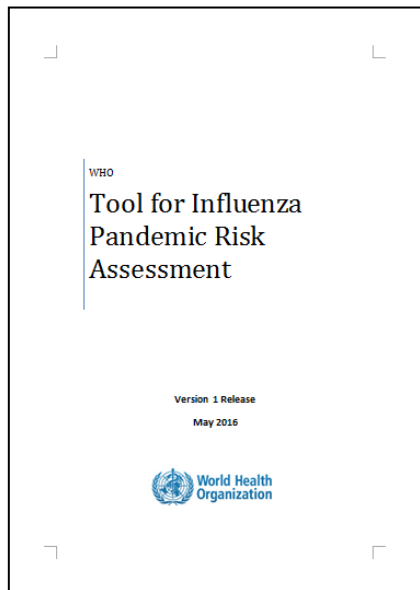
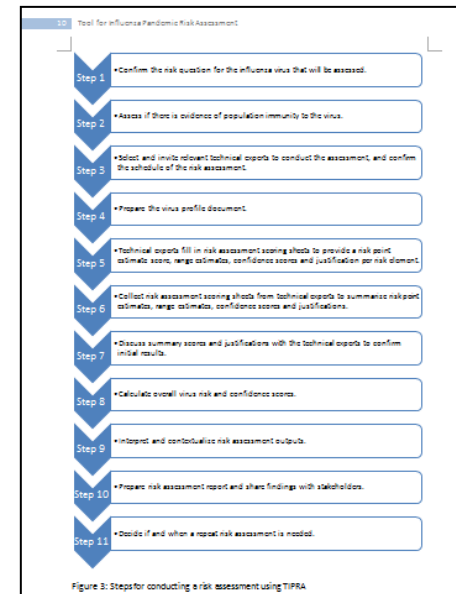


Tool for Pandemic Influenza Risk Assessment (TIPRA)



Presented by Gina Samaan
Global Influenza Programme



Pandemic Influenza Risk Management
WHO Interim Guidance



Context

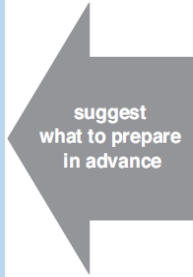
Pandemic influenza preparedness Framework

for the sharing of influenza viruses and access to vaccines and other benefits



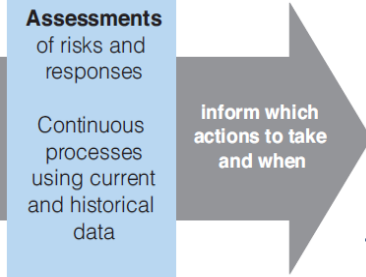
Preparedness

of capacities for emergency risk management
Based upon what could happen (planning assumptions)



Assessments

of risks and responses
Continuous processes using current and historical data



Response

proportional to identified risks
Based on current event and available data



Recovery

of systems and services
Based upon what happened

6.2 Pandemic risk assessment and risk response

6.2.1 WHO GISRS laboratories will make available to the WHO Secretariat and the originating Member State, in a rapid, systematic and timely manner, a summary report of laboratory analyses and on request any other available information required regarding PIP biological materials to enable the affected countries and in particular, developing countries, to make an effective and meaningful response.

