# COVID-19 Vaccine Trials
# Standard of Care, Serous Adverse Events (Injuries and Deaths), Compensation

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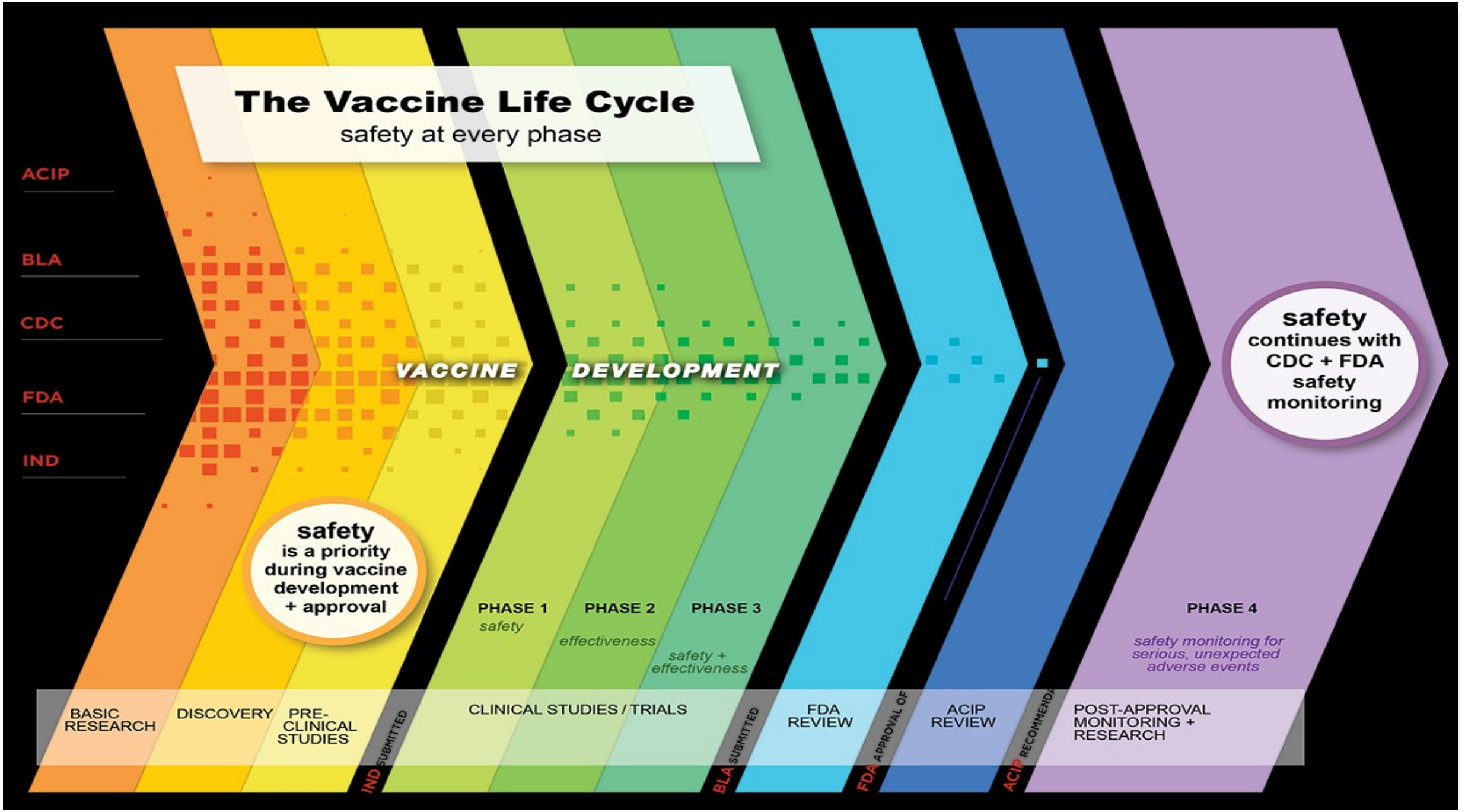
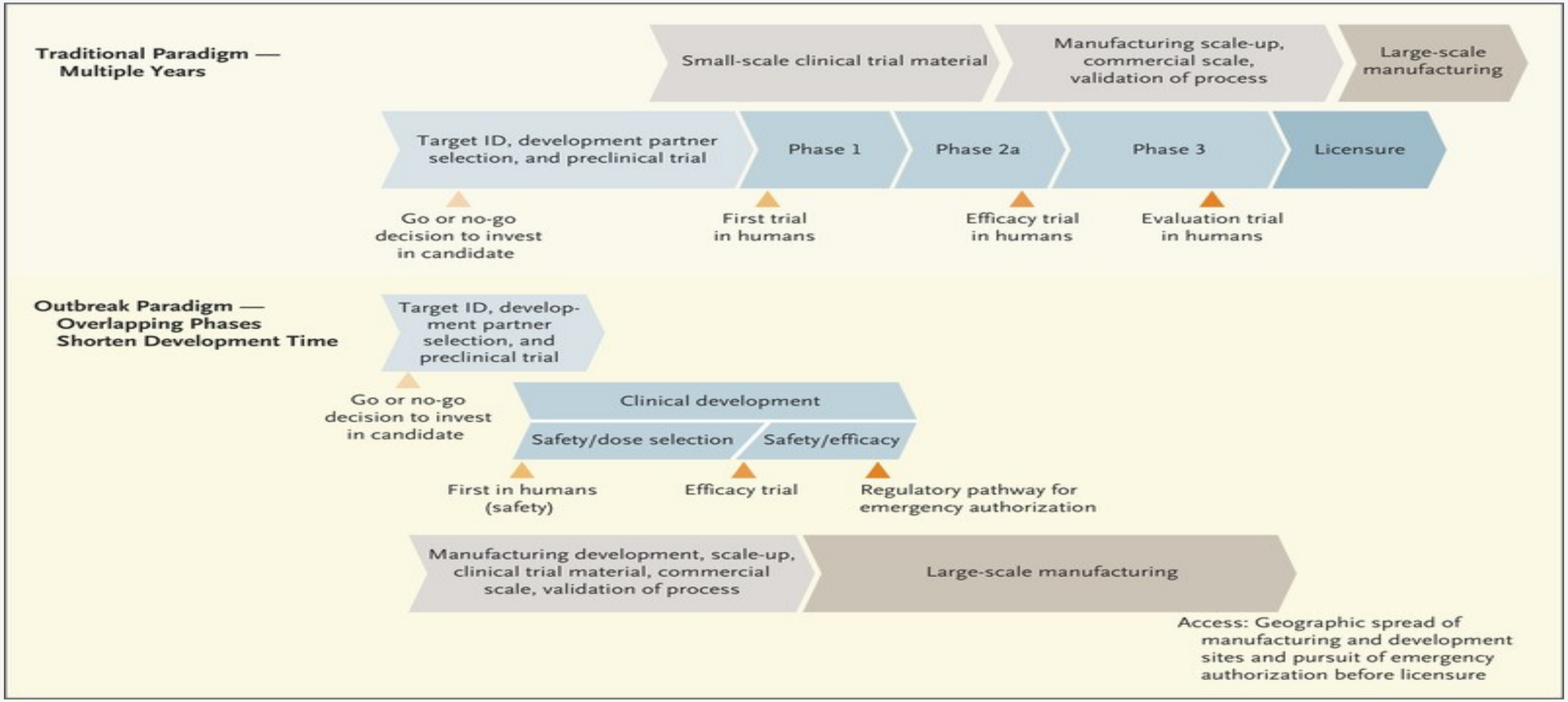

