can result in unexpected implications for laboratory safety

Recent examples include:

- Use of whole organism inactivated vaccines
- infectious vaccines
- Distributed, modular BL3 capability
- Uneven reporting of surveillance

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PROPHECY Surveillance



Observation: Several Asian live attenuated vaccines** for quasi- syngeneic broilers appear to influence heterogeneity of escape viruses (confirmatory sequencing under way)

Issue: could intentionally infectious vaccines reassort?

** LPAI; Haemophilus, Vibrio

-- A Disruptive Innovation for Biomanufacturing



Air-bearings allow pod to be pushed onto flat bed truck, ship, or plane for transport



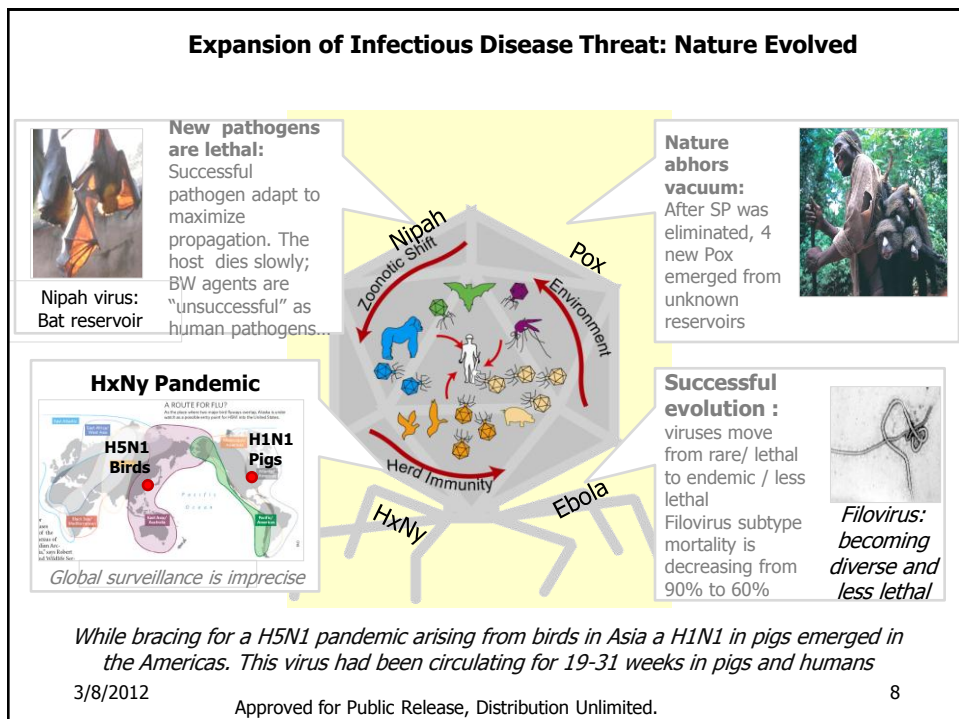
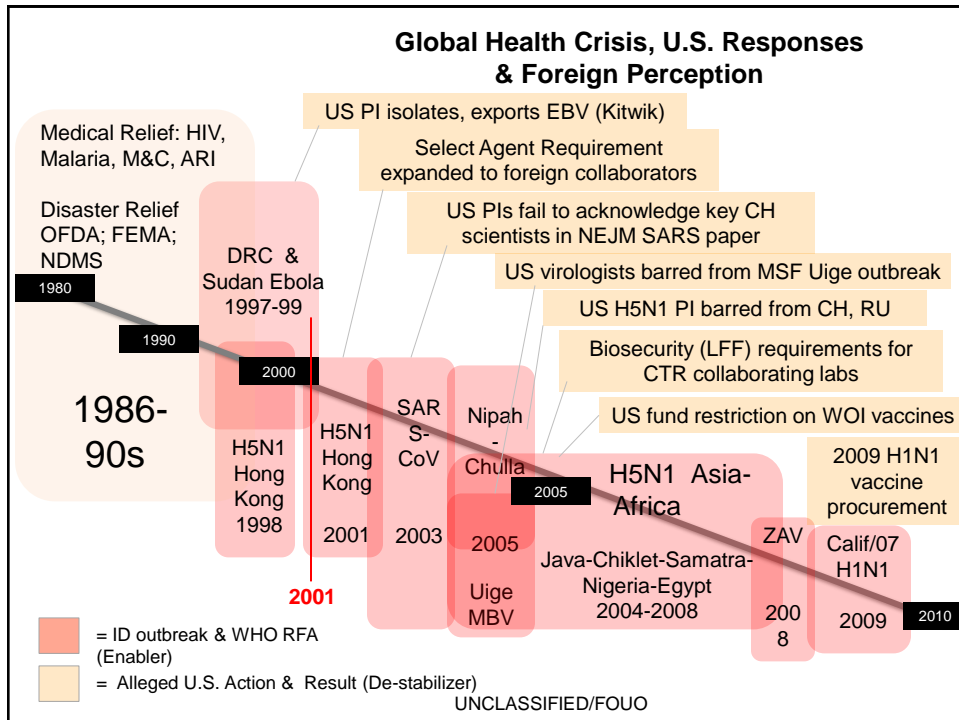
Requires only electrical hook-up and chilled water

