ANVISA and the Brazilian Medicine Inspection System

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Office of Medicine and API Inspection - GIMED
Inspection General Office – GGFIS

Tokyo, November 16th, 2019

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Brazilian Health Regulatory Agency

Brazilian Pharmaceutical Market in Numbers

Year of Reference: 2018

- Worth U$ 23,24 Bi
- Is the 7th World Biggest Market
- Exported U$ 1,008,42.00
- Imported U$ 6,896,55.00

ANVISA

ANVISA's Engagement on International Regulatory Convergence Initiatives

ICMRA

Member since 2012: Better collaboration among Regulations.

World Health Organization

Active participation on:
. WHA;
. Working Groups;
. Share non-public information
(confidential agreement)

List of third countries with a regulatory framework applicable API equivalent to that in the Union, since 2015

ICH harmonisation for better health

Member since 2016: Update of regulatory Framework; Participation on new guidelines.

PIC/S

In the process of adhesion. Expectation to become member in 2020

Programme to rationalise international GMP inspections of active pharmaceutical ingredients/active substances manufacturers

Anvisa requested adhesion. Expectation to share and receive GMP inspection information, participate at joint inspection.

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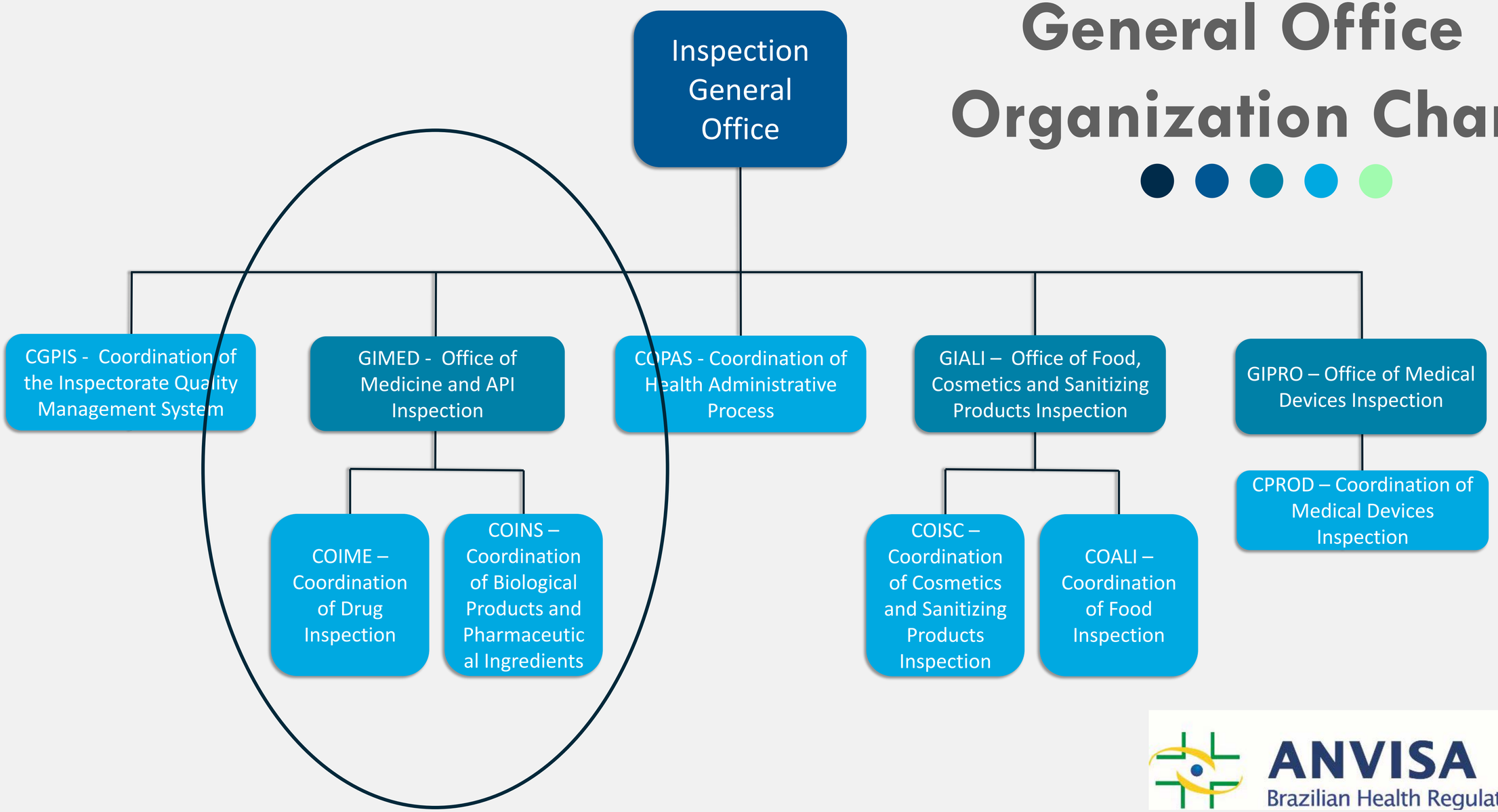
Inspection General Office Organization Chart



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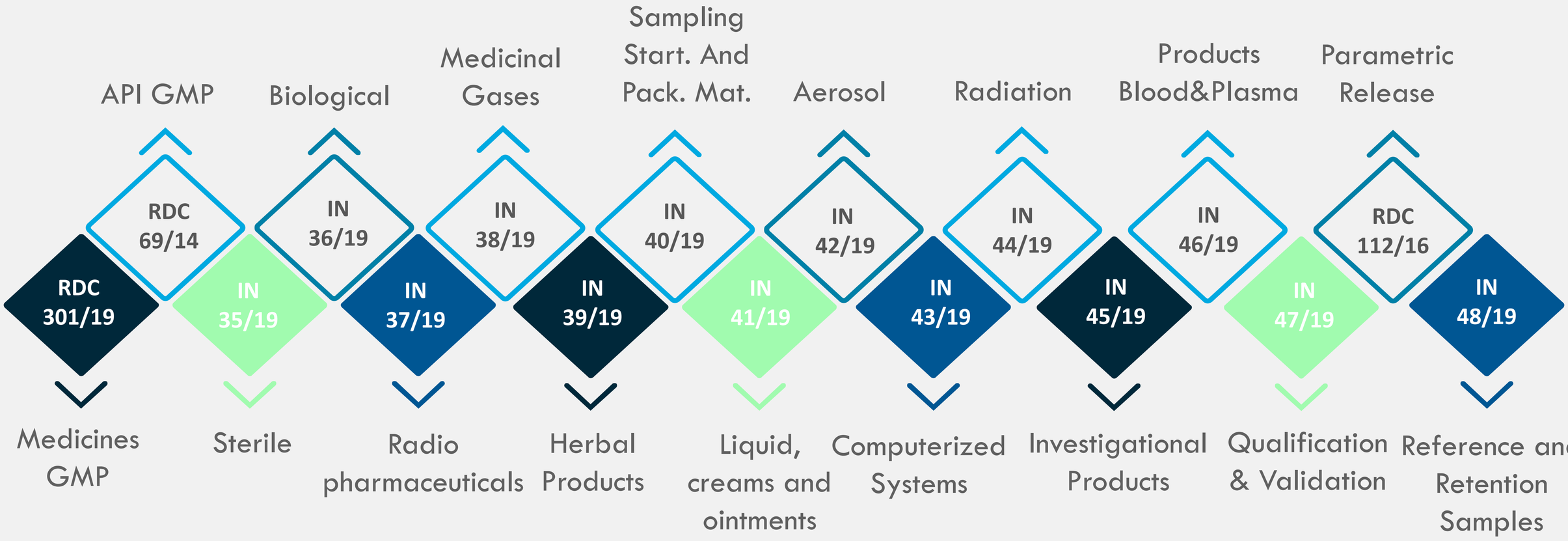
Regulation on Good Manufacturing Practices

