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)

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Introduction

Intervention Technologies

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

Introduction

Inspection

- 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 Responsabilities
- 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

Regulation

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?)

Regulation

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

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Regulation

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)

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Regulation

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

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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

cGMP Request Evaluation

- 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

1st – Remote Inspection

2nd – PIC/S, MDSAP or ECA

3rd – On site or RDC 336 (cGMP without inspection)

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Working flow

Remote inspections during pandemic

National – 1st choice

International – 1st choice

Investigation – 2nd choice

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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

Working flow

Remote Inspections Agenda

GMP topic

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

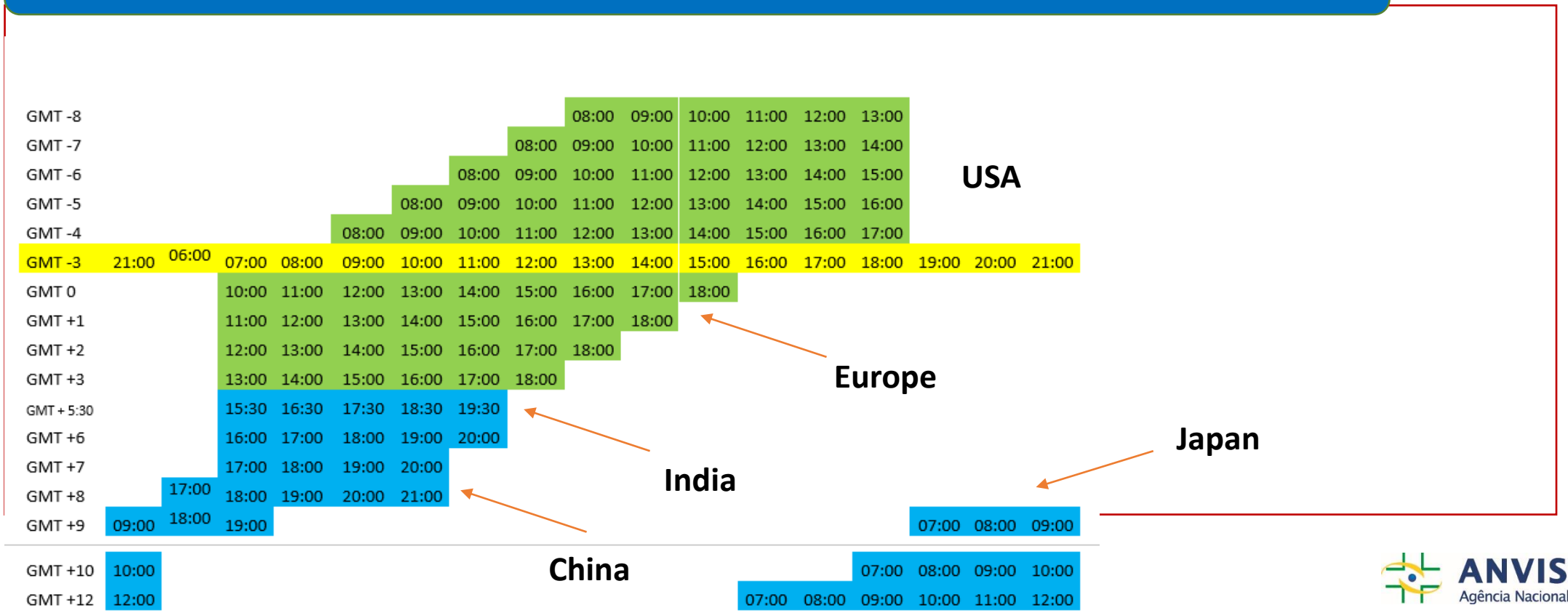
Synchronic Interactions

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

Document evaluation – desk documentation review

Working flow

Remote Inspections – Time zones



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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)

Perspectives

Reliance

- 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

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Perspectives

Domestic Inspections

- Onsite inspection – working using safety protocols
- Hybrid inspection– Anvisa's team by desk, Visa's team by onsite inspection

Perspectives

International Inspections

- 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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