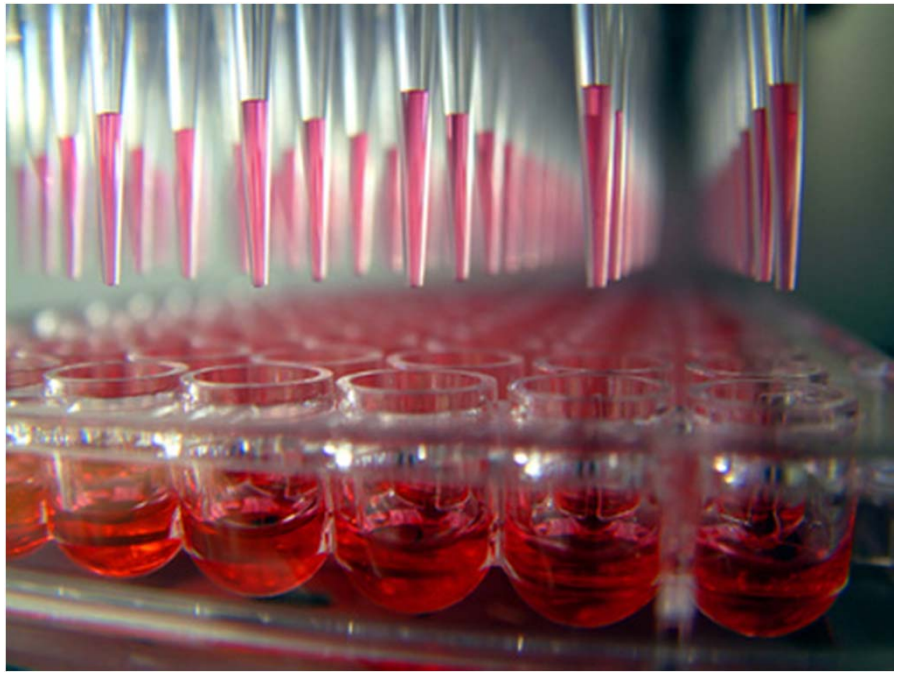
Regulatory Assessment of IVDs for the Diagnosis of Zika Virus in Brazil



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Office of *In Vitro* Diagnostics

ANVISA

Rio de Janeiro, 19 April 2016

National Health Surveillance System

ANVISA – Regulatory Agency

Integrated with the public healthcare system
Sistema Único de Saúde (SUS)

Established by law in 26 January 1999 – Lei nº 9.782

Products Regulated by the Office of IVDs – GEVIT

- *In Vitro* Diagnostics Medical Devices
  - Reagent kits, calibrators and controls for analytes available on human specimens
    - Proteins
    - Nucleic acids
    - Pathogens
    - Immunoglobulins
    - Metabolites
    - Drugs
    - Other substances
  - Instruments
    - Analysers
    - Sample preparation

Main Tasks

- Analysis of submissions for registration, notification, renewal, changes and cancellation of IVDs;
- Technical reports to:
  - Departments of Anvisa;
  - Ministry of Health;
  - Public organizations;
  - Users, laboratories and healthcare professionals.
- Answer questions regarding the importation of regulated products to Anvisa inspectors on borders;
- Issuance of IVDs registration requirements;
- Support to Good Maufacturing Practices inspections for certification processes.

Applicable Regulations

- RDC ANVISA 36/2015
  - Registration and notification (“cadastro”) of IVDs
    - Lower risk products (classes I and II) – “Cadastro”
    - Higher risk products (classes III and IV) – “Registro”
  - Risk classification rules
    - Based on GHTF proposal
  - Documental requirements for submission
  - Labelling requirements (including Instructions for Use)
    - Professional or Point of Care User
    - Lay user
  - Technical Dossier
    - Based on the IVD Market Authorization Table of Contents (IMDRF)
  - Good Manufacturing Practices Certification
    - RDC ANVISA 16/2013

Applicable Regulations

- Technical Dossier
  - Product description based on intended use
  - Risk Management
  - Performance Studies
    - Accuracy of measurement
    - Analytical sensitivity
    - Analytical specificity
  - Stability Studies
    - Claimed shelf-life
    - In use stability
    - Shipping stability
  - Clinical Performance
  - Labelling
  - Production flow

Applicable Regulations

- Laboratory Evaluation ("Análise Prévia")
  - Instituto Nacional de Controle de Qualidade em Saúde
  - Kits tested against comercial serological panels and qualified panels developed by the laboratory reflecting the epidemiologic reality in Brazil, including seroconversion samples
  - IVDs submissions that requires "Análise Prévia":
    - Chagas disease
    - HBV
    - HCV
    - HIV
    - HTLV
    - Syphilis
    - Immunohematology reagents