Equivalent/Translation from PIC/S Guidelines



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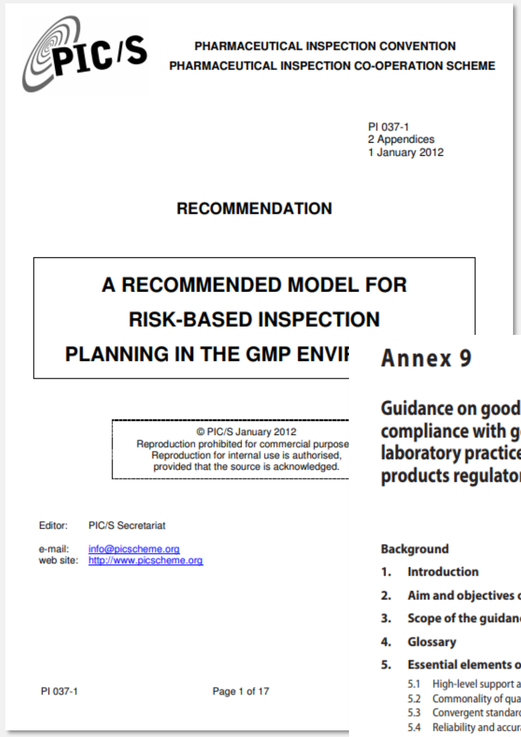
Risk Based Inspection Scheduling Procedures



PIC/S

PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

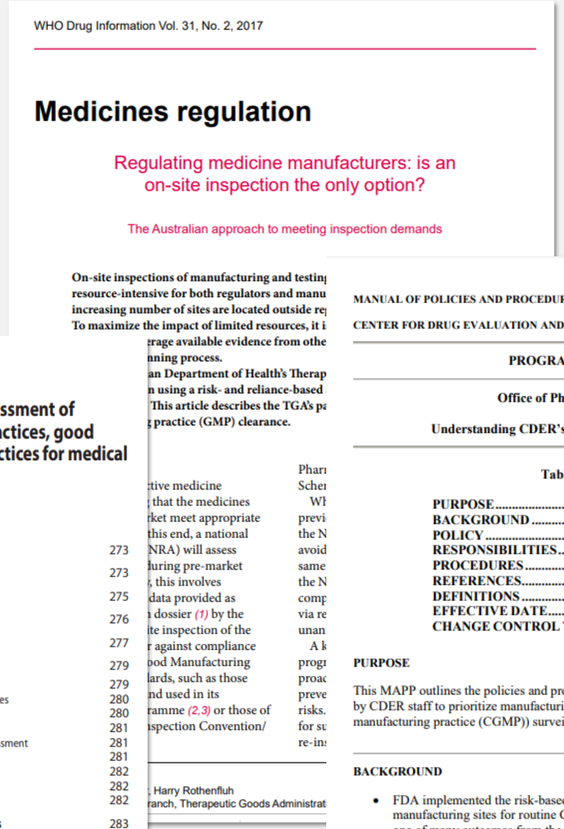
PI 037-1
2 Appendices
1 January 2012

RECOMMENDATION

A RECOMMENDED MODEL FOR
RISK-BASED INSPECTION
PLANNING IN THE GMP ENVI

Editor: PIC/S Secretariat

e-mail: info@picscheme.org
web site: http://www.picscheme.org



WHO Drug Information Vol. 31, No. 2, 2017

Medicines regulation

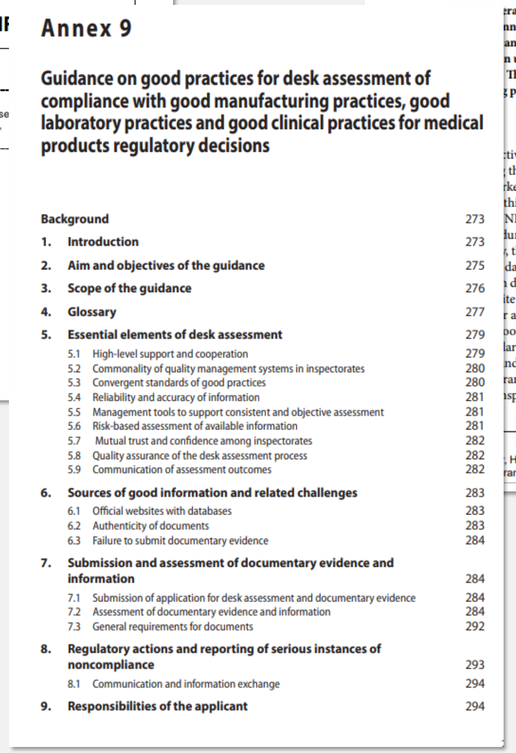
Regulating medicine manufacturers: is an on-site inspection the only option?

The Australian approach to meeting inspection demands

On-site inspections of manufacturing and testin
resource-intensive for both regulators and manu
increasing number of sites are located outside re
To maximize the impact of limited resources, it i
erage available evidence from othe
nning process.
an Department of Health's Therap
n using a risk- and reliance-based
This article describes the TGA's pa
g practice (GMP) clearance.

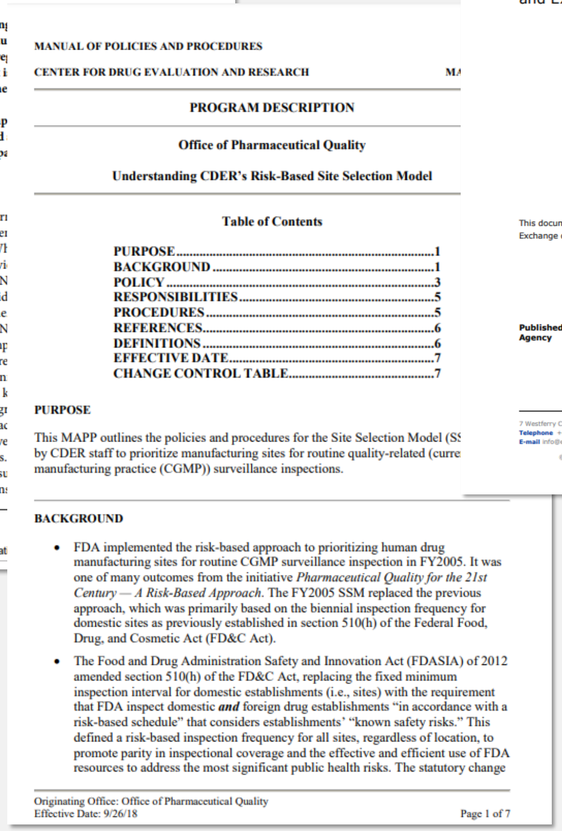
tive medicine
that the medicines
rket meet appropriate
this end, a national
NRA) will assess
luring pre-market
this involves
data provided as
dossier *(1)* by the
ite inspection of the
against compliance
ood Manufacturing
ards, such as those
nd used in its
ramme *(2,3)* or those of
spection Convention/

Harry Rothenfluh
ranch, Therapeutic Goods Administrat



Annex 9

Guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions



MANUAL OF POLICIES AND PROCEDURES

CENTER FOR DRUG EVALUATION AND RESEARCH MA

PROGRAM DESCRIPTION

Office of Pharmaceutical Quality

Understanding CDER's Risk-Based Site Selection Model

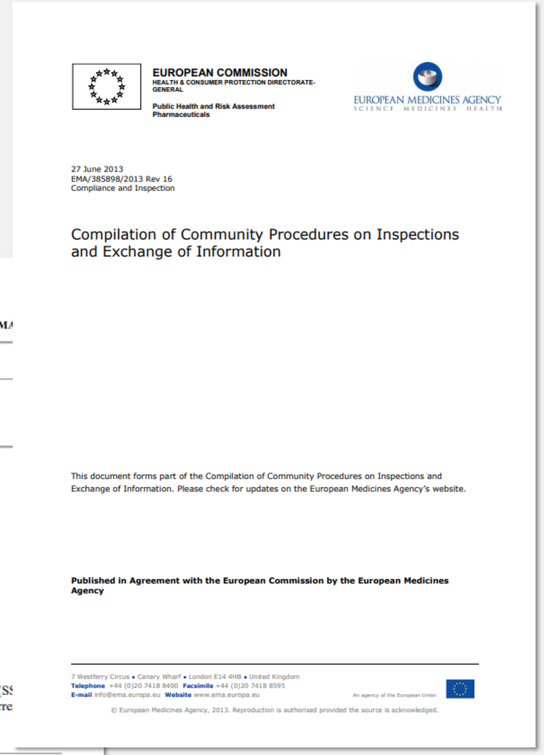
Table of Contents

PURPOSE

This MAPP outlines the policies and procedures for the Site Selection Model (SS by CDER staff to prioritize manufacturing sites for routine quality-related (curre manufacturing practice (CGMP)) surveillance inspections.