The Vaccine Life Cycle
safety at every phase
ACIP
BLA
CDC
FDA
IND
VACCINE DEVELOPMENT
safety
is a priority
during vaccine
development
+ approval
PHASE 1
safety
PHASE 2
effectiveness
PHASE 3
safety +
effectiveness
PHASE 4
safety monitoring for
serious, unexpected
adverse events
safety
continues with
CDC + FDA
safety
monitoring
BASIC RESEARCH
DISCOVERY
PRE-CLINICAL STUDIES
IND SUBMITTED
CLINICAL STUDIES / TRIALS
BLA SUBMITTED
FDA REVIEW
FDA APPROVAL OF
ACIP REVIEW
ACIP RECOMMENDA
POST-APPROVAL MONITORING + RESEARCH

# Pandemic Vaccine Development




**Laurie N et al. Developing Covid-19 Vaccines at Pandemic Speed. N Engl J Med 2020; 382:1969-1973 DOI: 10.1056/NEJMp2005630**

# What Does Standard of Care Mean?

# The Standard of Care in general refers to –
the degree of care (watchfulness, attention, caution, and prudence) that *a reasonable person* should exercise *under the circumstances*.

**PROVIDER**
**Physician / Researcher**

**CONTEXT**
**Therapy / Research**

# The context of research can vary – it can be a therapeutic or a non-therapeutic experimentation.

# The Standard of Care in therapeutic clinical trials mainly refers to the treatment that subjects in the control arm are allocated to.

# The Standard of Care in non-therapeutic clinical trials (e.g., phase 1 drug trials, vaccine trials) actually refers to Standard of Prevention.

# The Standard of Care in Clinical Trials

# In 2000, the WMA modified the Helsinki Declaration to state that "the benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods."
# In 2002, the CIOMS guidelines took the debate a stage further by using the term "established effective therapy" to indicate a degree of consensus and acceptability among health professionals about the nature of treatment.

*Notably neither specify if established effective therapy applies to a* ***local*** *or* ***global*** *context.*

# The Standard of Care in Clinical Trials

Currently, there is a wide variety of standards for the SoC in *therapeutic* clinical trials –

*# the highest attainable care*
*# the best available care*
*# the best current care*
*# a proven treatment*
*# an established effective treatment*

Perhaps none of the current standards is adequate to serve as a universal standard for the standard of care.

# Injury or Death of Participants in Vaccine Trials

# Emergency Use Authorization (EUA)

- Does not constitute approval of the drug/ biologic/ vaccine; instead authorizes regulators to facilitate availability of the product
- Is based on a reasonable (but incomplete and insufficient) empiric evidence or rationale in favor of its utility (i.e., purported/ expected benefit) and on *contemporary and quick R-B assessment* – risk associated with use of the medicine *versus* the risk of not allowing EUA (risk of the disease being not treated by the drug at all).
- Employed during a state of public health emergency or a material threat of any kind, in absence of adequate, approved, available alternatives

# Emergency Use Authorization

- The decision is certainly based on a *contemporary and quick R-B assessment* – risk associated with use of the medicine *versus* the risk of not allowing EUA (risk of the disease being not treated by the drug at all).

# Compensation Issues

# Medical Management of Injury in Trial Participants in India

**# 40. Medical Management in clinical trial or bioavailability and bioequivalence study of new drug or investigational new drug.—**
(1) Where an injury occurs to any subject during clinical trial or bioavailability and bioequivalence study of a new drug or an investigational new drug, **the sponsor, shall provide free medical management** to such subject as long as required as per the opinion of investigator or till such time it is established that the injury is not related to the clinical trial or bioavailability or bioequivalence study, as the case may be, whichever is earlier.
(2)The responsibility for medical management as referred to in sub-rule (1), shall be discharged by the sponsor or the person who has obtained permission from the Central Licensing Authority. ....."

***Ref: ND&CT Rules, 2019 Govt of India***

# Relatedness Assessment of Injury/Death in Trial Participants in India

**# "41. Consideration of injury or death or permanent disability to be related to clinical trial or bioavailability and bioequivalence study.— Any injury or death or permanent disability** of a trial subject occurring during clinical trial or bioavailability or bioequivalence study **due to any of the following reasons** shall be considered as clinical trial or bioavailability or bioequivalence **study related** injury or death or permanent disability, namely:-

(a) adverse effect of the investigational product;

(b) violation of the approved protocol, **scientific misconduct or negligence by** the sponsor or his representative or **the investigator** leading to serious adverse event;

(c) failure of investigational product to provide intended therapeutic effect where, the required standard care or rescue medication, though available, was not provided to the subject as per clinical trial protocol;

(d) not providing the required standard care, though available to the subject as per clinical trial protocol in the placebo controlled trial;