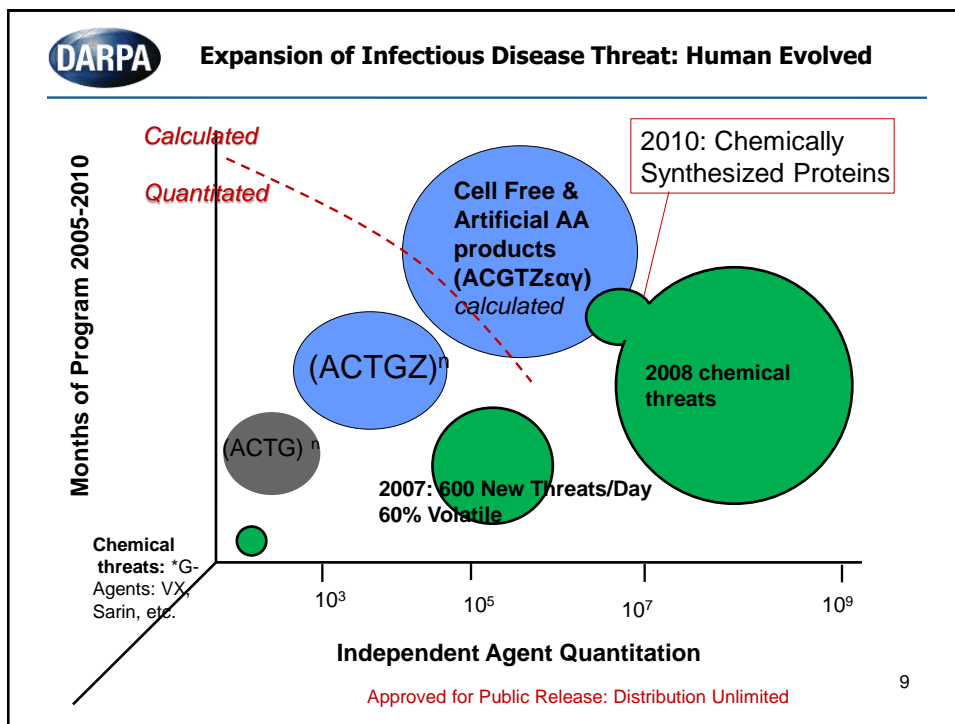


Superstructure 42 x 18 feet



Redundant core systems with automatic failover





Biocontainment Accidents: Case Studies

Examples of foreign biocontainment facilities:
Southeast Asia and Russia

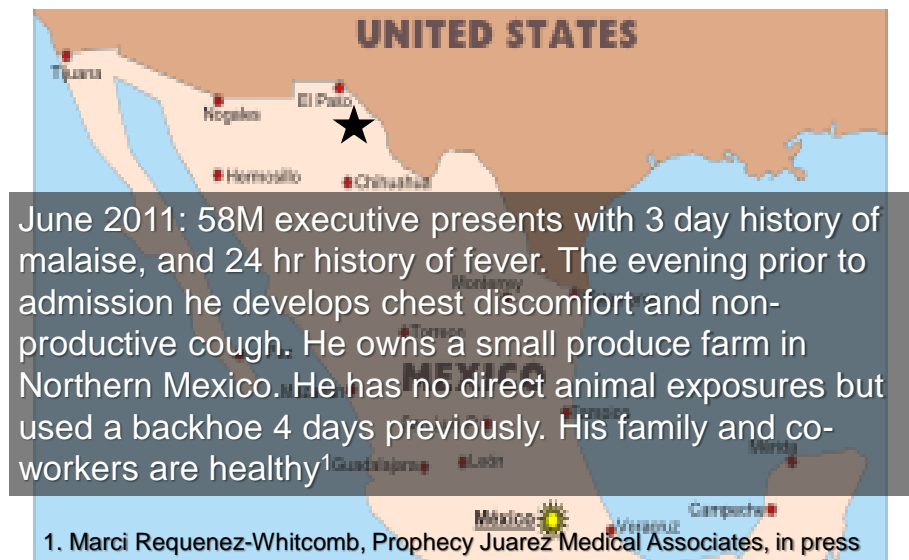


Live Agent Reference
Laboratory, Bogor, Indonesia



1970s-era Ministry of Health
BL4/III Koltsovo, Russia

Case Study : Gentleman farmer with cough

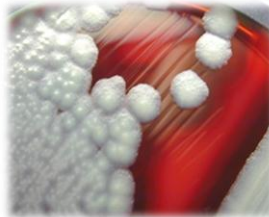
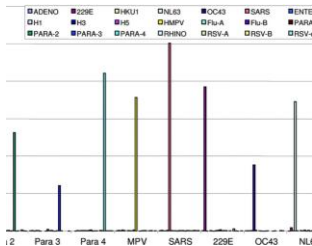


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Challenges with Fixed Detection: Select Agent PCR

Day 0	Day 4	Day 5	Day 6	Day 7	Day 9	Day 13
<i>Exposure</i>	<i>URI-CFX</i> <i>OP culture</i>	<i>Admitted</i> <i>+blood Cx</i>	<i>ICU/PPV</i> <i>-PCR RV</i> <i>+B hemolysis</i>	<i>ARDS</i> <i>(-)BA PCR</i>	Death	<i>G9241</i>