BACKGROUND

- FDA implemented the risk-based approach to prioritizing human drug manufacturing sites for routine CGMP surveillance inspection in FY2005. It was one of many outcomes from the initiative *Pharmaceutical Quality for the 21st Century — A Risk-Based Approach*. The FY2005 SSM replaced the previous approach, which was primarily based on the biennial inspection frequency for domestic sites as previously established in section 510(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).
- The Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 amended section 510(h) of the FD&C Act, replacing the fixed minimum inspection interval for domestic establishments (i.e., sites) with the requirement that FDA inspect domestic ***and*** foreign drug establishments "in accordance with a risk-based schedule" that considers establishments' "known safety risks." This defined a risk-based inspection frequency for all sites, regardless of location, to promote parity in inspectional coverage and the effective and efficient use of FDA resources to address the most significant public health risks. The statutory change



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL
Public Health and Risk Assessment
Pharmaceuticals

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

27 June 2013
EMA/385898/2013 Rev 16
Compliance and Inspection

Compilation of Community Procedures on Inspections and Exchange of Information

This document forms part of the Compilation of Community Procedures on Inspections and Exchange of Information. Please check for updates on the European Medicines Agency's website.

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An agency of the European Union

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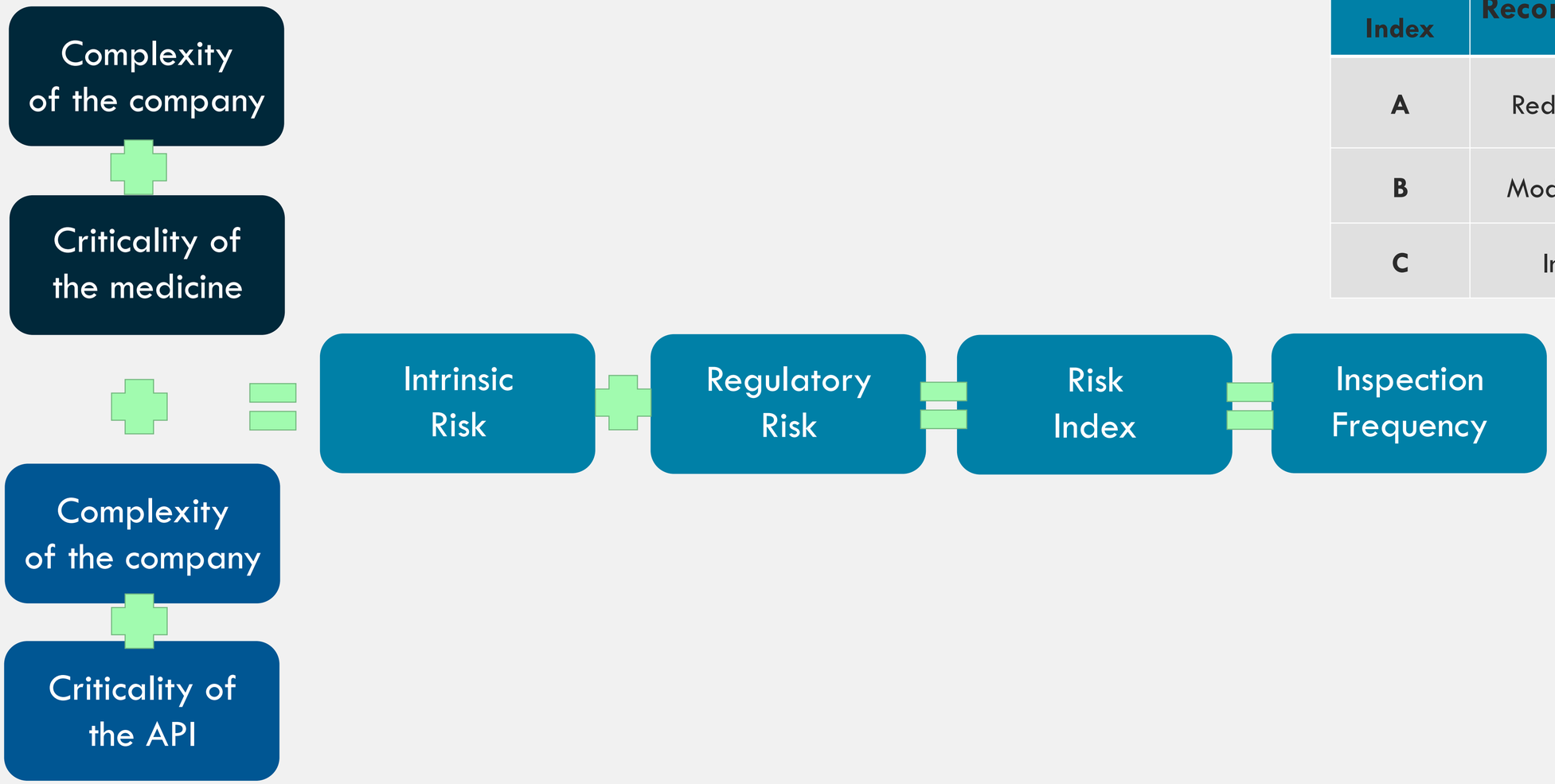
Risk Based Inspection Scheduling Procedures
(National Inspections)



Risk Index	Recommended Inspection Frequency
A	Reduced Frequency (24 to 36 months)
B	Moderate Frequency (12 to 24 months)
C	Intensive Frequency(≤ 12 months)