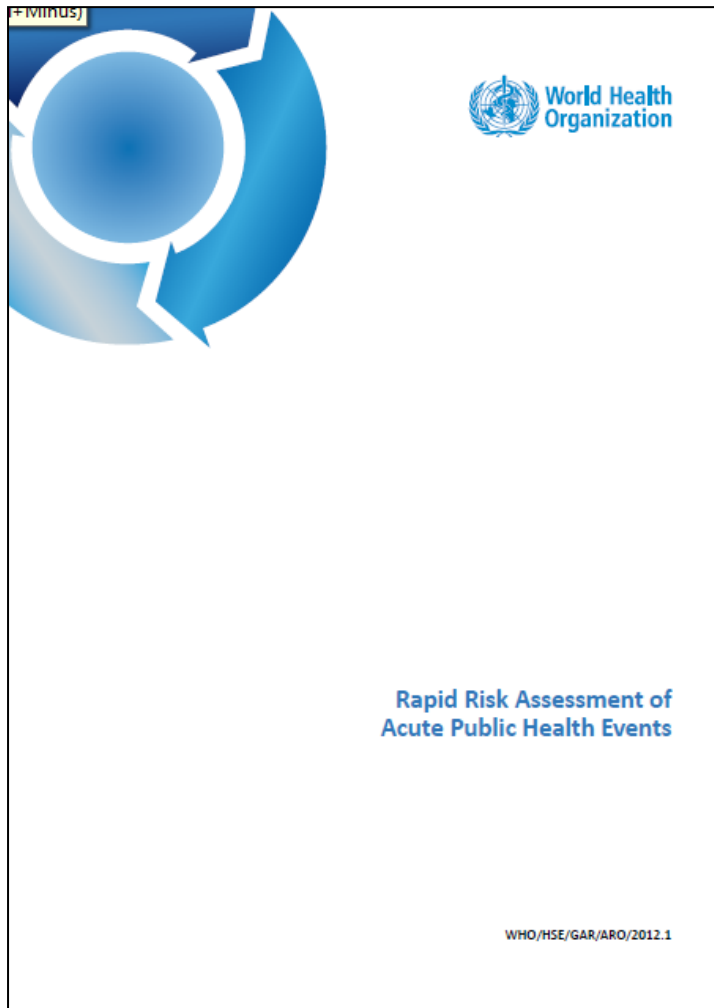
6.2.2 WHO will provide information, including, but not limited to, technical assistance to Member States, including developing countries, to support their risk assessment and pandemic risk response.

Which risk assessment tool?

6.3 Provision of PIP candidate vaccine viruses

6.3.1 The Director-General will ensure that WHO Collaborating Centres on Influenza/H5 Reference Labs and Essential Regulatory Laboratories, as

Rapid Risk Assessment of Acute Public Health Events (WHO, 2012)



Need for specific risk assessment tool

- Generic tools: good for undefined events (e.g. outbreak of a virus? a chemical event etc.?)
