

Dr Dipesh Tamrakar

- **Dr Dipesh Tamrakar** is an Associate Professor in the Department of Community Medicine, KUSMS. He is an infectious disease epidemiologist with extensive experience in disease burden estimation, sero-surveillance, and clinical trials related to infectious diseases. He also serves as the Member Secretary of the KUSMS Institutional Review Committee (KUSMS-IRC)

Operational Challenges of Conducting a clinical trial in Nepal

Dr Dipesh Tamrakar

Associate Professor, Community Medicine

Kathmandu University School of Medical Sciences

Contents

- Clinical trials in Dhulikhel Hospital
- Challenges during Regulatory Approval
- Challenges during Study Start-up and Recruitment
- Challenges during Follow-up and Study Conduct
- Conclusion

CLINICAL TRIALS IN DHULIKHEL HOSPITAL

2019 ONWARDS

IVI-T003
Statin study

2019
To evaluate the non-inferiority of the immunogenicity of the Vi-DT vaccine compared to the Vi-TT vaccine

Statins and Progression of Rheumatic Heart Disease: A Feasibility Study.

2021

To evaluate the immune non-inferiority and safety of OCV-S compared to Shanchol™ in healthy Nepalese participants aged 1 to 40 years old

To assess the efficacy, safety, and immunogenicity of two CoV preS dTM – AS03 vaccines (monovalent and bivalent) in adults 18 years of age and older in a multi-stage approach.

OCV-S
VAT00008

GBP510_004
KICC STUDY

2022
Heterologous Booster Vaccination of a SARS-CoV-2 Recombinant Protein Nanoparticle Vaccine (GBP510) adjuvanted with AS03 in Adults Aged 18 Years and Older

The effectiveness of Ketotifen fumarate and Indomethacin for improving clinical measures of respiratory function and /or resolution of COVID-19 symptoms

2023

To characterize immunologic biomarkers among vaccinated individuals from the Euvichol-S Phase III trial.

LTFU-OCVS

VAD00004

2024
To evaluate the efficacy, immunogenicity, and safety of a respiratory syncytial virus vaccine in infants and toddlers (PEARL)

Challenges during Regulatory Approval

Ethical regulation process in Nepal

Proposal submission to Nepal health research council(NHRC)

Review of proposal

Approval from NHRC

Approval from Department of drug Administration(DDA)

