

# Immunization Stress Related Responses (ISRR)\*



**Dr Madhava Ram MD DNB**

\* Developed based on the outline of the “*Immunization stress-related response - A manual for program managers and health professionals to prevent, identify and respond to stress-related responses following immunization*”

**Draft**

# Need for an ISRR guidance document



**GACVS December 2015:** Reports of clusters of anxiety-related reactions following immunization that impacted immunization programmes.



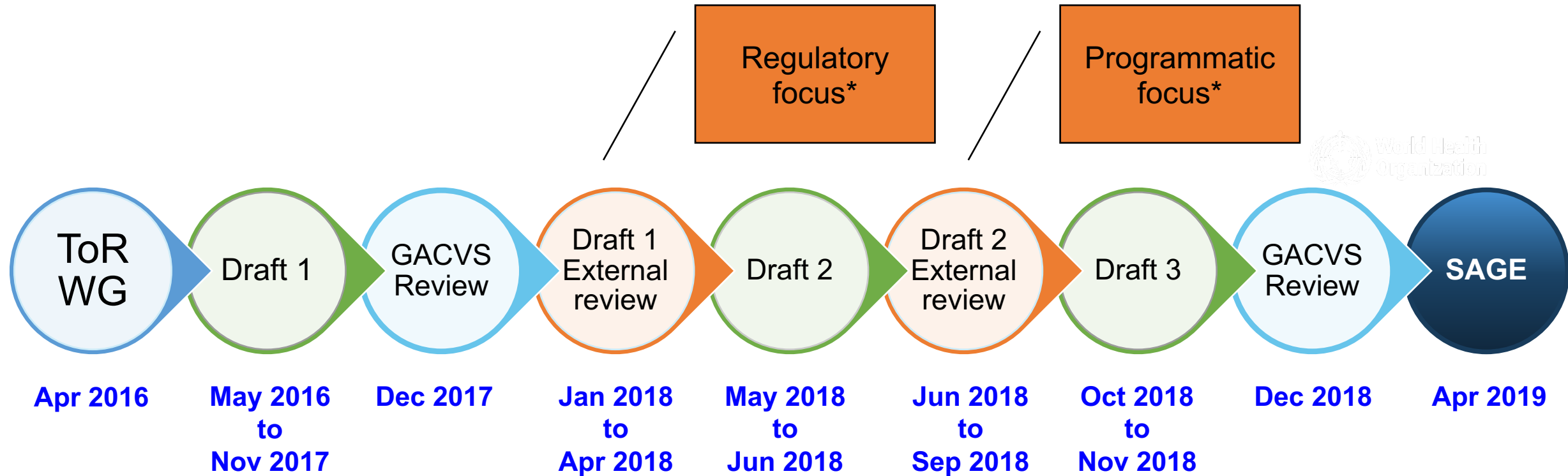
- Published reports<sup>1</sup> from - Iran, Italy, Jordan, India, Vietnam, Australia, Taiwan and the USA
- Media Reports<sup>2</sup> from - Canada, Columbia, Chad, Kazakhstan, China and Denmark

**GACVS convened an expert working group to understand the etiology, characteristics and prepare a guidance document for immunization staff and program managers**

1. Loharikar A et al. Anxiety-related adverse events following immunization (AEFI): A systematic review of published clusters of illness. Vaccine. 2018 Jan 4;36(2):299-305. doi: 10.1016/j.vaccine.2017.11.017. Epub 2017 Nov 29.

2. Suragh TA, et al. Cluster anxiety-related adverse events following immunization (AEFI): An assessment of reports detected in social media and those identified using an online search engine. Vaccine 2018; 36(40):5949-5954  
2019-04-05

# Developing the ISRR manual



\* Also Psychiatrists, Psychologists, Communication specialists, Pediatricians, Epidemiologists & Researchers

# CIOMS/ WHO cause specific definitions\* of AEFIs



**1**

**Vaccine product-related reaction**

An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.

**2**

**Vaccine quality defect-related reaction**

An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer.

**3**

**Immunization error-related reaction**

An AEFI that is caused by inappropriate vaccine handling, prescribing or administration.

**4**

**Immunization anxiety-related reaction**

An AEFI arising from anxiety about the immunization.