Bacillus cereus G9241 causes a fatal anthrax-like respiratory illness in humans; sequencing identified 2 virulence plasmids for anthrax toxin (pBCXO1) and capsule expression (pBC218)

On day 6 a 39F lab technician develops pleurisy, malaise and dry cough

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Category Pathogens: Surveillance Challenges

B. anthracis

C. botulinum toxin

E. tularensis

Y. pestis

Lethal genes transferred to uncontrolled species; risk of Detector Defeat is increased

Many nations use these pathogens to develop low cost, effective live-attenuated vaccines or more frequently, Whole Organism-Inactivated vaccines

Arena: Lassa

Bunya: Hantaan

Flavi: Dengue

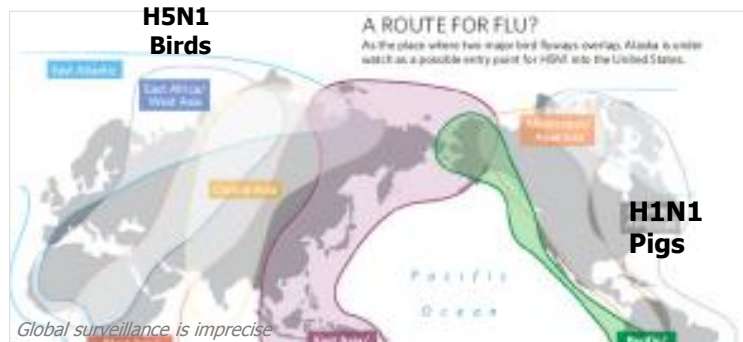
Filo: Marburg/Ebola

Other: V. Major Junin, Machupo, Guanarito, Rift Valley Fever

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Laboratory Transmission of ILIs



