Endemic country regulatory perspective on emergency vaccines against ZIKV (according to current TPP)
Current Scenario

WHO declared a cluster of microcephaly and other neurological disorders and their possible association with ZIKV, a Public Health Emergency of International Concern (PHEIC) – February, 2016

A Target Product Profile was drafted and sent forth to public consultation, which ended in May, 23rd

Brazil*:
7723 reported cases of microcephaly (until May, 28th)
• 1489 were linked to ZIKV
• 3072 were not linked to ZIKV
• 3162 remain under investigation.

*Epidemiological Bulletin of Microcephaly nº 28 (Epidemiologic week 21/2016), MoH
Challenges regarding ZIKV

• Many uncertainties;

• Urgency/emergency scenario;

• Lack of vaccines and therapeutics;

• Risk/Benefit evaluation.
TPP – Regulatory Perspective

• Overall, the drafted TPP seems to be in-line with what we would expect

• Future policy recommendations, to be derived from it, will be major milestones on promoting multi-regional understanding on evaluation criteria and protocol approval

• Anvisa counts on agreements and partnerships (ICMRA, FDA, WHO) to improve alignment and cooperation
  • Currently, Anvisa is leading cooperation networks such as the Zika Virus Network and the Global Health Crisis management framework (nested in ICMRA)
TPP – Current Regulatory Perspective

• Reduction of target population age to >9 yo likely to be very important in Brazilian context
  • Higher rates of pregnancy between 10-14 yo -> 393,370 women between 10-17 yo had children in a 12-mo reference period, 37,180 on 10-14 yo population (~9.45%)*

• Confounding factors from exposure to other flaviviruses to be considered (10+ types, interactions unknown, YF vaccination in some endemic areas)
  • Challenge studies are unlikely to be run in Brazil

• Surveillance for GBS should be present at all times

*data from 2010 Census (http://goo.gl/ZMz59h)
TPP – Current Regulatory Perspective

• Evaluating efficacy from neutralizing AB titers (if clinical endpoints are unfeasible) is still being discussed, specially considering previous DENV vaccine data, where high titers were not linked to protective efficacy as expected

• Robust ReproTox data from most appropriate animal models, as feasible

• IVD issues – validation, standardization are key issues bo the solved before moving into clinical trials
TPP – Regulatory Perspective

• Regulation regarding new approvals for vaccines:
  • **RDC 09/2015** – Drug Clinical Development Dossier (*DDCM*): **IND-like** submission for Protocol, Development Plan, CMC and related documentation
  
  • **RDC 55/2010** – MA for biologics, including vaccines
  
  • **RDC 37/2014** – Prioritization for MA, DDCM and in-vitro dx
    • 45d for DDCM, 75d for MA
    • Certainly applicable to ZIKV
RDC 09/2015

- Investigational Drug Development Plan
- Investigational Drug Dossier (CMC)
- Investigator’s Brochure
- CT Protocols

RDC 39/08
Accelerated Approval Possibilities

- Prioritization for evaluation through RDC 37/2014
- Emergency scenario: “Rolling submission”
- IMPD, CTD corresponding sections are acceptable
- No official emergency use authorization regulation in place
- Approvals are bound by RDC requirements
Regulatory advices for candidate Zika products

• Dialogue/schedule meetings with Anvisa;

• Narrow the distance between the development process and Anvisa (DDCM, regularly update documents);

• Transparency;

• Share info being discussed with other agencies.
Good experiences learned with Dengue Vaccines

- Meetings with manufacturers were overall very informative;

- Cooperative relationship and coordination between Clinical trials authorization and Marketing authorization area – gaps are being narrowed;

- Participation in international discussion groups: DCVRN (WHO), DVI;

- Discussion with other regulatory agencies;
Good experiences learned with Dengue

• Dengue Vaccine Initiative
• Consortium of four organizations: International Vaccine Institute, WHO, International Vaccine Access Center, Sabin Vaccine Institute.

• Mission: To encourage the development and consideration of vaccines to prevent dengue.

• DVI is focused on using the knowledge and expertise of its members to accelerate the development and country consideration of a dengue vaccine.

• Outcomes: Discussion with experts, interchange experience with other countries, sharing scientific publication.
Key considerations

- Cooperation;
- Prioritization;
- Transparency;
- Scientifically-driven development;
- Speed without loss of quality;
  - Protect the safety, welfare and rights of CT participants;
  - Scientifically sound CT so that they can generate interpretable results
- Discussion with stakeholders: NRAs, WHO, Manufacturers, EC.
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THANK YOU