- Specific tools: more rigorous and detailed approach to assess an event or a component.
- TIPRA focuses on HAZARD assessment: influenza viruses with pandemic potential.



Tool for Influenza Pandemic Risk Assessment (TIPRA)

Objectives of TIPRA

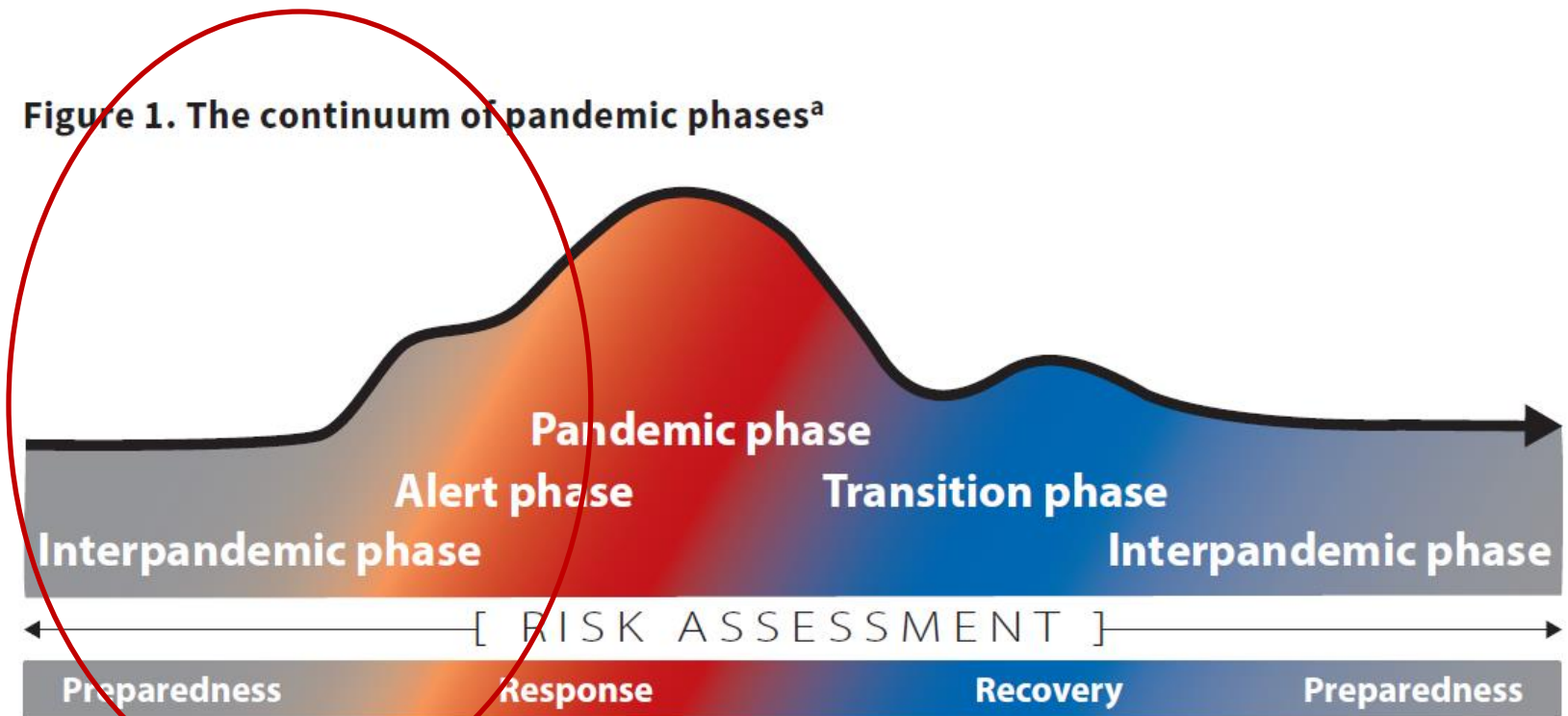
- Support a timely and updatable hazard risk assessment for influenza viruses with pandemic potential
- Transparently document features of the virus and the infections they cause
- Identify knowledge gaps and prompt further investigations including research and surveillance
- Facilitate sharing of information between scientists, policy-makers and other stakeholders