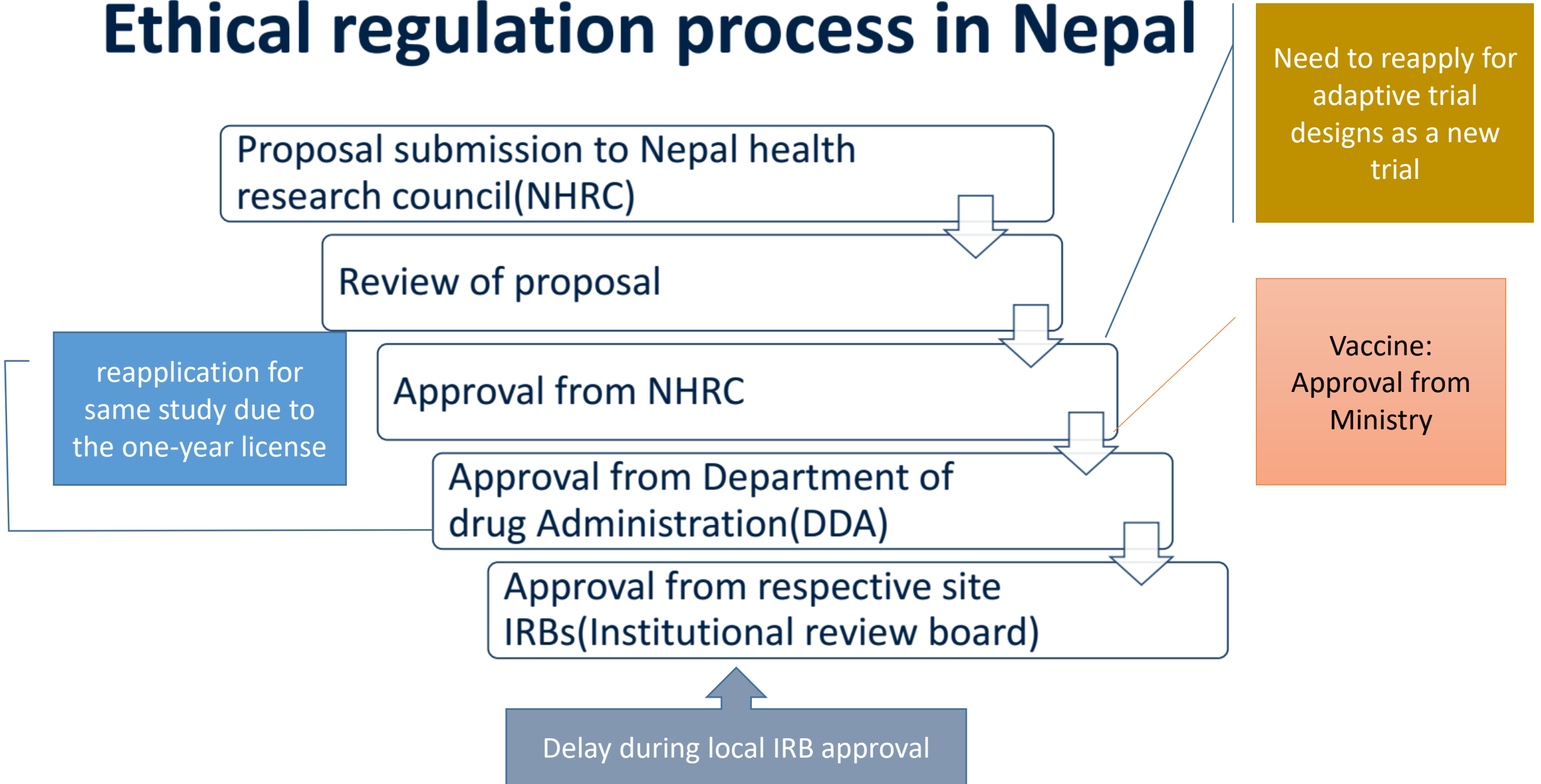
Approval from respective site IRBs(Institutional review board)