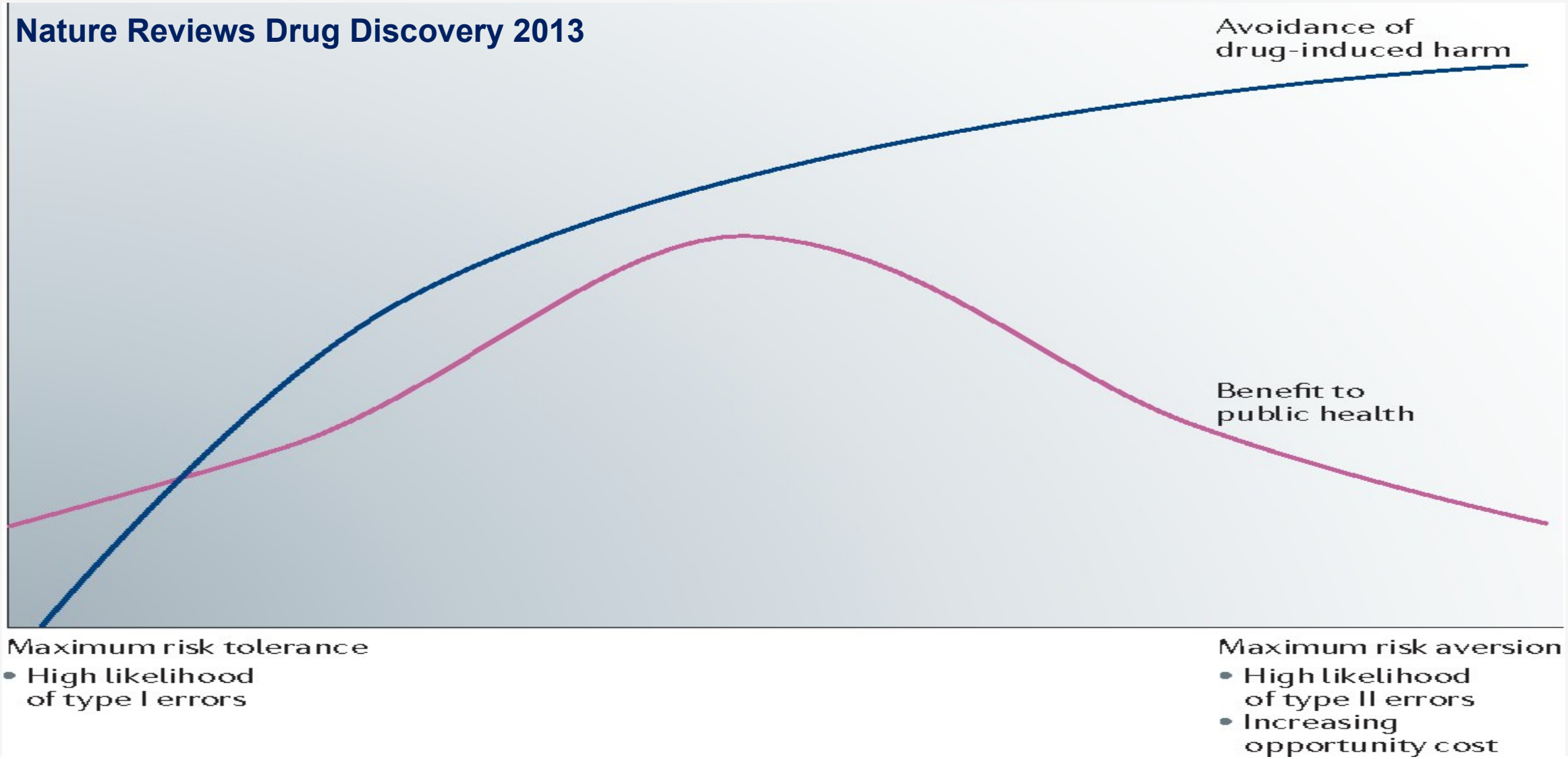
(e) adverse effects due to concomitant medication excluding standard care, necessitated as part of the approved protocol;

(f) adverse effect on a child in-utero because of the participation of the parent in the clinical trial;

(g) any clinical trial procedures involved in the study leading to serious adverse event.

***Ref: ND&CT Rules, 2019 Govt of India***

# Risks of Intense Risk Aversion by Regulators in Reference to Approval of New Drugs/Vaccines



# Thank You !!!