Influenza Viruses with Pandemic Potential

- Includes:
 - Animal viruses causing zoonotic infections (e.g. H5N1)
 - Viruses isolated from humans that are genetically related to viruses found in animals (e.g. swine-origin H3N2v)
 - Viruses (H1, H2 or H3) that previously circulated in humans but no longer circulate as seasonal epidemics.
- Excludes: seasonal viruses (already transmitting), viruses to which there is high population immunity (won't spread).

Risk Assessment Continuum

Figure 1. The continuum of pandemic phases^a



^a This continuum is according to a “global average” of cases, over time, based on continued risk assessment and consistent with the broader emergency risk management continuum.



Expectations from TIPRA



- TIPRA does not:
 - Predict which virus will cause the next pandemic
 - Eliminate need for technical experts
 - Quantify risk exactly or statistically, no cut-offs



Focuses on virus's qualitative pandemic potential, as evaluated by experts, based on different virus elements that are known to affect transmissibility and spread.

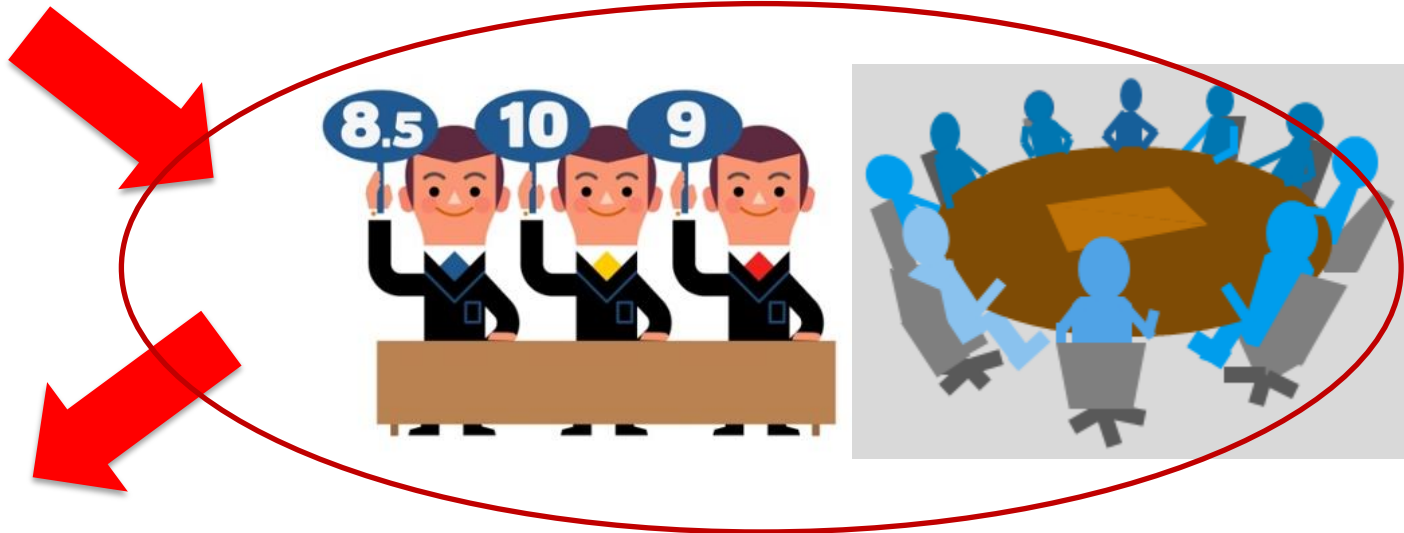
TIPRA Risk Question

What is the risk of sustained human-to-human transmission of the virus?

To evaluate this risk, two components, likelihood and impact, need to be evaluated:

- Risk Question Component A: What is the **likelihood** of sustained human-to-human transmission of the virus?
- Risk Question Component B: What is the **impact** to the human population of sustained human-to-human transmission of the virus?

TIPRA Process (11 detailed steps)



Risk Elements

A. Properties of the virus

- Receptor binding properties
- Genomic characteristics
- Transmission in animal models
- Susceptibility to antiviral treatment

B. Attributes in the human population

- Human infection
- Disease severity
- Population immunity

C. Virus ecology and epidemiology in non-human hosts

- Geographic distribution in animals
- Infections in animals

Transmission in Animal Models

For the purpose of the risk assessment tool, transmission in animal models is defined as the transmission of the virus in one or more accepted animal (mammalian) models of human transmissibility by *direct contact*¹ and/or through respiratory droplets² in the absence of direct contact.

Risk Stratification		Range of Point Estimate
Lower Risk	Viruses with no or rare evidence of either direct contact or respiratory droplet transmission in accepted animal models of human transmissibility.	1-3
Moderate Risk	Viruses with consistent transmission to uninfected direct contact animals co-housed with other animals inoculated by the intranasal route in addition to lack of transmission by respiratory droplets.	4-7
Higher Risk	Viruses with consistent transmission in animal models by both direct contact and respiratory droplets.	8-10