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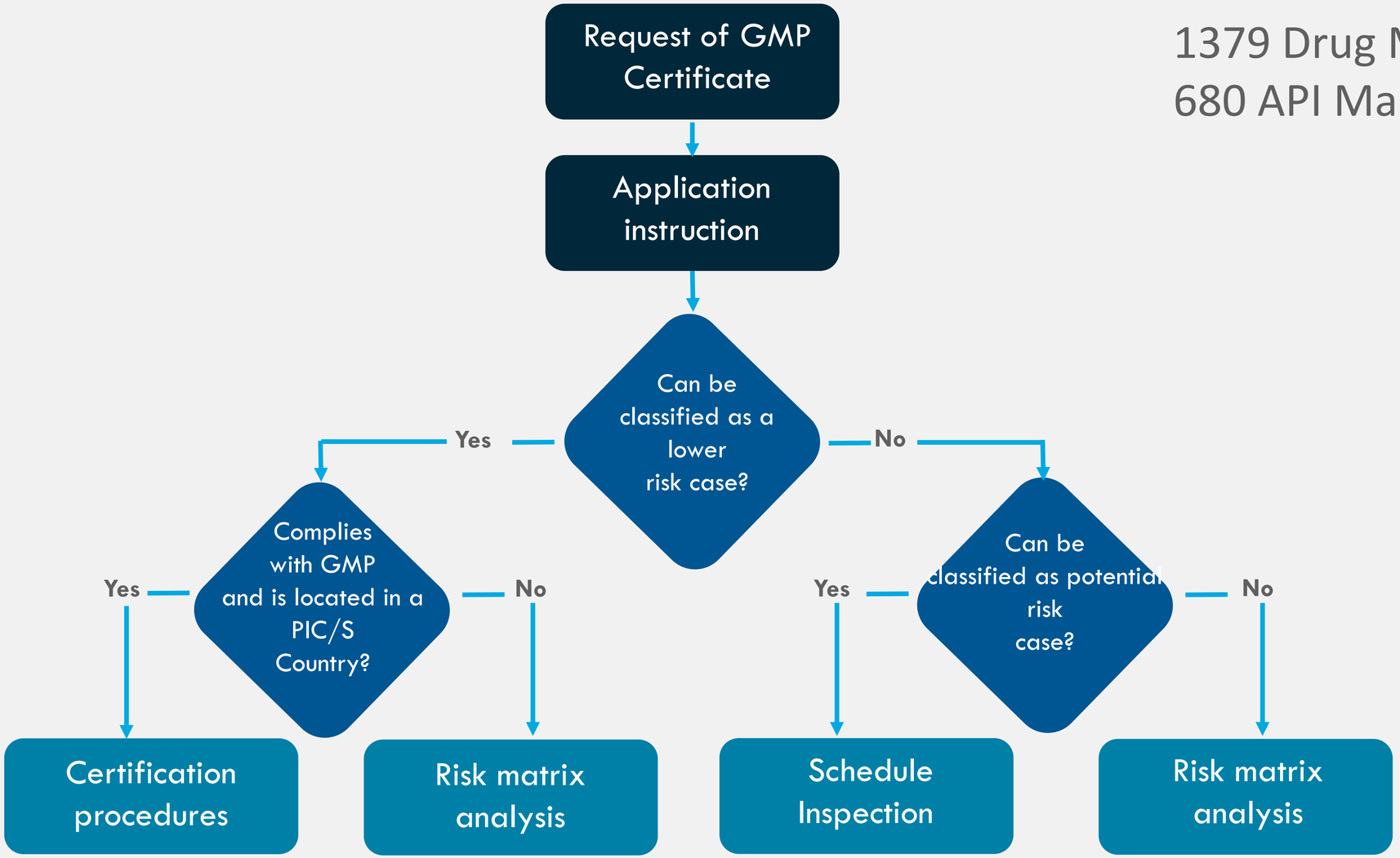
Risk Based Inspection Scheduling Procedures
Foreign Companies



1379 Drug Manufacturers
680 API Manufacturers

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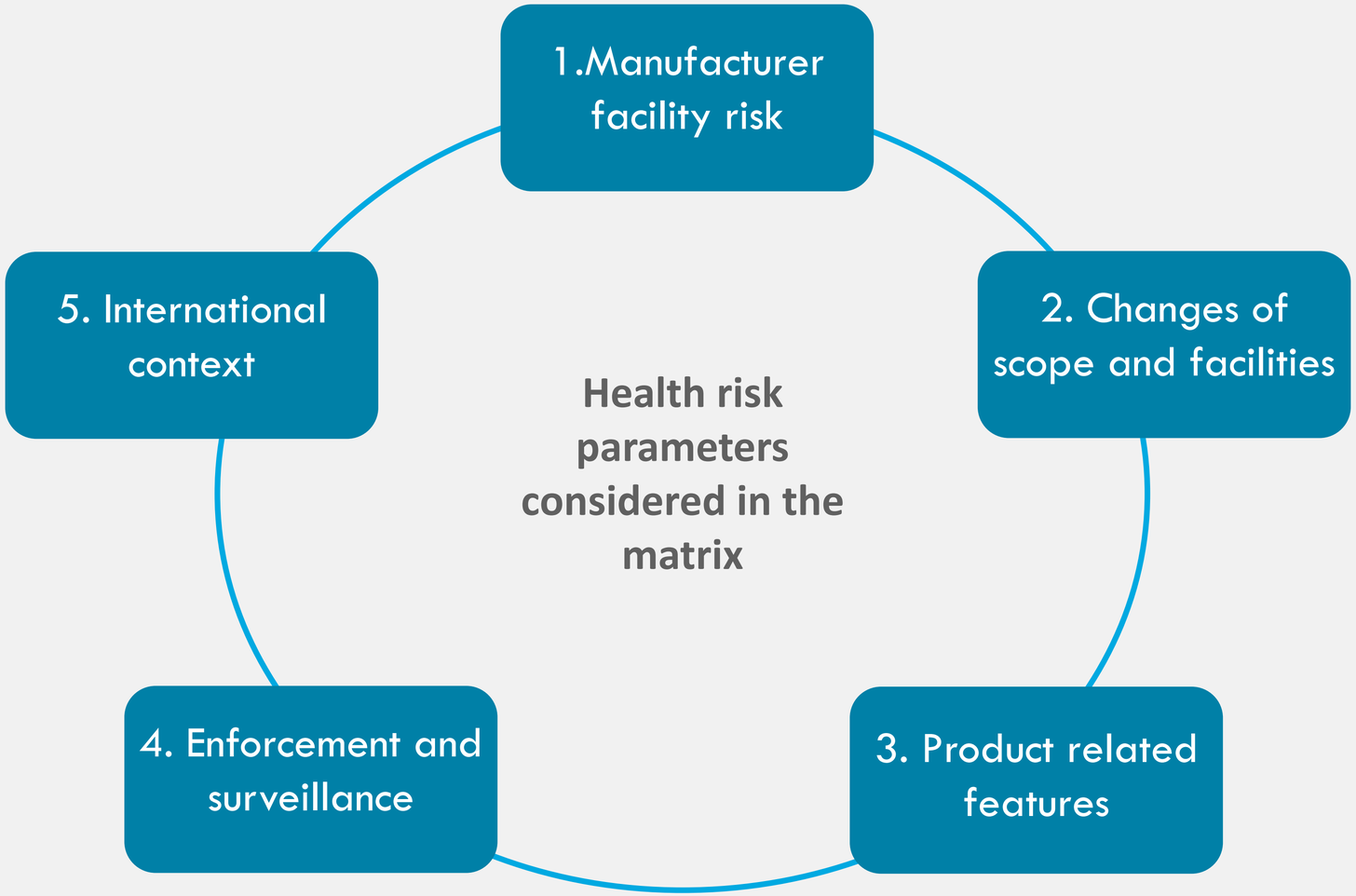
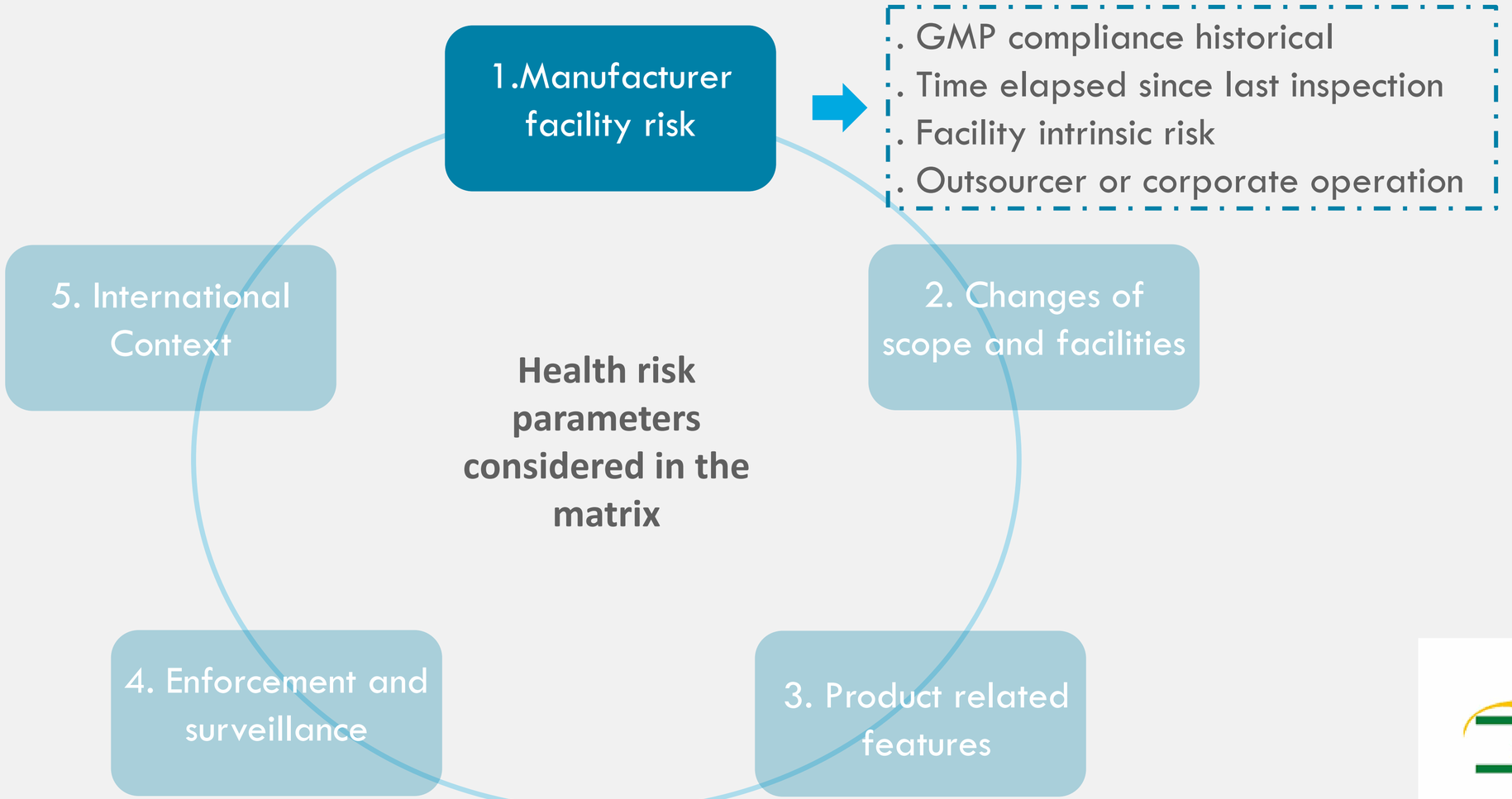
Risk Based Inspection Scheduling Procedures



