Reliance, Virtual Inspections and Regulations – Brazilian strategies during Covid-19 Pandemic

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Topics

Introduction

Regulation

Working Flow

Results

Perspectives
Introduction

National Surveillance System

- **Federal**: Anvisa (regulation, inspection, lab analysis, registration, post marketing, cGMP)

- **Local**: VISA (inspection, marketing license)
Introduction

- Regulation / legislation
- Post-Marketing Surveillance
  - Inspection
  - Monitoring
  - Fiscal Analysis
  - Adverse Event
  - Epidemiologic Researches
  - Information, communication and education
Introduction

• Systematic observation
• Technical and scientific oriented
• Sanitary condition examination for premises, processes, products and transports
• International/National standards
• cGMP request vs routine basis
Regulation

RDC nº 301/2019
GMP requirements/guides

• Quality System, Periodic Quality Review, Top Management, Quality Indicator and Goals, Quality Manual, Quality Management, Attribution and Responsibilities
• Continuous Process Validation - QdD
• Quality Risk Management
• No retrospective validation allowed
• Reprocessing rejected products
• Efficacy evaluation after change control
• Process Analytical Technology (nondestructive analysis in lab)
Regulation

Resolution RDC nº 336, 30/jan/2020
Time to response in cGMP requirements

• 365 days to issue cGMP
• Non inspected or already inspected sites
• cGMP valid for 2 years
Resolution RDC nº 346, 12/mar/20
GMP Certification

• Extraordinary and Temporary Procedures and Criteria for cGMP
• GMP requests
• External information vs Anvisa reports (Reliance?)
Resolution RDC nº 346, 12/mar/2020

GMP Certification – Alternative Inspection Tools

- Remote Inspection (virtual/desk)
- Replace on-site inspection
- Video streaming
- Document evaluation
- Online tour on facilities
Resolution RDC nº 346, 12/mar/2020

GMP Certification – “One Way Reliance”

- Pharmaceuticals and API: PIC/S
- Medical Devices: MDSAP
- API and Excipients: ECA Academy - Program to rationalize GMP inspection for API
Regulation

Resolution RDC nº 497, 20/may/2021
GMP Certification – Documentation 1st cGMP

- Anvisa and VISA inspection reports
- Audit Organization – Recognized
- Equivalent Regulatory Authorities (RA)
Resolution RDC nº 497, 20/may/2021

GMP Certification – Documentation for further cGMP

- GMP compliance history
- Technical complaints,
- Quality deviations or
- Sanitary infringements/violations
- Confidential information from RA
Regulation

Resolution RDC nº 497, 20/may/2021
GMP Certification – Automatic cGMP Renewal

- 270 to 180 days before cGMP expiration
- cGMP published even if the inspection is not performed yet.
Work Flow

- Manufacturer - Inspection History
- Products and Process – criticality and complexity
- Post Marketing – quality complaint and recall
- PIC/S – Already inspected by PIC/S RA
- Reliance – Mutual Recognition (Switzerland, Argentina, Uruguay, etc.)
Working flow

cGMP Request Evaluation

GMP inspection

Information Request

cGMP issuance

cGMP rejection
Working flow

Inspection Report for cGMP – During Pandemic

1\textsuperscript{st} – Remote Inspection

2\textsuperscript{nd} – PIC/S, MDSAP or ECA

3\textsuperscript{rd} – On site or RDC 336
\hspace{1em} (cGMP without inspection)
Remote inspections during pandemic

National – 1st choice

International – 1st choice

Investigation – 2nd choice
Working flow

Remote inspections steps

E-mail notification (optional)

- Manufacturers are informed about remote inspection and requested to confirm (not mandatory)

Preliminary meeting

- Virtual evaluations for video streaming and sharing documentation systems
- Agenda details (date, days, time zones, time for synchronic interactions)

Remote Inspection
Remote Inspections Agenda

GMP topic

- All GMP elements, or selected ones (history basis)

Synchronic Interactions

- Virtual tours on manufacturing (running), warehouse and labs
- Document, information and discussion

Document evaluation – desk documentation review
Working flow

Remote Inspections outcomes

Positive conclusion
• cGMP issuance

Negative conclusion
• cGMP Rejection
• Marketing Restrictions

On-site Inspections
Results

**Inspection numbers**

**2019 – 223 on site inspections (none remote inspection)**
- 102 domestic (64 pharmaceutical – 38 IFAs)
- 121 international (85 pharmaceuticals – 36 IFAs)

**2020 – 79 on site inspections (8 hybrid inspections)**
- 39 domestic (5 hybrid) – 28 pharmaceutical and 11 API
- 40 international (2 hybrid) – 35 pharmaceutical and 5 API

**2021 – 58 on site inspections (15 remote/hybrid inspections)**
- Planed and Performed
Results

Certification numbers

2020 - publications (per manufacturing lines)

• 1,417 cGMP for pharmaceuticals and biologics – 539 domestic
• 180 cGMP for API – 25 domestic

2021 – publications (per manufacturing lines)

• 967 cGMP for pharmaceuticals and biologics – 296 domestic
• 161 cGMP – 15 domestic
Perspectives

Remote inspections

- Temporary and Extraordinary — during the Pandemic
- Low risk facilities — case by case (depending on budget and personnel availabilities)
- Hybrid models — Must thing about.
- Report Review — No need for special evaluation (remote inspection replaces onsite inspection in every term)
• One way reliance – during the Pandemic
• PIC/S members – case by case after initial contact
• Mercosul, Switzerland, Cuba – Still working.
• Regulations – Guides are in discussion
Domestic Inspections

• Onsite inspection – working using safety protocols
• Hybrid inspection – Anvisa’s team by desk, Visa’s team by onsite inspection
• **Onsite inspection** – only for vaccines, Covid-19 supporting treatment and specific cases (complaint, risk of drug shortages)

• **Remote Inspection** – Anvisa tem by desk, Visa team by onsite inspection
Obrigado.
Thanks.

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