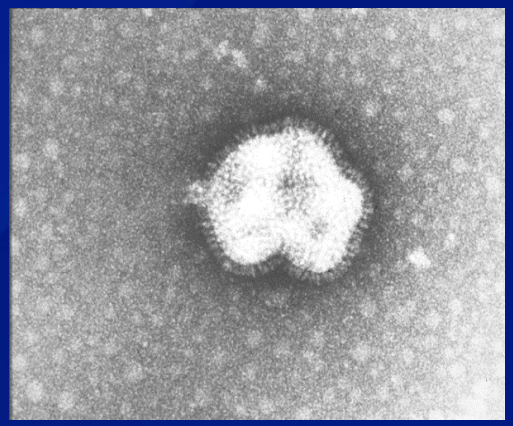
Development of an Influenza Risk Assessment Tool



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Influenza risk assessment framework

- Continued risk of influenza pandemics
- H5N1 enzootic in at least 6 countries
- H9N2, other avian influenza subtypes have infected mammals
- Maximize return on global investments in human & animal influenza surveillance/laboratories
- Chose viruses to prioritize work

Benefits of the Tool

- Objective measure applied consistently (minimizes bias)
- Transparent
- Provides documentation to support decisions
- Evaluated and reviewed regularly in an iterative process
- Can be updated with new information
- Effective communication method for policy makers

Expectations of the Tool

What it can do

- Identify key gaps in information/knowledge, i.e. prompt additional studies
- Assist with clear documentation of the thought process
- Focus Risk Management Efforts

What it can't do

- Predict the next pandemic
- Remove the need for subject matter expertise
- Make exact risk estimates

Consider utilizing an additive, multi-attribute ranking tool to rate novel influenza viruses

Serves to assess relative potential impact on health
[not a 'prediction' tool]

Relatively simple model

Involves consensus of experts

Easily modified as new data becomes available

Generates a 'score' for each virus

Uses for an Influenza Risk Assessment Tool

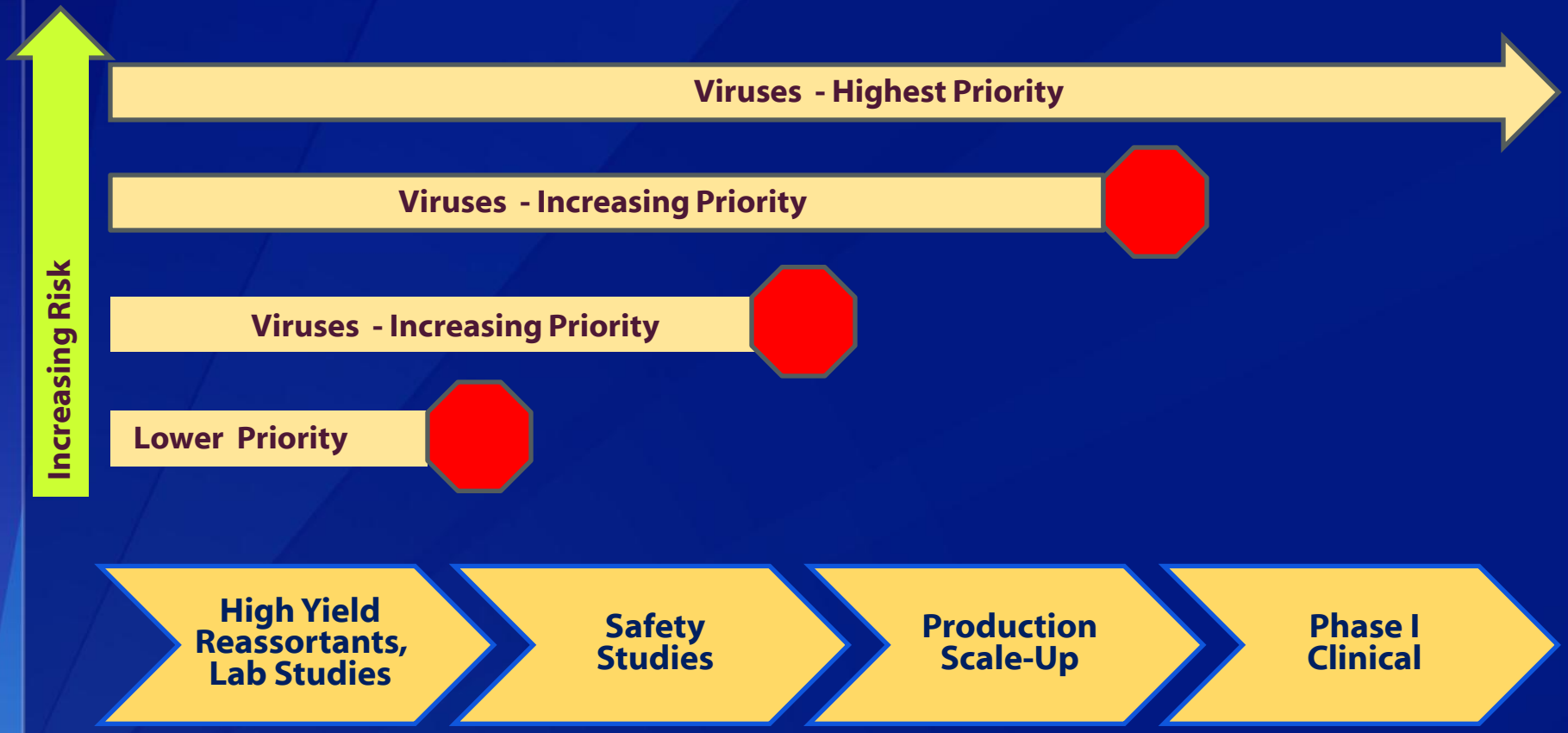
For high scoring viruses develop diagnostics and candidate vaccine libraries of high growth reassortants along with dx reagent development & seroprevalence surveys