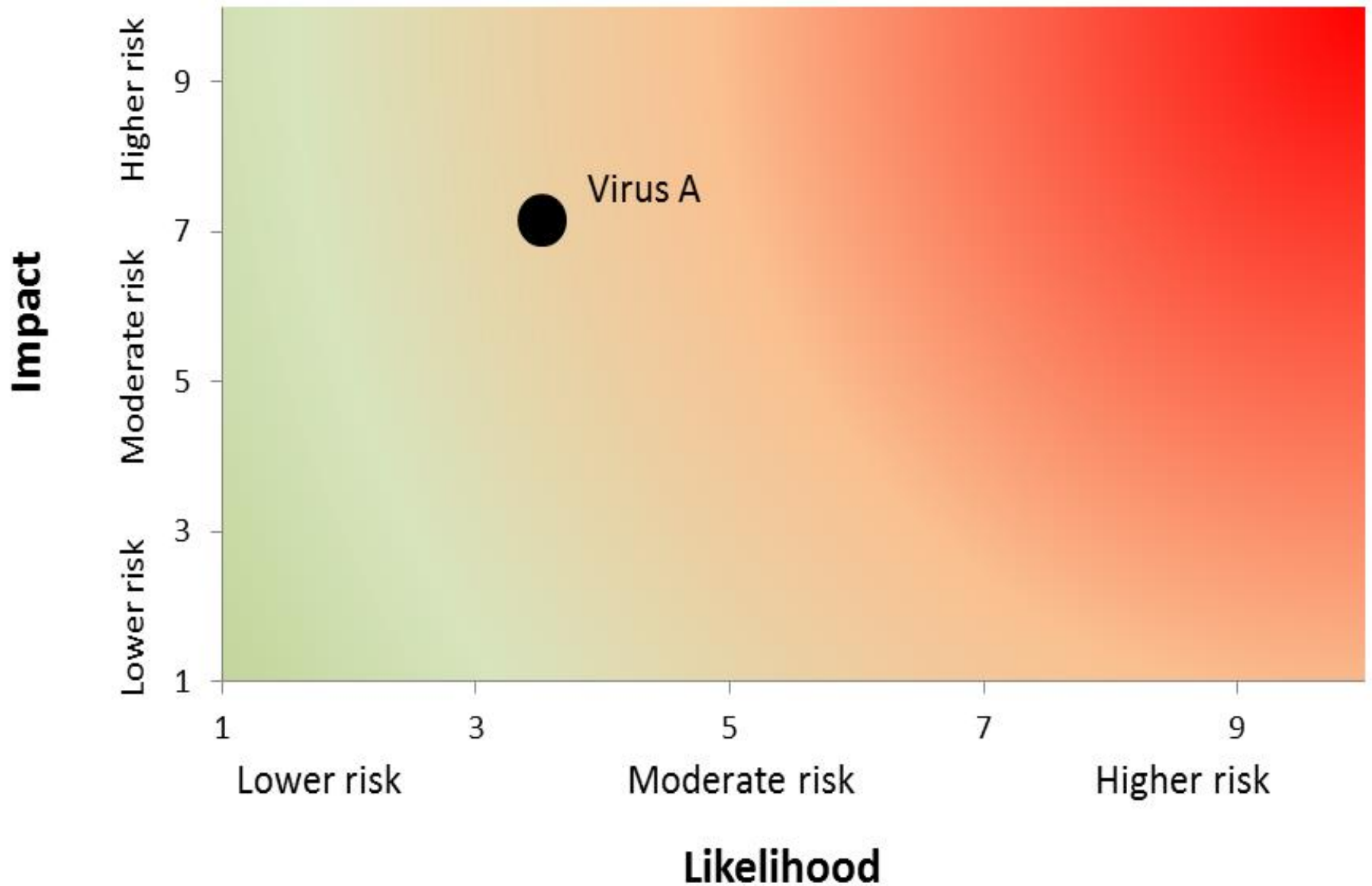
Terms:

1. Direct contact – naive animals are housed together with the virus-infected animals, allowing free contact to each other, sharing food and water.
2. Respiratory droplet transmission – naive animals are housed closely to the virus infected animal but without direct contact. Virus transmission can only occur via air-borne respiratory droplets.

TIPRA Process



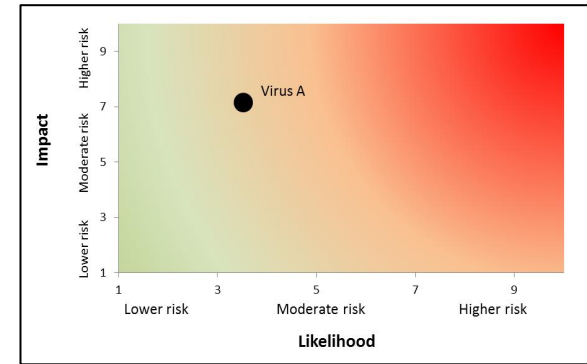
Visual Output: Risk Characterized



Risk Assessed

Risk:

Virus A can be deemed to have low likelihood for sustained human-to-human transmission with moderate impact on public health if the event occurred.



Overall Confidence:

As judged by technical experts in that risk assessment for likelihood and impact.