**5**

**Coincidental event**

An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety

# Why “ISRR” and not “immunization anxiety”?

**Too narrow  
and too  
"medically"  
focused.**



**Immunization  
anxiety**

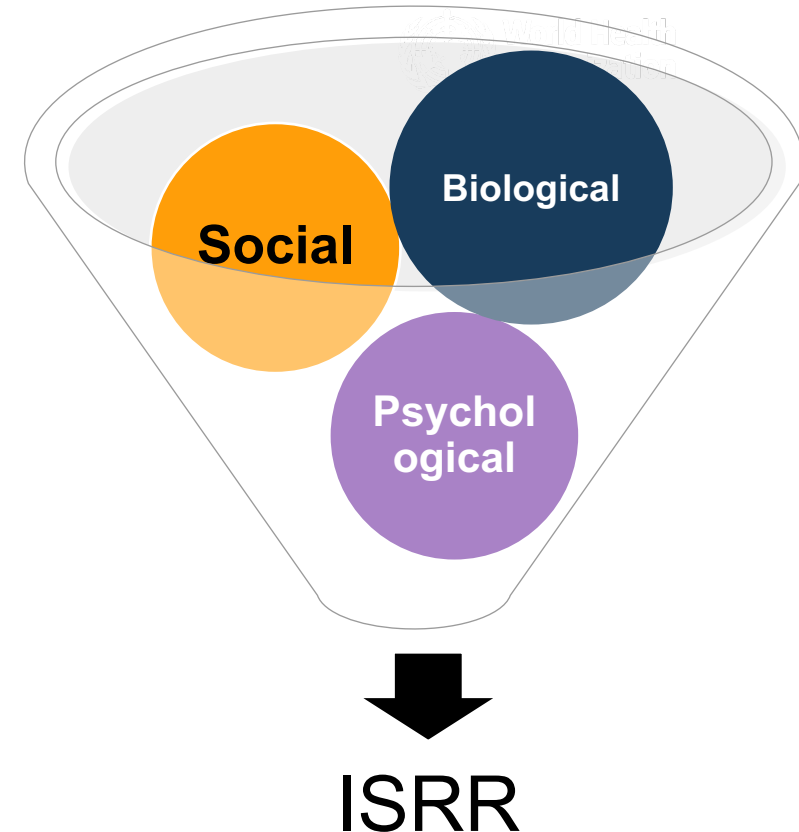
**Immunization  
stress related  
response**

**Includes the entire  
spectrum of signs  
and symptoms  
seen in a stress  
response  
(*not just anxiety  
symptoms*)**