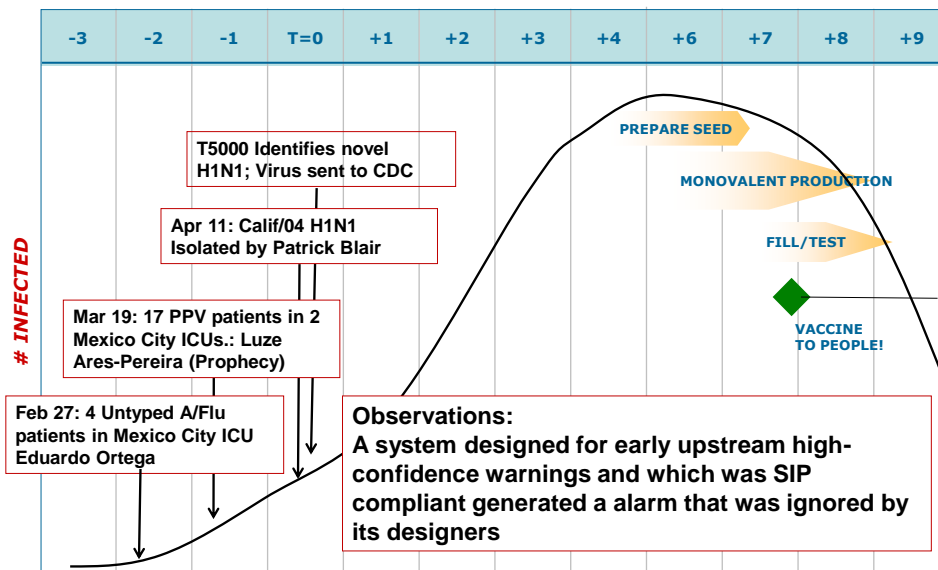
March: 5 Mexico City admissions with ILI pneumonia, negative RVP PCR and positive shell vial assay. BAL samples sent to laboratory result in horizontal transmission to lab personnel and family members.

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Case: Emerging Infectious Disease Surveillance



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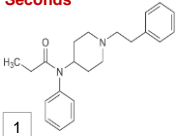
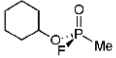
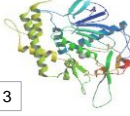
Post Exposure and Agnostic Agent Screening and Triage

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Challenges in Acute Incapacitating Agent Detection: *Clinical*

onset	CN II-XII (Blurred vision/ Nystagmus)	Motor: (Ataxia/ Weakness)	Mental Status: (Confusion/ Somnolence)	Clinical differential	Field Diagnostic capability
Seconds  1	++	++	++++	2/11	N
Seconds-Days  2	++++	++++ (fasciculations>rigid> paralysis)	++++	1/11	Y/N
Minutes-Days  3	++++	++++ (fasciculations> flaccid>paralysis)	-	3/11	Y/N

1. Fentanyl citrate
2. cyclosarin
3. light chain botulinum A

Nov 14, 2011

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Predicting Health and Disease

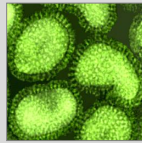
Capability: Highly accurate disease detection prior to symptoms appearingResults to date:

- 85-90% sensitivity for detection within hours of exposure (10% false positive rate)
- 100% detection within days (0% false positive rate)

Normal disease / infection
symptoms appear 7 – 10 days
after exposure
Infectious Pathogens



Respiratory
Syncytial Virus



Influenza

Medical data and
mathematics

Detection prior to the onset of
symptoms facilitates
containment and early
treatment for infected
Individuals



Distinguish between sick,
contagious and well

Highly accurate disease detection prior to the onset of symptoms enables prevention of disease propagation and treatment for infected individuals

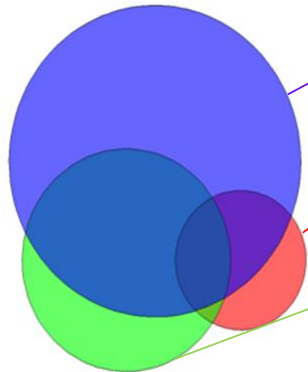
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PHD Biomarker Discovery

- Exposure to disease resulted in changes in hundreds of biomarkers
- Small subset (2-5 per disease) were used in non-linear, predictive classifiers for emergence of symptoms of specific diseases
- Secondary subset of markers used to create a classifier indicative for all three viruses studied