Delay during local IRB approval

reapplication for same study due to the one-year license

Need to reapply for adaptive trial designs as a new trial

Vaccine:
Approval from Ministry

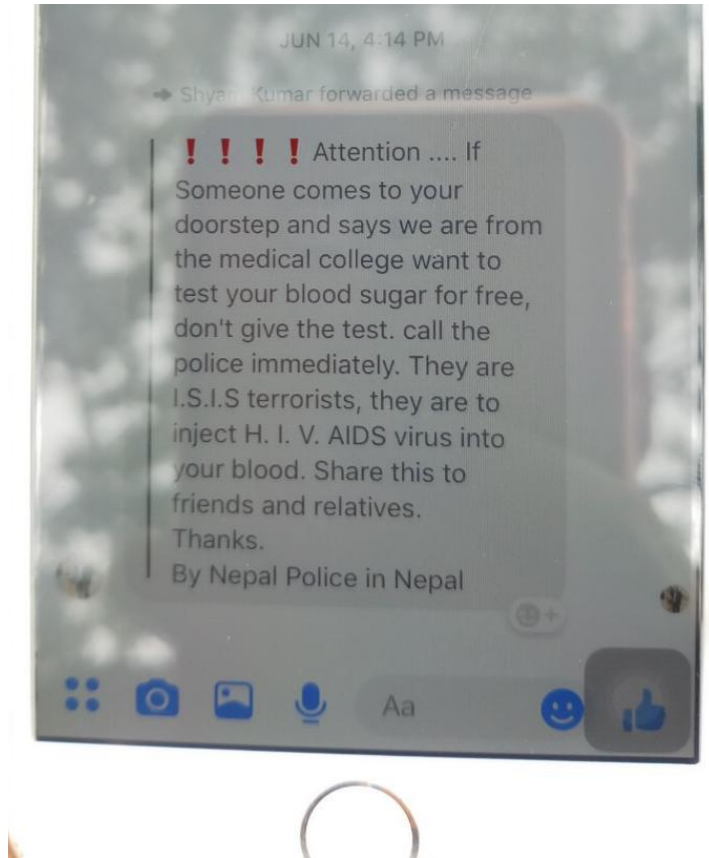


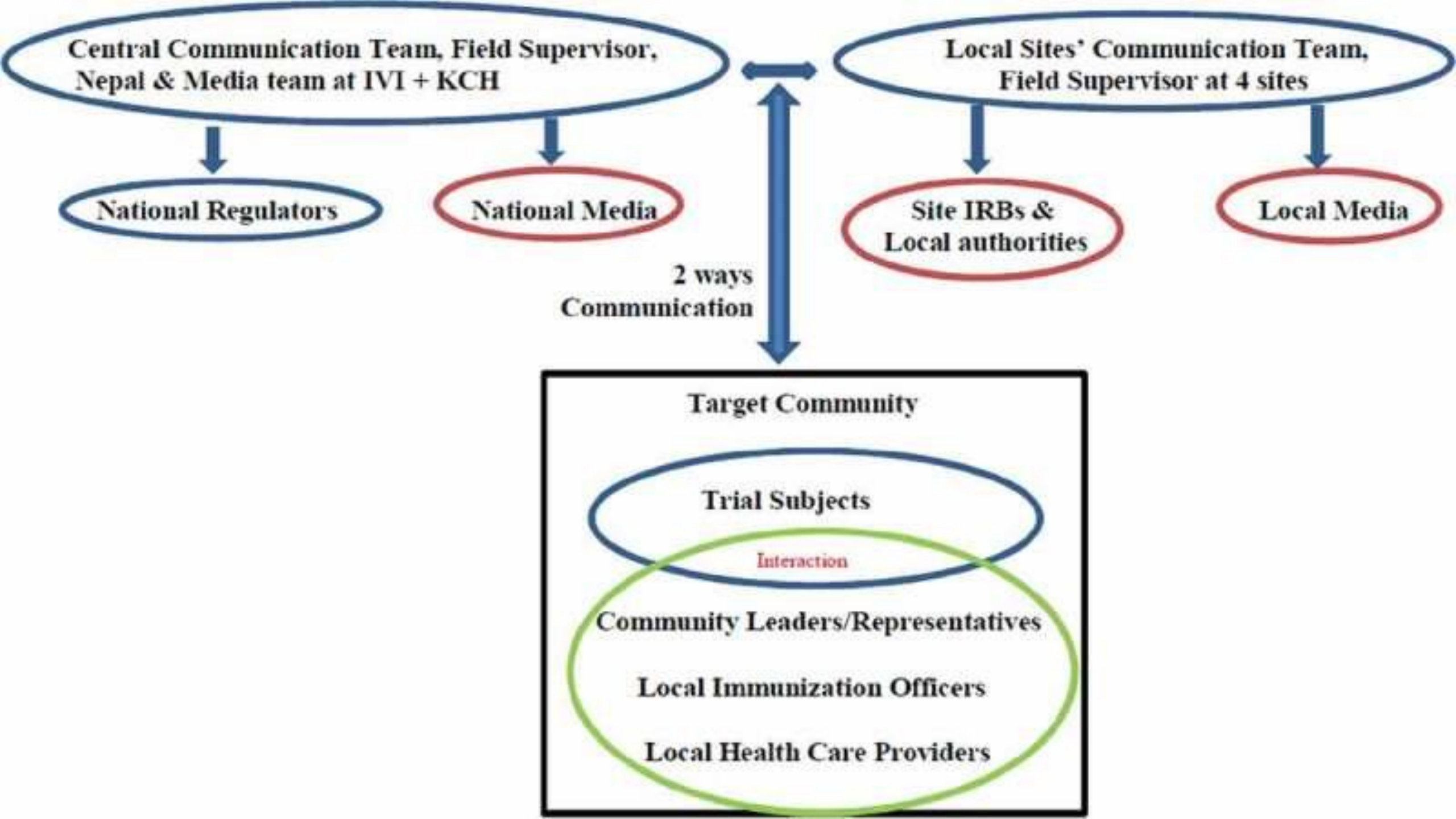
Challenges during Study Start-up and Recruitment