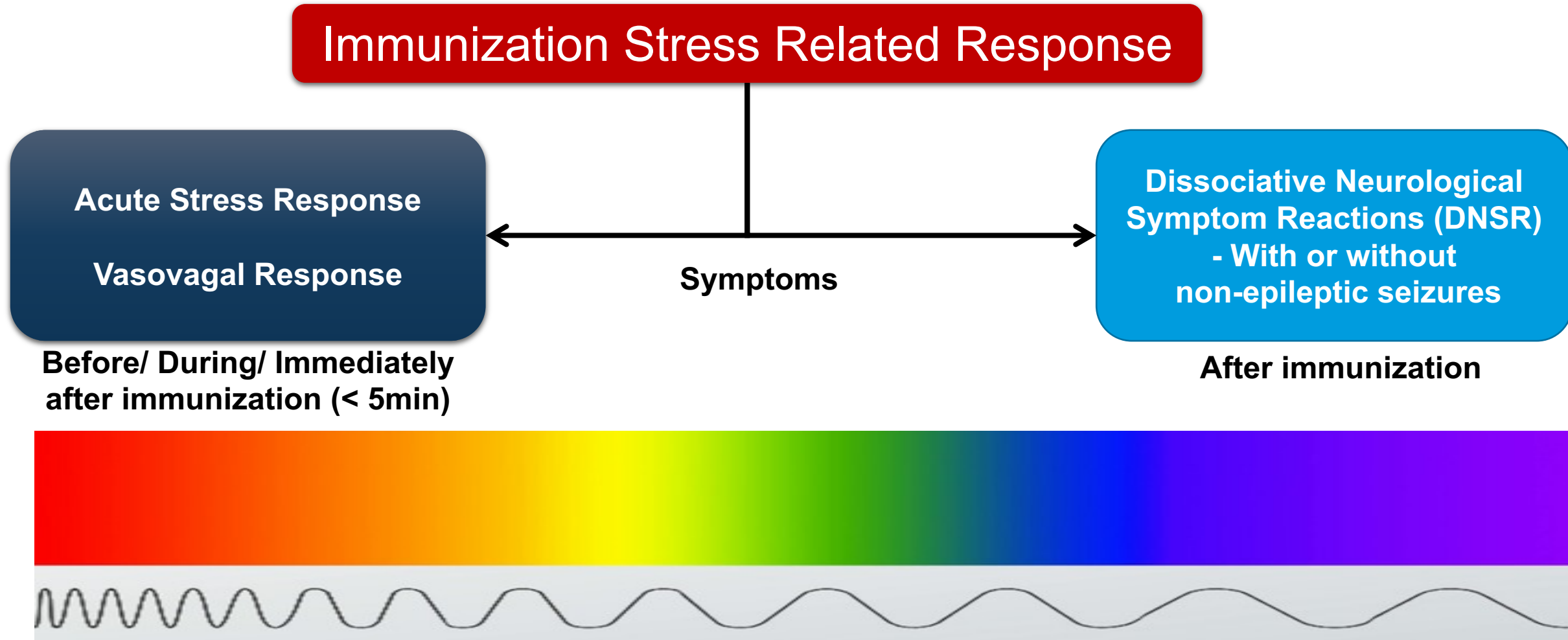
# Characteristics - ISRR

Can happen before, during, or after immunization

- **Biopsychosocial framework:** Helps understand a person's response to immunization
  - **Pre-disposing factors:** Historical, pre-existing factors brought into the immunization context
  - **Precipitating factors:** Dynamic, factors occurring in the peri-immunization context
  - **Perpetuating factors:** Factors occurring in the post-immunization context



# Classification - The ISRR spectrum



**Remember: These responses can also occur unrelated to immunization**

# Why differentiate ISRR from other serious AEFI?

## ISRRs

- More Common
- Not usually life threatening
- No need for Epinephrine
- Usually no Meds needed

**VS**

## Anaphylaxis

- Rare
- Life-threatening
- Need Epinephrine
- Medication

## Epileptic Seizures

**Wrongly diagnosing and treating ISSR as Anaphylaxis (or other serious medical conditions) can have serious implications on the health of the vaccinee**



# ISRR Clusters

Multiple (two or more) ISRRs → a cluster

Common in schools and large campaigns

Mass Immunization Stress-Related Response (MISRR)

Social Factors

- Peers
- Media/ Social Media



<https://www.youtube.com/watch?v=3ikEycuJ1yE>

# Non ISRR: Events, disorders or syndromes

## Reported as AEFI post-immunization

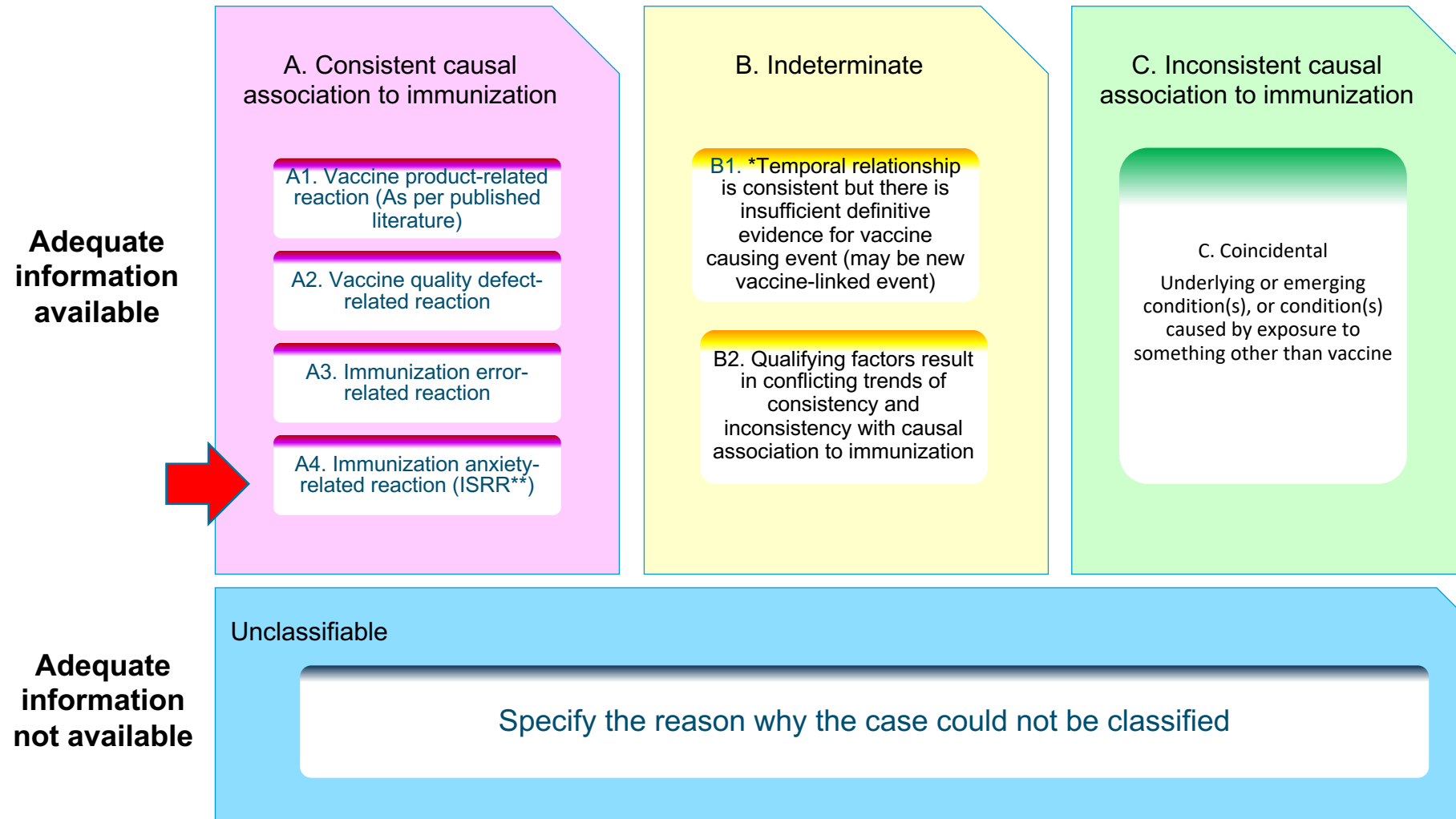
- Signs and symptoms are unexplained after appropriate medical investigations
- **Causal association** with immunization has **not been established**.