Risk Based Inspection Scheduling Procedures



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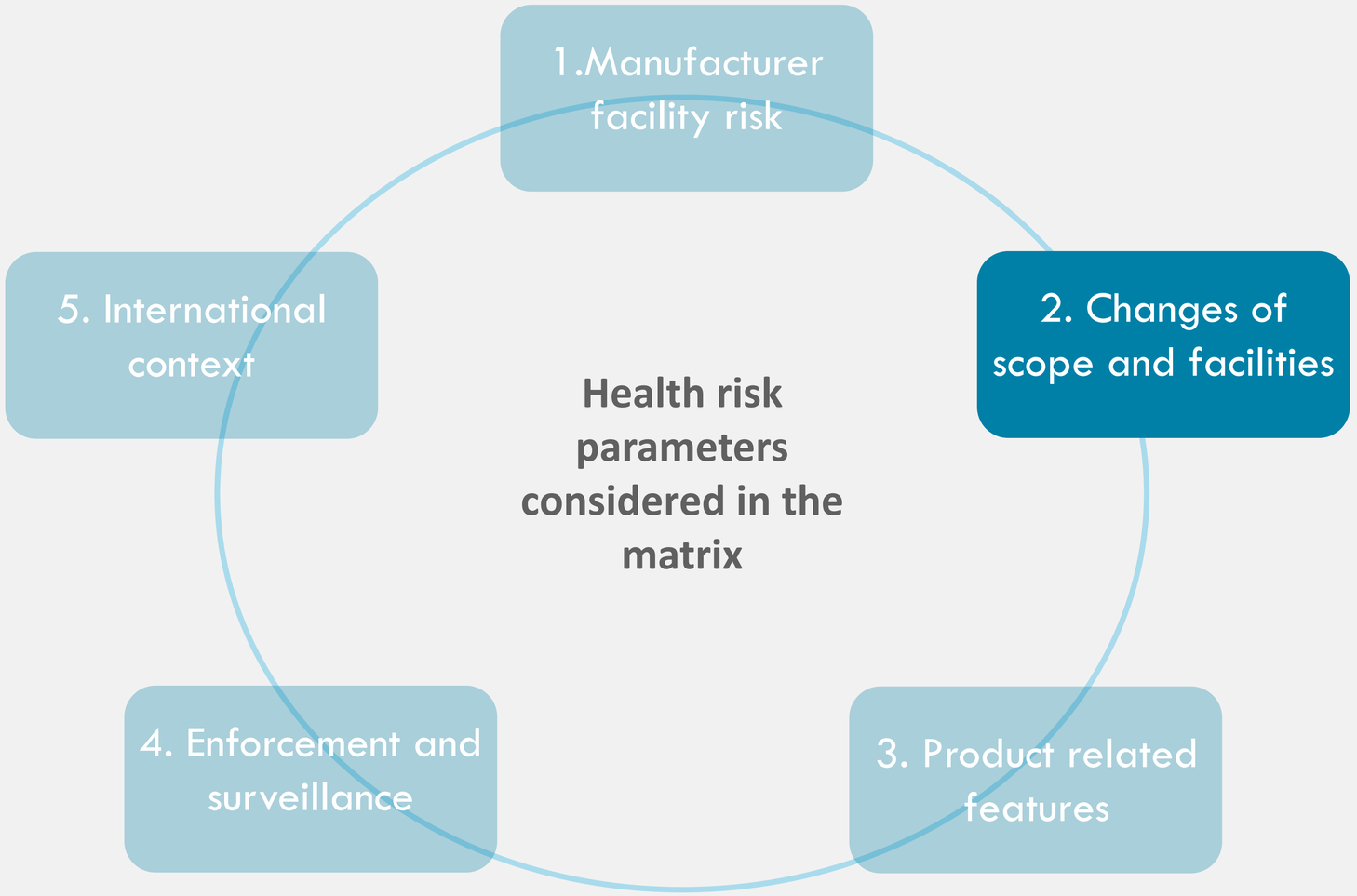
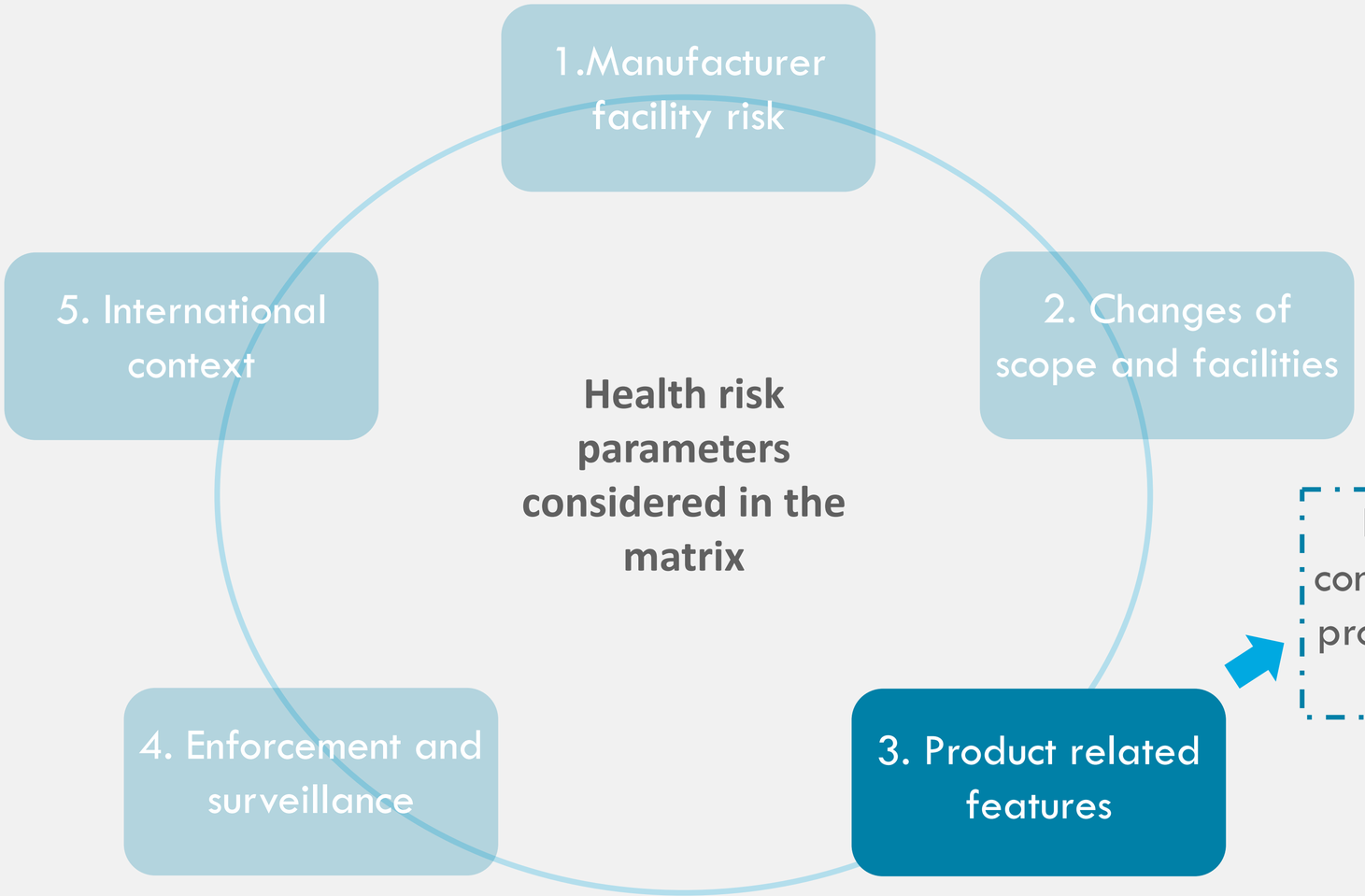