Total Biomarkers Discovered

Platform/Tissue: RNA
blood

Pathogen: **HRV** **RSV**
INF

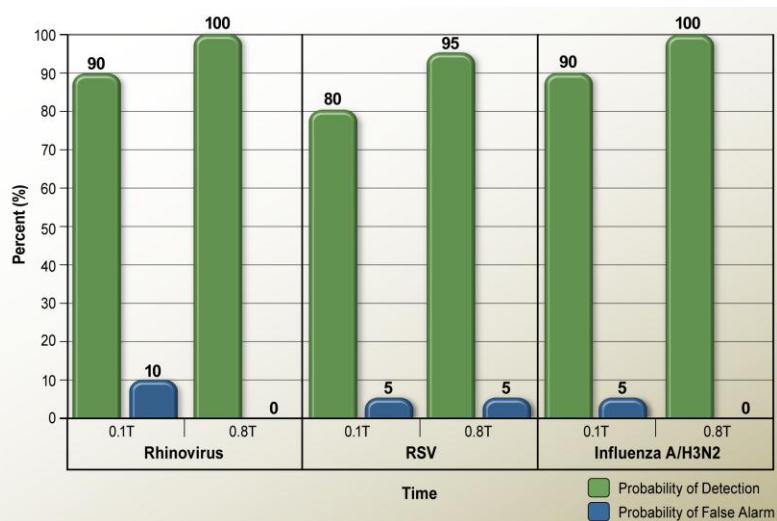
Discovered: **781**
1986 **3893**

Biomarkers Used in Classifier

Influenza Biomarkers	General Viral Infection Biomarkers	
HOXA6	Known Role in Host Response	
EXTL2	RSAD2	PLSCR1
TLR8	IFI44	IFI6
UAP1L1	IFIT1	IFIT5
HRASLS3	OAS3	IFIT2
HRV Biomarkers	SIGLEC1	GBP1
QRSL1 (218948_at)	OASL	IFI35
OAS1 (205552_s_at)	DDX58	LY6E
CNDP2 (217752_s_at)	OAS2	IFIT3
HMBOX (219269_at)	OAS1	LOC26010
GSTK1 (217751_at)	IFIH1	
RSV Biomarkers	CXCL10	Possible Role in Host Response
CD72 (971_at)	IFI27	HERC5
CD177 (57126_at)	ISG15	XAF1
	MX1	DDX60
	IFI44I	
	IFITM3	
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PHD: Phase 1 Challenge Results

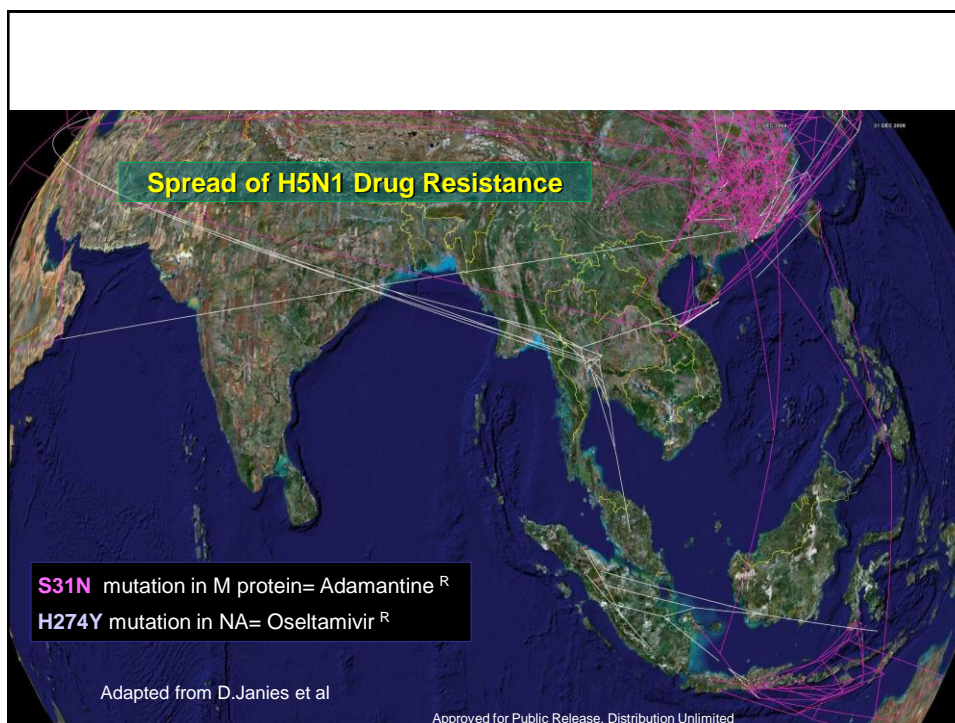


Research results based on limited experiments

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Biocontainment Good Practices

Foreign nations, economies and regulatory bodies agree on safe practices but do not agree on a international standard

Western style practices are infrastructure and human capital intensive; in current form they are not sustainable.

New solutions involving technologies and health-based processes can serve as examples of new, sustainable lab safety systems.

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