## Examples

- *Complex Regional Pain Syndrome (CRPS) -Type 1 with delayed onset*
- *Postural Orthostatic Tachycardia Syndrome (POTS)*
- *Chronic Fatigue Syndrome (CFS).*
- *Somatic Symptom Disorders*

- Pathogenies of these conditions are poorly understood
- All occur as background conditions which are unrelated to immunization
- When the *onset of symptoms is proximate to immunization* this should be reported as an AEFI

# Causality assessment of ISRR



\*B1 : Potential signal and maybe considered for investigation

\*\*Immunization Stress Related Response

## Step 2 (Event Checklist) ✓ (check) all boxes that apply

I. Is there strong evidence for other causes?	Y N UK NA	Remarks
1. In this patient, does the medical history, clinical examination and/ or investigations, confirm another cause for the event?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
<b>II. Is there a known causal association with the vaccine or vaccination?</b>		
<b>Vaccine product</b>		
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
2. Is there a biological plausibility that this vaccine could cause such an event?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
3. In this patient, did a specific test demonstrate the causal role of the vaccine ?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
<b>Vaccine quality</b>		
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
<b>Immunization error</b>		
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
8. When this patient was vaccinated, was there an error in vaccine administration by the vaccinator (e.g. wrong product, wrong dose, wrong route, wrong site, wrong time)?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

### Immunization anxiety (Immunization stress related response - ISRR)

11. In this patient, could this event be a stress response related to immunization (e.g. acute stress response, vasovagal reaction, hyperventilation, dissociative neurological symptom reaction etc)?

☐ ☐ ☐ ☐

II (time). If "yes" to any question in II, was the event within the time window of increased risk?

☐ ☐ ☐ ☐

12. In this patient, did the event occur within a plausible time window after vaccine administration?

1. In this patient, did such an event occur in the past after administration of a similar vaccine?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
2. In this patient did such an event occur in the past independent of vaccination?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
3. Could the current event have occurred in this patient without vaccination (background rate)?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
5. Was this patient taking any medication prior to the vaccination?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

# Examples of other key topics addressed in the manual

## Differentiating

- Anaphylaxis from acute stress response (General and vasovagal)
- Pseudo seizure and seizure

## Prevention

- Environment and Attitude
- Communication and Pain Reduction
- Identify high risk persons

## Responding to ISRR

## Identifying and responding to ISRR clusters

## ISRR Surveillance

## Addressing media queries related to ISRR

# Chapters in the ISRR Manual

Chapters	Topic addressed
Chapter 1	An introduction to immunization stress-related response
Chapter 2	Manifestation and classification of immunization stress-related response
Chapter 3	Epidemiology of immunization stress-related response
Chapter 4	Prevention, diagnosis, management and causality assessment of immunization stress-related response
Chapter 5	Clusters of immunization stress-related response
Chapter 6	Reporting mechanisms and support structures for immunization stress-related responses
Chapter 7	Communication strategies for prevention and management of Immunization stress-related response
Chapter 8	Research gaps and the way forward

# Appendices in the ISRR Manual

Number	Topic addressed
1	Glossary of Terms and Definitions
2	Schematic biopsychosocial conceptualization of immunization stress-related response
3	Physiological effects of an acute stress response
4	Developmental approach to the prevention and management of pain
5	Information to collect to inform communication planning to prevent an immunization stress-related response
6	Common questions asked by the media, preparing a holding statement and message mapping

# Who will use this manual?

# What are the plans for its dissemination?

- Primarily intended for program managers and health professionals
- Manual to be translated to major languages and made available in WHO website
- To increase awareness among health professionals, synopsis will be proposed for publication in an international peer reviewed journal
- Training materials (cases for teaching, e-module, addressing needle phobia etc.) tailored to the target audience will be developed.