. Information from PQR, SMF and variations to score.

Risk Based Inspection Scheduling Procedures



PQR demonstrates that consistent assessments of the process control and stability have been conducted

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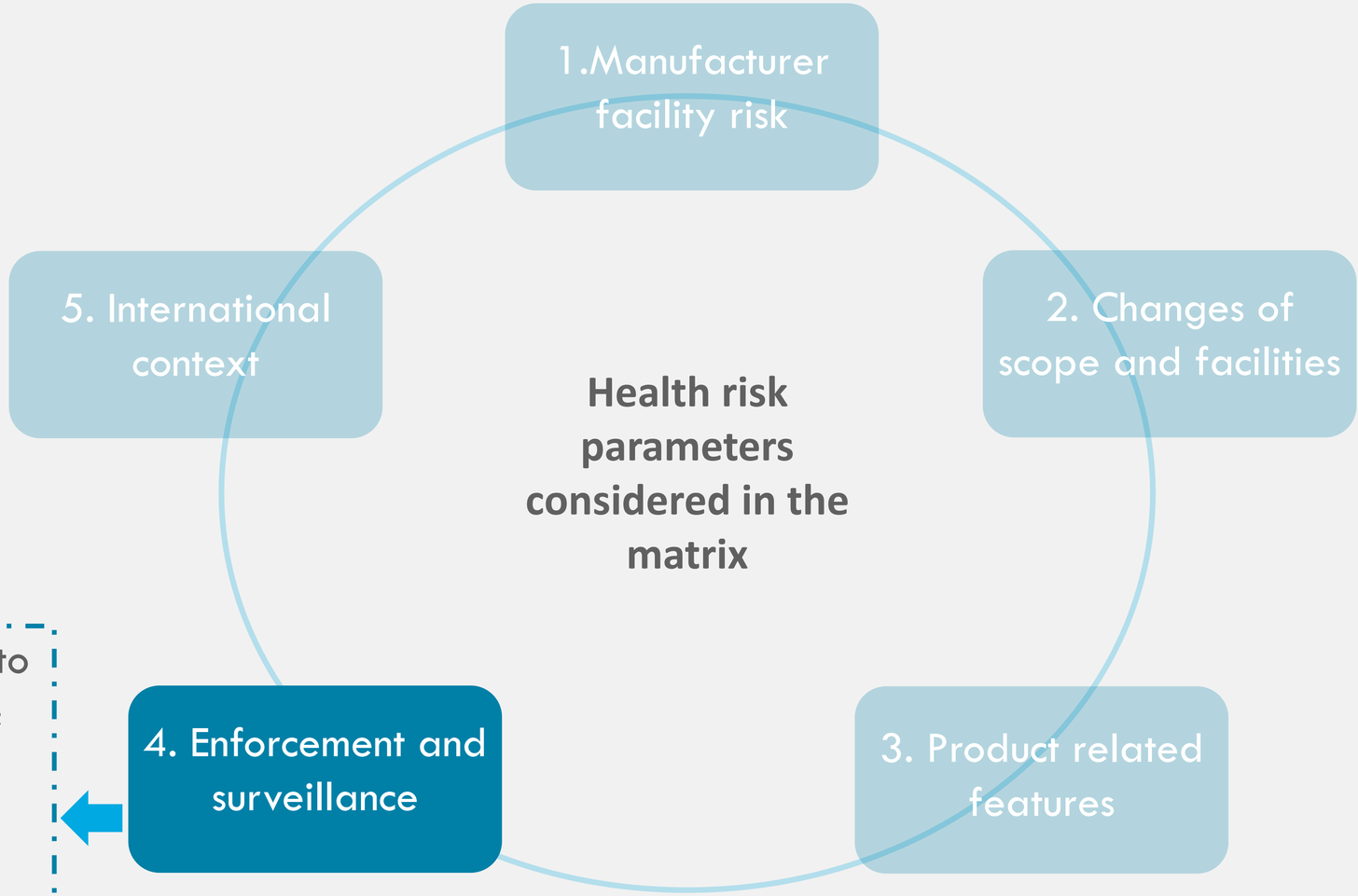
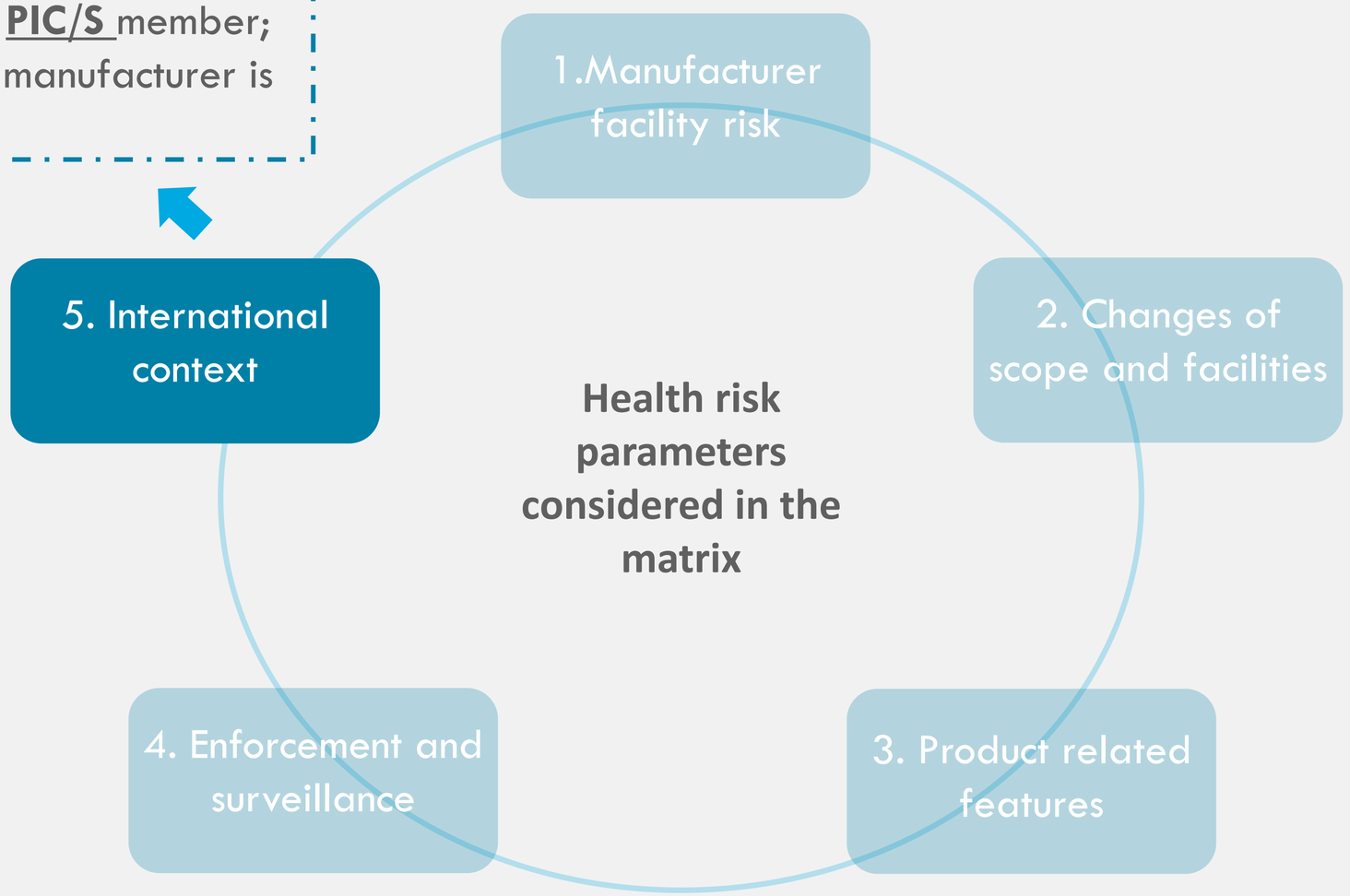
Risk Based Inspection Scheduling Procedures