For very high scoring viruses develop pre-pandemic vaccines

- Vaccine stockpiles
- Pre-pandemic vaccine use to prime the population

Expectations for an Influenza Risk Assessment Tool

Possible application



Vaccine Development

Developing an Influenza Risk Assessment Algorithm – Identify the Elements

Use to compare and discriminate between alternatives (i.e. viruses)

- Identify the elements to consider when assessing influenza viruses - risk of public health threat
- Define elements
- Ranking/Weighting each element

Influenza Risk Assessment Tool

What elements are included in the influenza risk assessment algorithm?

Identified 3 categories of consideration

- **Properties of the virus**
- **Attributes of the population**
- **Ecology & epidemiology**

Influenza Risk Assessment Tool

Properties of the virus [4 elements]

1. Genomic variation
   rates of reassortment & mutation
2. Receptor binding
   α 2,6 vs α 2, 3 sialic acid receptor binding
   avian vs mammal
3. Transmission in lab animals
   ferret/guinea pigs – droplet, direct contact
4. Antiviral/treatment susceptibility/resistance
   oseltamivir, zanamivir, M2 blockers

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Attributes of the population [3 elements]

1. Existing population immunity
   cross reactive antibodies; age groups
2. Disease severity and pathogenesis
   severity of illness in people and/or animals
3. Antigenic relationship to vaccine candidates
   cross reactive antibodies (ferret antisera) to current vaccine strain or other previous prepared vaccine(s)

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Ecology and epidemiologic considerations [3 elements]

1. Global distribution (animals)
   - wild animals vs domestic (containment)
   - limited geographic area vs widespread
2. Infection in animal species
   - wild birds; domestic birds; mammals
   - animal – human interaction opportunities
3. Human infections
   - none; rare event-no H-2-H transmission; clusters

Assigning a Score to a Virus

Virus evaluation is to be based on expert judgment and consensus using Risk Element definitions

Determine scores according to a physical or judgmental measure applied to the virus on a scale of 1 -10

Example Scoring Template

Selected Virus	Low ←							→ High		Range	
										Low	High
	1	2	3	4	5	6	7	8	9	10	

Risk Assessment Tool Elements

Example: Human Infections

Expert Scoring

Low Risk
Score (1 – 3)

no known human infections

Moderate Risk
Score (4 – 7)

sporadic, isolated human cases
rare H-2-H transmission

High Risk
Score (8 – 10)

several, simultaneous clusters in
in multiple geographic areas




Risk Assessment Tool Elements

Example: Receptor binding

Expert Scoring

Low Risk Score (1 -3)	aquatic bird-like α 2,3 sialic acid linkage
Moderate Risk Score (4 – 7)	dual receptors α 2, 6 and α 2,3 sialic acid linkage
High Risk Score (8 – 10)	human-like receptor binding sites primarily α 2, 6 sialic acid linkage

Scoring a Risk Element

Subject matter expert input

Example: receptor binding [SAα 2,3 Gal vs SAα 2,6 Gal]

Risk Element Ranking & Weighting

Determine the relative rank order of the elements

Low, Moderate and High importance categories

Risk elements are not weighted the same

Weighting of Elements

Situation/Question 1 (Emergence):

What is the risk that a novel* virus has the potential for sustained human-to-human transmission?

***novel = a virus that is not currently circulating in humans**

Rate the elements from 1 - 10 as you would consider them based on your concern that a virus posed a risk of emergence from its current known niche to become a virus that can spread among people.