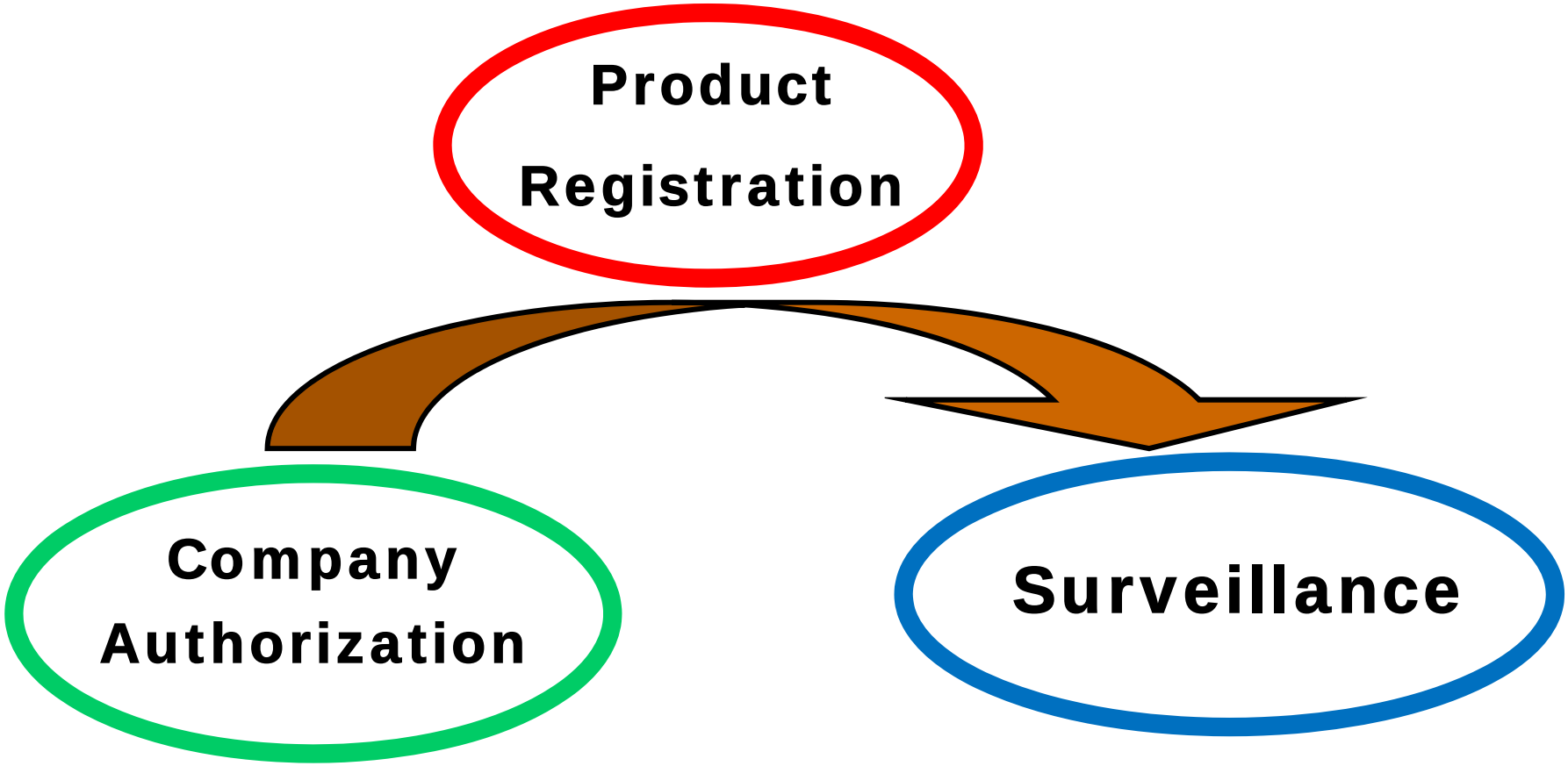
Zika IVDs

- Increased number of reported cases of microcephaly in the northeast of Brazil

- Director of Authorizations and Registrations decided on mid January:
  - To prioritize (fast-track) the analysis of submissions for Dengue, Chikungunya and Zika IVDs

- 4 product submissions were reviewed in January-February and considered minimally satisfactory
  - RT-PCR for Zika Virus
  - Indirect Immunofluorescence (IIFT) Mosaic for IgG – DENV-1, DENV-2, DENV-3, DENV-4, CHKV and ZIKV
  - Indirect Immunofluorescence (IIFT) Mosaic for IgM – DENV-1, DENV-2, DENV-3, DENV-4, CHKV and ZIKV
  - Immunocromatographic Rapid Test for IgG and IgM for Zika Virus

Sanitary Control of Medical Devices



Zika IVDs

- Concerns raised during the review of dossiers:
  - Low number of positive confirmed samples
  - Samples obtained in different regions
    - Same strain available in Brazil?
    - Would affect sensitivity?
  - Cross-reactivity with Dengue virus

Zika IVDs

- Anvisa requested studies to evaluate cross-reactivity and interference with known positive samples for Dengue Virus of all four serotypes

- Validations performed by the brazilian representatives in private laboratories being followed by Anvisa

Zika IVDs – Perspectives

- Intention to extend the collaboration with Instituto Nacional de Controle de Qualidade em Saúde
  - Inclusion of Dengue and Zika virus to the “Análise Prévia” scheme (Laboratory Evaluation)
  - Obtain and validate positive samples for Zika virus
  - Reference materials?

INCQS
Instituto Nacional de Controle de Qualidade em Saúde

- Adopt WHO recommendations for review of future submissions


Thank you
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