a. Recall related to quality deviations;
b. Restrictive measures; and;
c. Technical Complaints.

Risk Based Inspection Scheduling Procedures

a. Historical data of inspections by MRAs of reference;
b. Certification issued by **PIC/S** member;
c. Country risk where the manufacturer is located.



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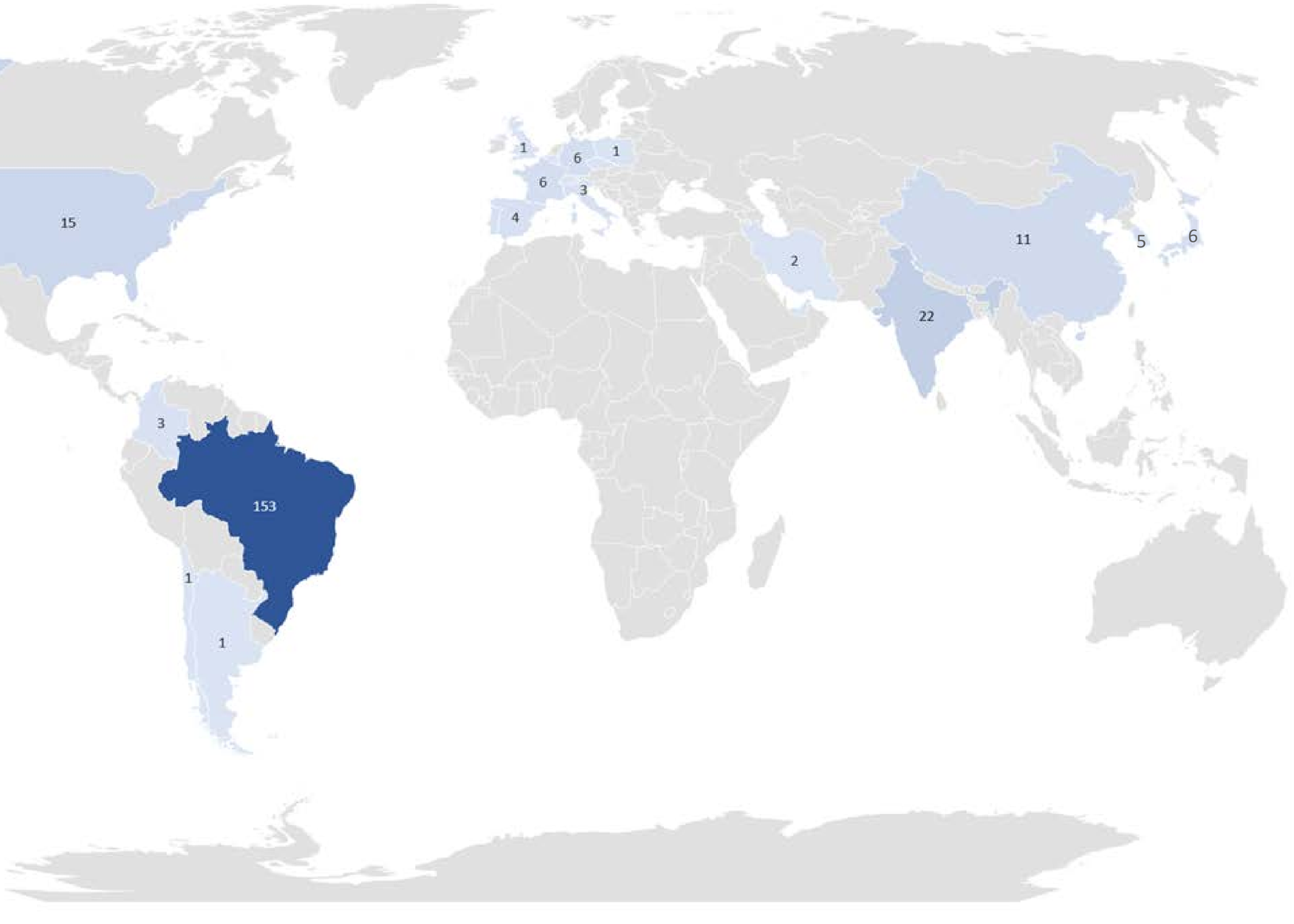
Inspections Conducted

2019



153 National
97 Abroad

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DEFICIENCY CLASSIFICATION

Critical	• Generated or leads to a significant risk of manufacturing a product that is dangerous to patients, or when it is detected fraud and misrepresentation, or falsification of data and/or products, or when combining different non-critical NCs that together can be explained in the report as a critical situation for the product.
Major	• Denotes that a product does not complies with its MA specifications, or does not represent the effective implementation of the required control measures in GMP, or indicates a serious breach of the other conditions stated in the MA, or which represents a failure related to batch release procedures;
Minor	• Cannot be classified as either critical or major, but is a deviation from the GMP