- Stigma and Fear regarding clinical trial
 - At Institutional Level
 - At Community Level



Typhoid Conjugate Vaccine test in Nepali children: Is Nepal a lab?





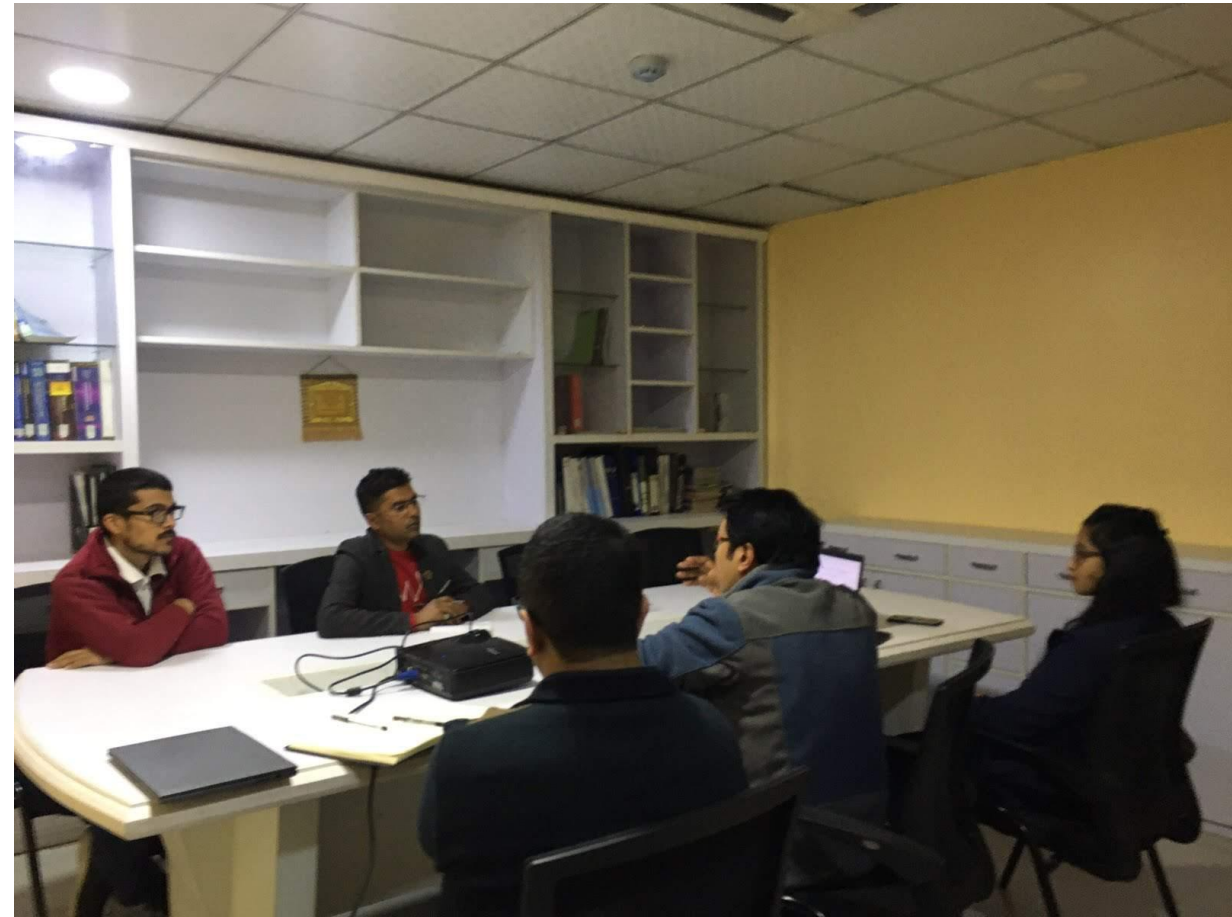


Faculty Orientation

Local
Stakeholder
Orientation



Media Personal Orientation



Challenges during Study Start-up and Recruitment

- Stigma and fear regarding clinical trial
 - At Institutional level
 - At community level
- Site preparedness and Operational readiness

2019

Activity	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec		
Central Training	<ul style="list-style-type: none"> Basic knowledge of clinical trials Site PI and study coordinator from each site & Government officials 3 times (combined for all sites) 										SIV/IM ★	★ Enrolment starts
Site Specific Training				<ul style="list-style-type: none"> Operational aspects of clinical trials in addition to the basic training All sites staff 3 times per site 								
Mock Drills /Dry Run				<ul style="list-style-type: none"> Simulate real situation of the trial as per study protocol operation manual and site-specific SOPs All sites staff 3 times per site 								
Hands on Training				<ul style="list-style-type: none"> Real experience of know how Site CRC, lab personnel/study nurses and Field Supervisor 1 time per site 								
Contracted Services				<ul style="list-style-type: none"> ★ Contracting CRO <ul style="list-style-type: none"> Clinical Trial Monitoring Site Management Clinical Trial Supply Management 								
Hiring Local Site Management Coordinators				<ul style="list-style-type: none"> Experienced in clinical trials Involved in training Responsible for Site Management 								
Stakeholders Engagement				<ul style="list-style-type: none"> Stakeholders Engagement (e.g., Local authority, Community Leaders, Media, ...) 								

Pharm

tor

V

