The Brazilian Experience in Pharmacovigilance

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REGULATORY RELATIONSHIPS
Pre-Marketing Time  Post-Marketing Time

Clinical Trials Assessment
Safety Issues
Pharmacovigilance

Drug Registration
Safety/ Rational Issues
Laboratory Assays
Batch Release

Quality Inspection
Laboratory Assays

Pharmacovigilance
Major Aims
• early detection of unknown safety problems
• detection of increases in frequency
• identification of risk factors
• quantifying risks
• preventing patients from being affected unnecessarily

Laws Framework of Vaccines and Pharmacovigilance
Constitution – art. 197

Pharmacovigilance Laws and decrees
• Law 6360/76 – creation of Products and Services Public Health Surveillance System
• MH Resolution (CNS) 3/89 – Institution of Pv System
• National Drug Policy – Decree n 391/98
• Law n 9782/99 – Anvisa’s creation
• M. Health decree 696/MS – 2001 – National Center creation (CNMM)
• Anvisa’s Service Bulletin – nº 16 – 15/03/2007 – institution of Pharmacovigilance Office
• Anvisa’s resolution - RDC Nr 04/2009 Pv for Pharmaceutical Industries

Brazilian Pharmacovigilance system
Why do we need Risk Management?

- Many new drugs/new technologies in the marketing;
- Sub-standard products in the marketing;
- A large number of imported products and raw material.

Why Risk Management is a challenge?

- Lack of regulatory effort by some Governments
- Post-marketing surveillance is not a priority, but license.
- Not many resources and structure available for regulation
  - Human, materials, legal bases, regulatory legislations
- Limited expertise in Drug Regulatory Authority
  - Employees and lack of advisory committees
- Drug companies with limited resources
- Drug companies’ lobby
  - Risk Management resistance
- Good formation/information only in English.
  - Pharmacovigilance courses and literature

Brazilian Drugs Exportation and Importation data


Adverse Event Reporting System

Brazilian Adverse Event Reporting System

Vaccines
- Clinical Trials
- Medicines AE
- Medical products
- Medical equipment
- Diagnostic reagents
- Calorimetrics
- Sanitizer
- Fluid
NOTIVISA

Codes:
- Product:
  - ATC-WHO
- ADR:
  - WHO-ART
  - MedDRA/WHO-ART Bridge
- Therapeutic indications:
  - ICD 10

SENTINEL HOSPITALS NETWORK

- Maintenance of 224 high complexity hospital network, able to report adverse drug reactions and other problems

SENTINEL HOSPITALS - COMPONENTS

Problems with Medicines? Call for the Pharmacist

Brazilian cases exemples of drug-related problems

QUALITY DEVIATION PROBLEM AND REGULATORY INTEGRATION

Brazilian Case Example

Date: May of 2003
Product: barium sulphate, 150g
Use: x-Ray for esophagus and stomach
Route: Per oral

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CASE EXAMPLE
QUALITY DEVIATION PROBLEM (CELOBAR)

ADR: hypokalemie, cardiac and pulmonary arrest possibly leading to death
Number of cases: Around 200 disabilities reported and 22 deaths.
Geographic distribution: 6 states involved
Reaction onset: 10 minutes to 3 hours (mean 30 min)

INVESTIGATION:
Celobar® = 21g barium carbonate (7 times lethal dose)
First Death Patient and Celobar body concentration = 143 mg/Kg
Lethal dose = Around 3 grams*
*Source: POISINDEX, THOMSON MICROMEDEX, 2003:

Brazilian Risk Management Documentation

- Development of “Brazilian Guideline for Risk Management in Pharmacovigilance”
  - Health Authorities Document;
  - from 2006 to 2007 – 3 Regional Seminars;
- Creation of Macro flow for Brazilian Pharmacovigilance System;
- New rules for Industries – Phv Regulatory Resolution
  - including Phv Plan and RMP

Key points of new brazilian regulation in pharmacovigilance (RDC N# 04/2009)
New Brazilian Regulation in Pharmacovigilance

- Having a system of pharmacovigilance located in Brazil;
- Coordination of professional demonstrably qualified;
- Structure physical and documentary organization that meets the implementation of proposed activities;
- Have detailed document describing its system of pharmacovigilance implanted in the company.

New Brazilian Regulation in Pharmacovigilance

- There must be on pharmacovigilance communications without prior or simultaneous information to Anvisa;
- The actions adopted in Brazil or by regulatory agencies in respect of pharmaceutical product, safety should be communicated;
- Encourage Health professionals and consumers to be notified;
- Must do Risk Management Plan when asked for.

New Brazilian Regulation in Pharmacovigilance

Deadline for report:
- Life-threatening and death adverse reaction: 7 days from their knowledge;
- Other serious adverse reactions: 15 days from their knowledge;
- Non-serious adverse reaction expected to be incorporated into the PSUR.

New Brazilian Regulation in Pharmacovigilance

Primary Sources:
- Health professionals;
- Users with evaluation by a health professional;
- Users without individual assessment, but that generated safety signal.

Chapter 6 - Pharmacovigilance Plan and Risk Minimization Plan

- Article 11. Anvisa may request at the time of licensing, or at any time, the Pharmacovigilance Plans for pharmaceutical companies, describing the actions of routine or description of additional actions proposed for the monitoring of medicines.
- Article 12. May be required at the time of licensing, or any time for any product, in addition to the Pharmacovigilance Plan, a Risk Minimization Plan, where the situations that require additional action. In this plan the company should explain how will evaluate the effectiveness of their actions to minimize the risks of their products.
  - §1. The RMP referred to in this article aims to management of new risks in the post-registration or even monitoring of known risks in populations already studied. Also they aim to implement in situations where the product will likely use one that has not been studied adequately in pre-registration.
  - §2. In addition to routine pharmacovigilance, the RMP should submit a proposal based on methods pharmacoepidemiological for the assessment of critical points related to security medicine.
New Brazilian regulation in pharmacovigilance

- Inspections: programmatic or sporadic;
- It should be made self-inspection at least once a year;

The knowledge-driven model of decision-making

Data Collection
Analysis
Sorting/Selection
Interpretation
Weighing options
Interpretation
Weighing options
Interpretation

Decision
Judgement
Valuation

Knowledge
Information
Understanding


Thank you!

Brasilia - DF during sunset
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