Report and recommendations

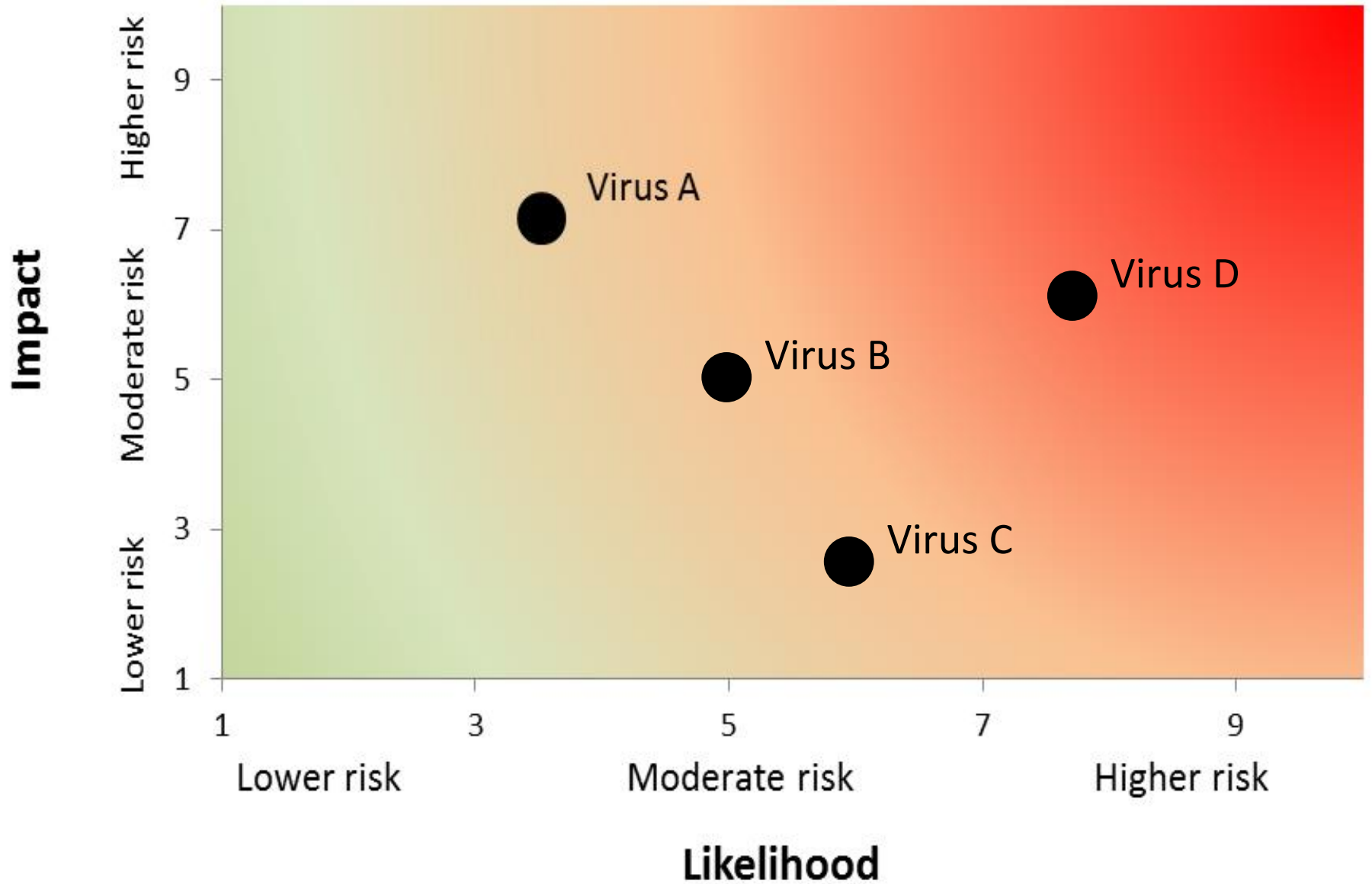
Risk Assessment for Influenza A(H5N6) Virus

Executive Summary:

Date of Assessment: 2-4 March and 26 April 2016	
Countries affected: China, Vietnam, Lao PDR	
Assessment Team: Shu Yuelong, Dayan Wang, Ian Barr, Jackie Katz, John McCauley, Richard Webby, Malik Peiris, Ron Fouchier, Pasi Penttinen, Susan Trock, Charles (Todd) Davis, David Swayne, Mia Kim Torchetti, Gwen Dauphin, Sophie Von Dobschuetz, Gounalan Pavade, Philip Gould, Rakhee Palekar, Caroline Brown, Tsutomu Kageyama, Zhibin Peng, Chengjun Li, Yuzo Arima, Stephan Burke, Diane Gross, Erica Dueger, Wenqing Zhang, Kaat Vandemaale, Terry Besselaar, Julia Fitzner, Thedi Ziegler, Gina Samaan	
<p>Results:</p> <p>Risk Question: What is the risk of sustained human to human transmission of the influenza A(H5N6) virus?</p> <p>Risk: A(H5N6) virus has low risk to develop sustained human to human transmission capacity with moderate impact on the human population if that event occurred.</p> <p>Confidence: Pending due to changes in TIPRA process for ascertaining overall confidence in risk assessment.</p>	
Recommendations: Address gaps in evidence available for risk assessment	

