# Gaps and opportunities in moving candidate vaccines from Pre-clinical studies to phase I clinical trial

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| Vaccine R & D | Examples: Laboratory research |
| --- | --- |
| • Seed & Ag development<br>• Pre-clinical studies<br>• Clinical studies | • Characterization<br>• Testing on safety, immunogenicity in vivo & in vitro<br>• Testing subject's specimen (Ab, CMI, MI, disease diagnosis), defining correlate of immunity<br>• Assays development |

# Important points of vaccine R&D

- The lab research should be conducted in line with the regulatory concept and procedure.
- Assays used need to be validated/ standardized .
- The research results must be reliable and should be interpreted in combination with the knowledge on vaccine characteristics and experiences in the past.

# Pre-clinical studies of vaccines

- To ensure safety and immunogenicity in animal model
- Quality management system: OECD-GLP requirements

# Preclinical studies (1)

- Characterization
- Immunogenicity/ pharmacodynamic studies provide
  - "Proof of concept" information for clinical development plan
  - Information to guide selection of the doses, schedules and routes of administration in clinical trials
  - HIR & CMIR (e.g. neutralizing antibodies, opsonophagocytic activity, sinterference between antigens, etc.)

Note: Animal models frequently fail to predict immunogenicity and efficacy in humans. It may be used in to measure the potency of vaccine if appropriate.

# Preclinical studies (2)

## Safety assessment : Toxicity assessment

- Basic toxicity assessment : single dose, repeated dose, (+ local tolerance):
  - Dose used should be equal or more than SHD
  - Animals used should be more than one species
- Additional toxicity assessment
  - Special immunological investigations

    To investigate immunological aspects of toxicity (e.g. precipitation, autoimmune pathology, etc.)

# Preclinical studies (3)

- Additional toxicity assessment
  - Developmental and reproductive toxicity studies
  - Genotoxicity and carcinogenicity studies
  - Safety pharmacology

    To investigate the effects of the candidate vaccine on vital functions (e.g. central nervous system, respiratory, cardiovascular and renal functions)
  - Pharmacokinetic studies:

    Novel adjuvants, alternative routes of administration

# Preclinical studies (4)

- Special considerations: adjuvants, additives, vaccine formulation and delivery device, alternative routes of administration
- Specific considerations for particular types vaccines: live attenuated vaccines, combined vaccines, etc.

# Mandatory requirements for QMS in Preclinical studies

- OECD-GLP for Safety Assessment only
- OECD-GLP
  - Characterization (in vivo & in vitro)
  - Animal test for safety

# Basic OECD Principles of GLP (1)

GLP

promotes

Quality and Validity

of test data

# Basic OECD Principles of GLP (2)

MAIN GOAL : To help scientists obtain results which are:

- Reliable
- Repeatable
- Auditable
- Recognized by scientists worldwide
- The purpose is not to assess the intrinsic scientific value of a study
- GLP principles are a set of organizational requirements

# Basic OECD Principles of GLP (3)

## GLP Aim

To make the incidence of

## False Negatives

more obvious

(e.g. Results demonstrate non-toxicity of a toxic substance)

# Basic OECD Principles of GLP (4)

- Limit waste resources
- Ensure *high quality* of results
- Ensure *comparability* of results
- Promote mutual recognition of results

(Preamble to Directive 87/18 EEC)

# Basic OECD Principles of GLP (5)

Defines conditions under which studies are

- Planned
- Performed
- Recorded
- Reported
- Monitored

# Basic OECD Principles of GLP (6)

## Five Basic Points

1. **RESOURCES**: Personnel, Facilities & Equipment
2. **RULES**: Guidelines, Procedures Protocols/Study Plans
3. **CHARACTERIZATION**: Test Article, Identification, Quality Test System
4. **DOCUMENTATION**: Raw data, Final Report, Archives
5. **QUALITY ASSURANCE**: Audit/Inspection - Training - Advice

# Gaps in pre- clinical studies (1)

- Limited experience in study design of toxicity studies and abnormal investigation
  - Animal model
  - Route of administration
  - Delivery device
  - Analysis of results
- Lacking of appropriate animal model
  - Limited service

# Gaps in pre- clinical studies (2)

- Limited experience in vaccine characterization as per regulatory requirements
- No testing facility is certified according to OECD-GLP requirements
- Lacking of veterinary pathologist who has experience in vaccine development
- National OECD-GLP certifying body has not been completely recognized by OECD members.

# Opportunities in moving from pre-clinical study to phase I clinical study (1)

- Lesson learned from Influenza vaccine development
- Interest of Academies in investment of testing facility to comply to OECD-GLP
- The national certifying body has established the OECD-GLP certifying scheme and applied to be OECD recognized members
- Thai FDA has established the pilot project for providing guidance on the regulatory requirements from R&D to licensing.

# Opportunities in moving from pre-clinical study to phase I clinical study (2)

- Research & development of vaccines and biological products is included in the national strategic plan 2017-2021
- NVI acts as national coordinator in vaccine area
  - HRD
  - Develop National strategic plan
  - Provide financial support on vaccine R & D
  - Coordinate networks to stimulate vaccine R&D
- OECD has accepted to inspect test facility certifying process and performance
- There are animal facilities complied with AALAC requirements

Thank you