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Inspection Flow

8.7. Da visão geral dos prazos aplicáveis

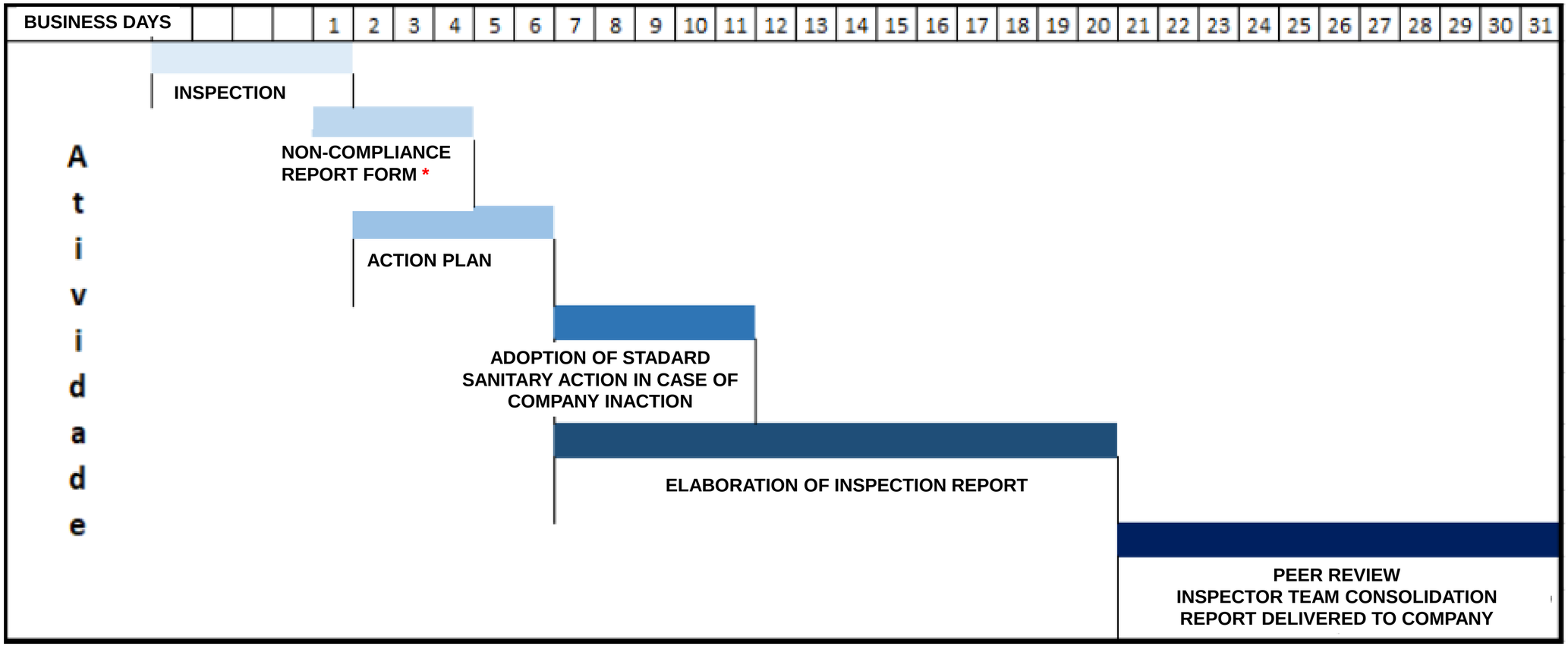

Figura 1 – Prazos aplicáveis a finalização do relatório após o término da inspeção

Company’s overall compliance rating
POP-O-SNVS-014

NO ACTION INDICATED (SAI)

Immediate Certification **
all lines

Voluntary Action Indicated (AVI)

Certification **

Exclusion:
Pharmaceutical form *
Production Line *

Official Action Determined (AOD)

Certification ** / ***

Exclusion:
Pharmaceutical form *
Production Line *

** For certification to occur, NCs that do not result in standardized sanitary action must have had satisfactory corrections and corrective actions.

* All products (pharmaceutical form or line): object of restrictive market action after adoption of standard sanitary actions

*** Does not result in certification: AOD classification for the 2nd consecutive time; NC related to fraud, forgery, tampering.

RDC 39/2013

- Valid for 2 years since its publication.
- Published in the Government Official Journal www.in.gov.br
- Can be cancelled in case of marketing deviations or other significant events.
- Before expiration, the renewal may be requested to ANVISA.
- ANVISA will decide if another inspection will be needed based on a risk assessment

GMP CERTIFICATE

GMP Certificates:

http://portal.anvisa.gov.br/consulta-certificado-boas-praticas

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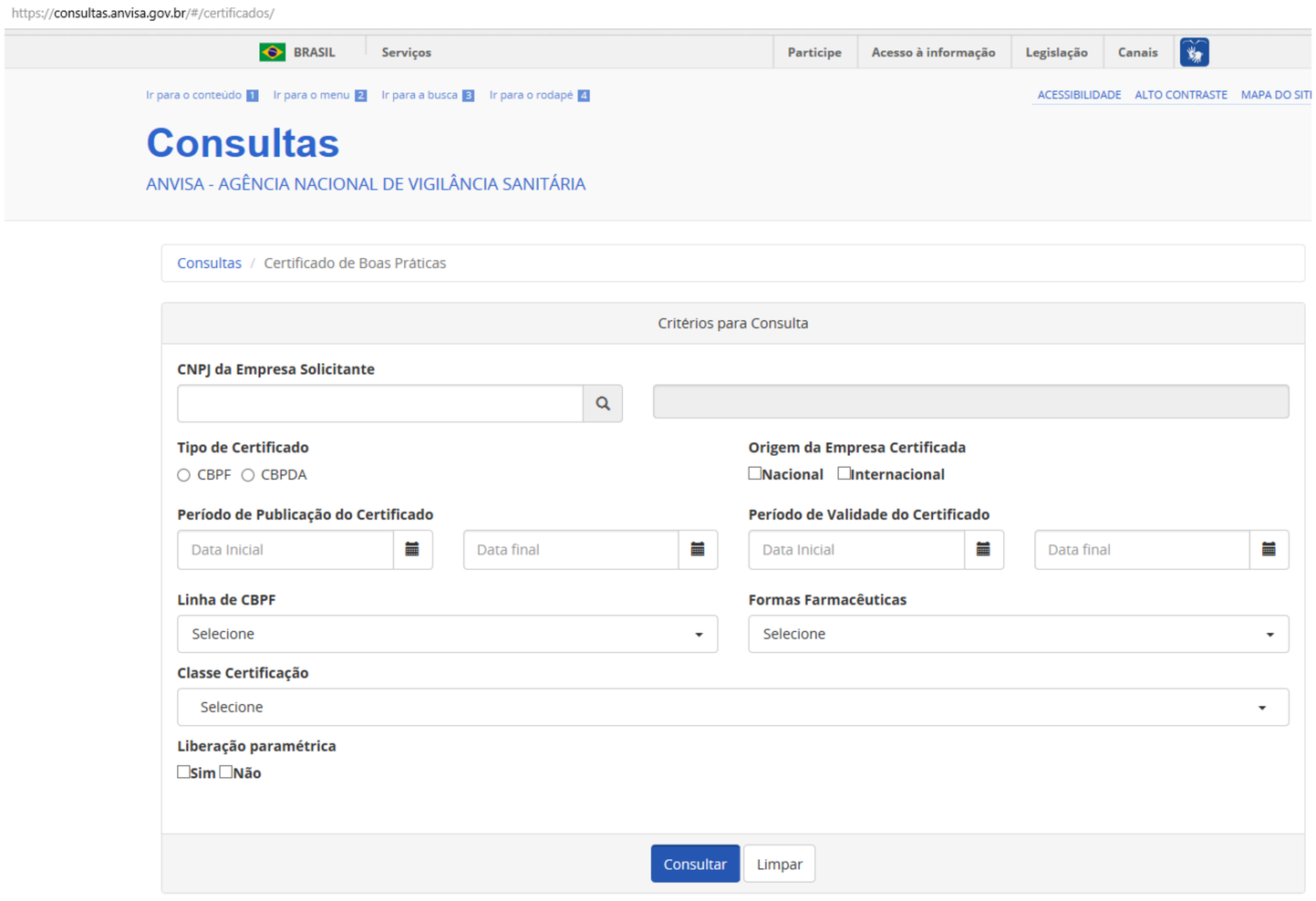
Drug Products https://consultas.anvisa.gov.br/#/certificados/



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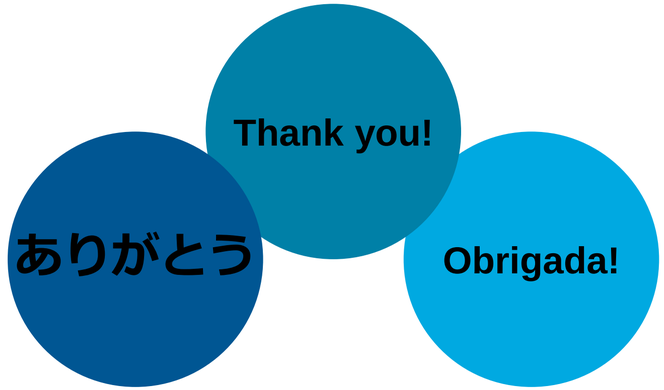

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