Adopting new technologies: Regulatory challenges and support platforms in LMICs

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New platforms need a clear regulatory pathway

- WHO TPP-May 2020
- FDA guidance-June 2020
- CDSCO-September 2020

- In general similar guidance on safety, immunogenicity and efficacy
- China, Russia and India gave some form of approval prior to even interim data on efficacy

- All studies depended on a placebo/comparator vaccine

But what is the path now that vaccines are approved for use?

- Can placebo controlled trials be done?
  - Some discussion on whether countries with low coverage in Africa will permit/want to have placebo controlled trials to fast-track testing
- In the absence of placebo controlled trials, what are the possible approaches?
- Superiority vs a partially effective vaccine with disease endpoint
  - New vaccine anticipated to have high efficacy
  - Run trial in locations where partially effective vaccines the only option
- Non-inferiority trials with disease endpoint
  - Compare new vaccine to a licensed vaccine
  - Show new vaccine is not appreciably worse than licensed vaccine
- • Immuno-bridging
  - Establish that an immune response (antibody) is reasonably likely to predict efficacy on a disease endpoint
  - Conduct an immunogenicity study to demonstrate sufficiently high immune response
  - Possibly link immuno-bridge to confirmatory efficacy or effectiveness study

Immune bridging is most likely approach, but what constitutes an appropriate study needs clarification

- Premise is vaccine induced antibody from new vaccine is reasonably likely to predict high Vaccine Efficacy-How?
  - Have mechanism of action similar to licensed vaccine
  - Possibly demonstrate protection and Ab/protection relationship in animal models
  - Cite other studies that demonstrate antibody's importance
  - Immunogenicity studies demonstrate antibody levels similar or greater than licensed vaccine with high efficacy
- Have a correlate of protection or a surrogate correlate of protection
  - Who decides?
  - Role of ECBS

Support platforms in LMICs

- Availability of comparator vaccines
- Pre-clinical testing
  - Animal models
- Clinical trial platforms
  - Mainly part of internationally funded networks
  - Issues with recruitment, follow up, outcome assessment, ability to handle AEs
- Clinical assay platforms
  - Assays-beyond antibodies-need for shedding? Memory B? T cell responses?
  - Standardization of methods and access to approved/accredited assays-CEPI
  - Use of international standards-NIBSC and secondary standards