Situation 1: Elements of most concern when considering the risk of virus emergence (potential for H-2-H transmission)

Element	Importance			
	Most	Very	Important	Not relevant
Human infections	27	2	0	0
Transmission (Lab Anim)	14	12	1	0
Receptor binding	13	12	2	0
Population immunity	16	3	8	1
Infections in animals	7	12	8	0
Genomic variation	4	10	12	0
Antigenic relationship	3	10	12	2
Global distribution	1	9	10	0
Disease severity	0	3	6	15
Antivirals/Treatment	0	0	5	24

Weighting of Elements

Emergence Question		Virus 1		Virus 2		Virus 3	
Element	Weight	R Score	W X RS	R Score	W X RS	R Score	W X RS
Human Infections	0.2929						
Transmission (Lab Animals)	0.1929						
Receptor Binding	0.1429						
Population Immunity	0.1096						
Species Distribution	0.0846						
Genomic Variation	0.0646						
Antigenic Relationship	0.0479						
Global Distribution (animals)	0.0336						
Dz Severity	0.0211						
Antivirals/TX	0.001						
Total	1.0						

Application

Example: Comparison of recent viruses

- Variant H3N2
- H5N1 HPAI
- North American avian H1N1 (Mallard)

Example of scoring w/weighted Elements

Situation 1: Emergence		HPAI H5N1		N.A. avian H1N1		Variant H3N2	
Element	Weight	R Score	W X RS	R Score	W X RS	R Score	W X RS
Human Infections	0.2929	5.67	1.66	2.33	0.68	4.33	1.27
Transmission (Lab Animals)	0.1929	3	0.58	2	0.39	9	1.74
Receptor Binding	0.1429	3.3	0.47	2	0.29	8.3	1.19
Population Immunity	0.1096	8.67	0.95	3	0.33	3.67	0.40
Infection in Animals	0.0846	7.25	0.61	2	0.17	8	0.68
Genomic Variation	0.0646	4	0.26	3	0.19	8	0.52
Antigenic Relationship	0.0479	6	0.29	2	0.10	8	0.38
Global Distribution (animals)	0.0336	5.5	0.18	2.5	0.08	7	0.24
Dz Severity	0.0211	8.5	0.18	2.25	0.05	6	0.13
Antivirals/TX	0.001	4.5	0	2.25	0	2.5	0
Total	1.0		5.18		2.28		6.55

Weighting of Elements

Application of model to different situations

Situation/Question 2 (Impact):

If the virus were to achieve sustained human-to-human transmission, what is the risk that a novel* virus has the potential for significant impact on public health?

***novel = a virus that is not currently circulating in humans**

Situation 2: Elements of most concern when considering the potential impact to human populations

Element	Importance			
	Most	Very	Important	Not relevant
Disease severity	26	3	0	0
Population immunity	21	8	0	0
Human infections	16	5	3	3
Antiviral/Tx options	7	14	6	0
Antigenic relationship	7	13	7	0
Receptor binding	0	13	9	6
Genomic variation	3	7	9	7
Transmission (Lab Animals)	2	8	12	6
Global distribution	2	3	12	11
Infections in animals	0	3	10	16

Example of scoring w/weighted Elements

Situation 2: Impact		HPAI H5N1 (clade 1)		North Amer avian H1N1		Variant H3N2	
Element	Weight	R Score	W X RS	R Score	W X RS	R Score	W X RS
Dz Severity	0.2929	8.5	2.49	2.25	0.66	6	1.76
Population Immunity	0.1929	8.67	1.67	3	0.58	3.67	0.71
Human Infections	0.1429	5.67	0.81	2.33	0.33	4.33	0.62
Antivirals/TX	0.1096	4.5	0.49	2.25	0.25	2.5	0.27
Antigenic Relationship	0.0846	6	0.51	2	0.17	8	0.68
Receptor Binding	0.0646	3.3	0.21	2	0.13	8.3	0.54
Genomic Variation	0.0479	4	0.19	3	0.14	8	0.38
Transmission (Lab Animals)	0.0336	3	0.1	2	0.07	9	0.3
Global Distribution (animals)	0.0211	5.5	0.12	2.5	0.05	7	0.15
Infection in Animals	0.001	7.25	0.01	2	0.002	8	0.01
Total	1.0		6.60		2.38		5.42

Who inputs into the Tool

Sharing of subject matter expertise

- Veterinary Health
- Public Health
- Laboratory
- Field Epidemiologists

Next steps

- Expand outreach to outside stakeholders and influenza experts
- Create international cadre of SMEs for the various elements (~ 60 SMEs currently engaged)
- Test run known viruses through the tool
- Refine elements, situations, application

Challenges

- Language/Terminology
  - Careful use of specific language for definitions and risk questions – need to avoid misunderstandings
- Agreement on specific risk questions
- Keeping the tool simple and intuitive for broad application and acceptance
- Funding and leveraging international resources
- Overall acceptance and use of the tool

Challenges – continual reminder

Influenza Risk Assessment Tool

NOT A PREDICTION OF THE NEXT PANDEMIC VIRUS!

Thank you

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www.cdc.gov/flu/weekly

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The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention.