ICH M10 GUIDELINE ADOPTION BY ANVISA

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Coordination of Therapeutic Equivalence

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ANVISA
Agência Nacional de Vigilância Sanitária

Internal Governance for ICH

- Ordinance (Portaria) 1.520/2019
- Service Orientation 75/2019

Internal Governance for ICH

- Ordinance 1.520/2019 -> Ordinance with Anvisa´s regulatory performance model for harmonizing and internalizing themes developed within the scope of ICH.
  - Governance structure;
  - Requirements for representatives participation;
  - Responsibilities;
  - Flow for harmonization and internalization of ICH themes -> detailing of activities will be in specific Service Orientation (OS).

Internal Governance for ICH

- OS 75/2019 -> Service Orientation on the flow to harmonization and internalization of themes developed within the scope of ICH.

After adoption on ICH -> Anvisa Internalization of ICH Guideline

- **Step 1:** Identification of the national legal basis related to the theme.

Brazilian Legislation on Bioanalysis

- RE 895/2003 -> Guide for elaborate technical report of relative bioavailability/bioequivalence study.
- RE 1170/2006 -> Guide for medicines relative bioavailability/bioequivalence evidences.
- RDC 27/2012 -> Minimum requirements for the validation of bioanalytical methods used in studies for the purposes of medicine marketing authorization and post approval changes.

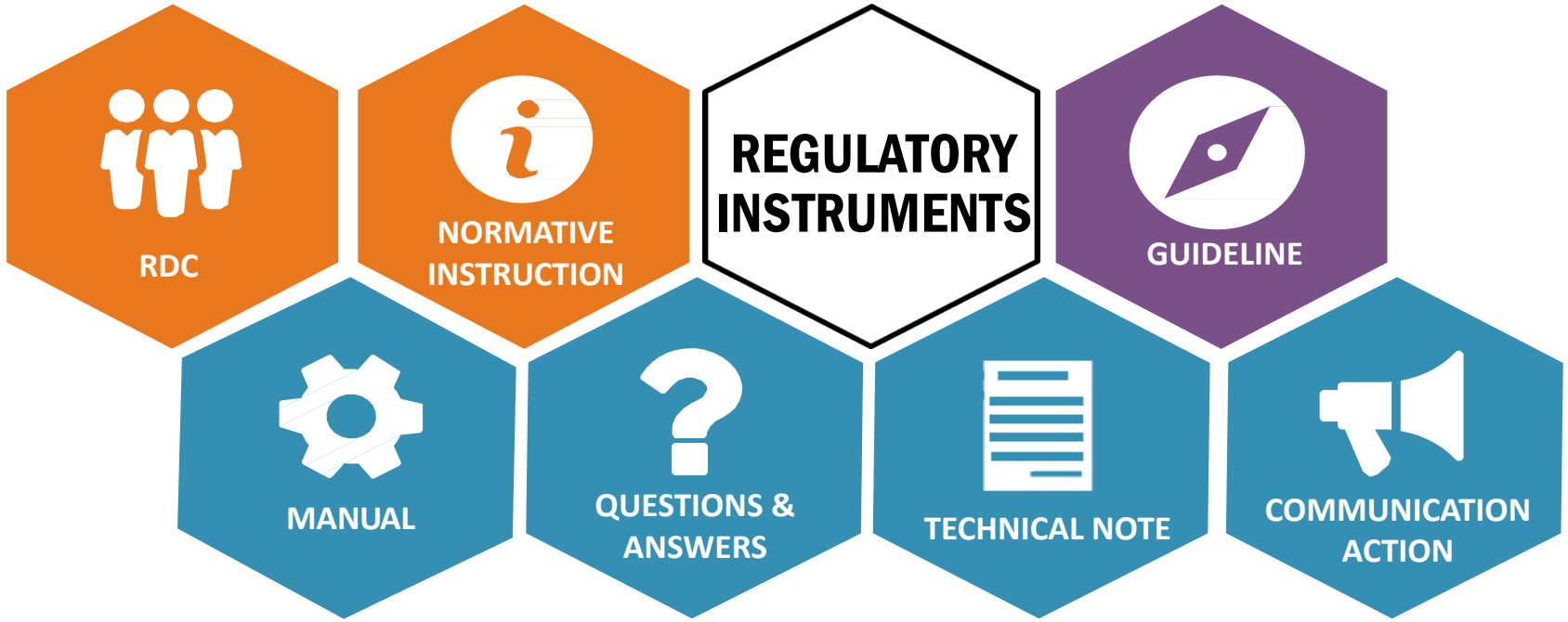
OS 75/2019

After adoption on ICH -> Anvisa Internalization of ICH Guideline

- **Step 2:** Internalization of ICH Guideline totally or partially.

- **Step 3:** Appropriate regulatory instrument for internalization.

Anvisa Regulatory Instruments



Service Orientation and Ordiance are instruments of internal scope

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Anvisa Regulatory Instruments

NORMATIVE ACTION - REGULATION

Resolution of Collegiate Board (RDC)

RDC is the act expressing collegiate decision to issue rules on matters within the agency's scope with provision for sanction in case of non-compliance.

Normative Instruction

Normative instruction is the act that expresses a normative decision of the collegiate board for the purpose of detailing rules and procedures of external scope, established in RDC.

OS 75/2019

After adoption on ICH -> Anvisa Internalization of ICH Guideline

- **Step 4:** Assessment of the need for a new consultation with external agents.
- **Step 5:** Deadline for internalization, including deadline for document translation.
- **Step 6:** Need to change or revoke a normative act.

Brazilian Legislation on Bioanalysis

- RE 895/2003 -> Guide for elaborate technical report of relative bioavailability/bioequivalence study -> tables and attachments
- RE 1170/2006 -> Guide for medicines relative bioavailability/bioequivalence evidences -> no impact
- RDC 27/2012 -> Minimum requirements for the validation of bioanalytical methods used in studies for the purposes of medicine marketing authorization and post approval changes -> almost all

Table of Guideline Contents

Table of Guideline Contents

3. Chromatography

- 3.1. Reference standards
- 3.2. Validation
  - 3.2.1 Selectivity
  - 3.2.2 Specificity
  - 3.2.3 Matrix effect
  - 3.2.4 Calibration Curve and Range
  - 3.2.5 Accuracy and Precision
    - 3.2.5.1 Preparation of Quality Control Samples
    - 3.2.5.2 Evaluation of Accuracy and Precision
  - 3.2.6 Carry-over
  - 3.2.7 Dilution integrity
  - 3.2.8 Stability
  - 3.2.9 Reinjection Reproducibility

Table of Guideline Contents

3. Chromatography (continued)

- 3.3. Study sample analysis
  - 3.3.1 Analytical run
  - 3.3.2 Acceptance Criteria for an Analytical Run
  - 3.3.3 Calibration Range
  - 3.3.4 Reanalysis of Study Samples
  - 3.3.5 Reinjection of Study Samples
  - 3.3.6 Integration of Chromatograms

4. Ligand Binding Assays

- 4.1 Key reagents
  - 4.1.1 Reference standard
  - 4.1.2 Critical reagents

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Table of Guideline Contents

4. Ligand Binding Assays (continued)

- 4.2. Validation
  - 4.2.1 Specificity
  - 4.2.2 Selectivity
  - 4.2.3 Calibration Curve and Range
  - 4.2.4 Accuracy and Precision
    - 4.2.4.1 Preparation of Quality Control Samples
    - 4.2.4.2 Evaluation of Accuracy and Precision
  - 4.2.5 Carry-over
  - 4.2.6 Dilution Linearity and Hook Effect
  - 4.2.7 Stability

Table of Guideline Contents

4. Ligand Binding Assays (continued)

- 4.3. Study Sample Analysis
  - 4.3.1 Analytical Run
  - 4.3.2 Acceptance Criteria for an Analytical Run
  - 4.3.3 Calibration Range
  - 4.3.4 Reanalysis of Study Samples

5. Incurred Sample Reanalysis

6. Partial and Cross Validation

- 6.1 Partial Validation
- 6.2 Cross Validation

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Table of Guideline Contents

7. Additional Considerations

- 7.1 Analytes that are also Endogenous Compounds
  - 7.1.1 Quality Control Samples
  - 7.1.2 Calibration Standards
  - 7.1.3 Selectivity, Recovery and Matrix Effects
  - 7.1.4 Parallelism
  - 7.1.5 Accuracy and Precision
  - 7.1.6 Stability
- 7.2 Parallelism
- 7.3 Recovery

Table of Guideline Contents

7. Additional Considerations (continued)

- 7.4 Minimum Required Dilution
- 7.5 Commercial and Diagnostics Kits
- 7.6 New or Alternative Technologies
  - 7.6.1 Dried Matrix Methods

8. Documentation

- 8.1 Summary Information
- 8.2 Documentation for Validation and Bioanalytical Reports

9. Glossary

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OS 75/2019

After adoption on ICH -> Anvisa Internalization of ICH Guideline

- **Step 7:** The internalization plan must be submitted to DICOL´s decision (fully approve, approve with reservations or request diligences from the organizational unit to carry out complementations).

- **Step 8:** After approval of the internalization plan, the ANVISA ICH coordinator must inform ICH secretariat of the way and deadlines defined by DICOL for internalization.

OS 75/2019

After adoption on ICH -> Anvisa Internalization of ICH Guideline

- **Step 9:** Elaboration of regulatory instrument (OS 56/2018).
  - Elaborate regulatory instrument;
  - Public consultation (analyze the contributions received and promote the relevant adjustments);
  - Legal analysis;
  - DICOL deliberation (approve, make adjustments, filing);
  - Publish the final regulatory instrument in the DOU.

Conclusion

Approval of ICH harmonised guideline of Bioanalytical method validation and study sample analysis -> november, 2021

After adoption by ICH, long way till its internalization in Anvisa.

Thank you!

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