Challenges during Study Start-up and Recruitment

- Stigma and fear regarding clinical trial
 - At Institutional level
 - At community level
- Site preparedness and Operational readiness
- Inclusion/exclusion criteria vs real-world population

Challenges during Follow-up and Study Conduct

- Loss to Follow-up

Proper consent and counselling



Transport facility



Trust building



Medical insurance



Challenges during Follow-up and Study Conduct

- Loss to Follow-up
- Maintaining Data quality

Date: 14 Feb 2020

Visit Strata	V2	V3	V4	V5	V6	Remarks
D3-	D3-250	D3-219	D3-158			2454 SF=10 +1
	D3-251		D3-160			
	D3-252	D3-221	D3-162			
	D3-258	D3-222	D3-163			
	D3-254	D3-223				
D2-	D2-137	D2-108	D2-055			139 SF=3
	D2-138	D2-109	D2-056			
	D2-139	D2-110	D2-057			
		D2-112	D2-058			
		D2-224				
		D2-118				
TOTAL:						393

Medication taken fill below details

N o.	Medication Name	Dose	Unit	Frequency	Route	Prophylactic medication	Start Date	Stop Date	Ongoing	Indication
1.	Syn. Aspirin 25mg	5	ml	Once a day	Oral	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	10 / Feb / 2020	14 / Feb / 2020	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Sore Throat and Fever
2.	Syn. Paracetamol 30mg	5	ml	Twice a day	Oral	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	10 / Feb / 2020	18 / Feb / 2020	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Cough
3.	Chlorpheniramine + Dextromethorphan (10:4:3)	2.5	ml	Once a day	Oral	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	10 / Feb / 2020	18 / Feb / 2020	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Cough



Conclusion

- Community and stakeholder engagement is critical for successful trial
- Anticipation and Preparation should be there for potential challenges rather than reaction to challenges
- “Operational excellence is as important as scientific rigor”

Thank you