Risk Element	Recommendations
Human infection	<ol style="list-style-type: none"> 1. Perform thorough contact tracing to assess extent of outbreaks (sub-clinical infections, case clustering). 2. Share detailed epidemiological information from human cases to assess epidemiological links to sources of infection.
Population immunity	<ol style="list-style-type: none"> 1. Perform serosurveillance studies using clade 2.3.4.4 viruses. 2. Perform NAI assays in laboratories with this test capacity.
Receptor binding properties	<p>To assess receptor binding properties from evidence other than genome sequencing data:</p> <ol style="list-style-type: none"> 1. Conduct experiments to inoculate the lower airways of ferrets or other suitable experimental animals. 2. Conduct experiments to infect differentiated human cells in culture or <i>ex vivo</i> tissues of human lower airways

Comparisons Feasible



Target Users and Beneficiaries of TIPRA

Target Users of TIPRA

Global Assessments:

- WHO: key convener and user of TIPRA, involving:
 - International experts in public health, animal health and research academia.
 - Member State(s) affected by the influenza virus.

Other Settings:

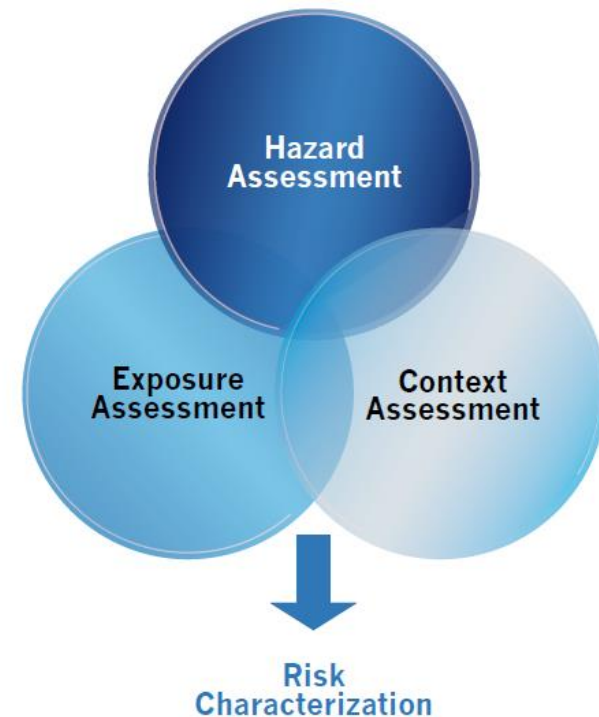
- Caution is needed to avoid conflicting risk characterization:
 - Multi-disciplinary experts score and evaluate the different virological, animal and public health risk elements.
 - Risk assessments are informed by comprehensive knowledge about the virus.
 - TIPRA processes are adhered to without modification.

Beneficiaries from TIPRA Outputs

Level	Stakeholders
National	Pandemic planning and policy-making teams
	Laboratories, e.g. National Influenza Centres (NICs)
	Public health, animal health surveillance and risk management teams
Global	Pandemic planning and policy-making team
	WHO Collaborating Centres and Global Influenza Surveillance and Response System (GISRS)
	FAO, OIE

Member States

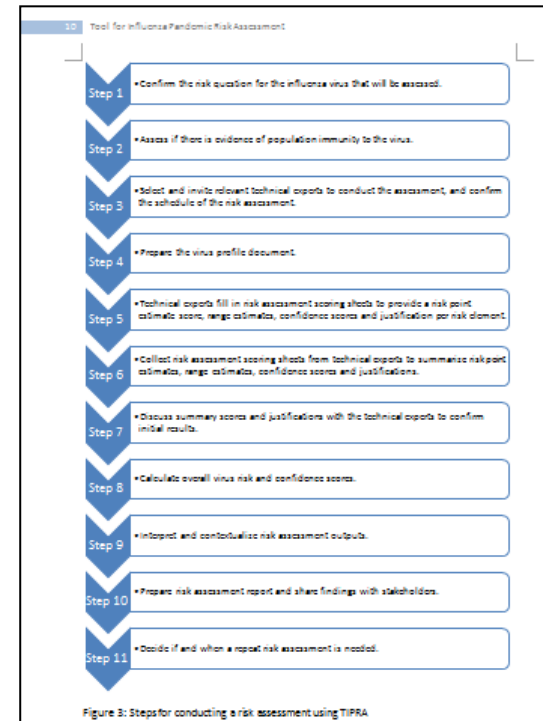
- TIPRA output: available from their investment in influenza surveillance (GISRS), research and the collaboration.
- Available to be incorporated into national risk assessments that also consider country's context and exposures.
- National level risk assessments that incorporate all three components will better determine the timing, scale, emphasis, intensity and urgency of the actions required.



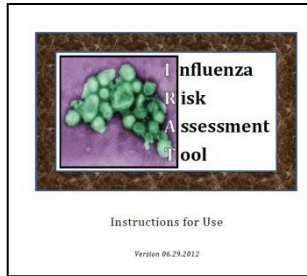
TIPRA Version 1 Release and Monitoring

WHO
Tool for Influenza
Pandemic Risk
Assessment

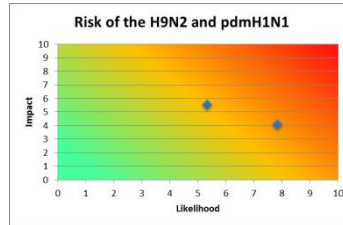
Version 1 Release
May 2016



TIPRA Development



US CDC
IRAT,
2011



Bangladesh
Pilot, 2015



Global
Pilot,
2016



**TIPRA
Version 1
Launch
May 2016**



China
Consultation
& Pilot, 2014



Egypt
Pilot,
2015



Monitoring TIPRA Version 1

- Soon to be on GIP website:
 - Clearance underway
- Plans to use it, monitor it and refine it.
 - Version 1 has only been applied once: A(H5N6)
 - Next virus risk assessment: H7N9

Acknowledgements

- US CDC Team: sharing expertise and IRAT approach.
- Crystal Wang and Hala Tolba: technical officers drafting TIPRA in initial stages.
- Technical experts who participated in pilots and provided feedback on draft documentation.
- Experts who supported finalization after global pilot: Steve Burke, Nancy Cox, Todd Davis, Ron Fouchier, Diane Gross, Andy Hill, Malik Peiris, David Swayne, Richard Webby.
- US CDC Cooperative Agreement

For more TIPRA information:

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Gina Samaan samaang@who.int

Triggers for Using TIPRA

Epidemiological triggers include:

- First documented human cases of a non-seasonal or animal influenza virus
- Increased detection of a virus with reduced antiviral susceptibility
- Cluster of cases with potential human-to-human transmission of the virus
- Cluster of human cases with infections beyond blood-related family members
- Changes in case trends associated with virus infection such as number of cases detected, disease severity, mortality ratio or geographic dispersion

Virological triggers include:

- Presence of amino acid substitutions at or near the hemagglutinin receptor binding pocket that would increase the capability of the virus to bind to mammalian alpha 2-6 receptors
- Transmission studies in laboratory animals indicating that the virus has the capability to transmit to uninfected animals by either direct contact or respiratory droplets

Benefits and Limitations

TIPRA Benefits

- Can be done **quickly**: mobilize the GISRS network experts and other focal points (OIE, FAO, Member State, Research Group).
- Provides a method for taking into account multiple risk elements and different types of information **systematically**.
- Enables **comparison** of risk characterized for different viruses or for the same virus assessed at different time points.
- Enables risk characterization **despite gaps** in information.
- **Captures confidence** in the risk characterized based on the information available at the time of assessment: transparent.

TIPRA Limitations

- Model construction:
 - Simplification of reality.
 - Need broader risk assessment tools for full characterization, especially at country level.
 - Risk elements defined by proxy indicators & not always capturing full spectrum.
- Data used to characterize risk:
 - Comprehensive virus profile relies on data to be available and shared.
- Risk assessment process:
 - Scoring contingent on technical experts adhering to the scoring process. To ensure adherence, need thorough discussions to review justifications and variations in scores.