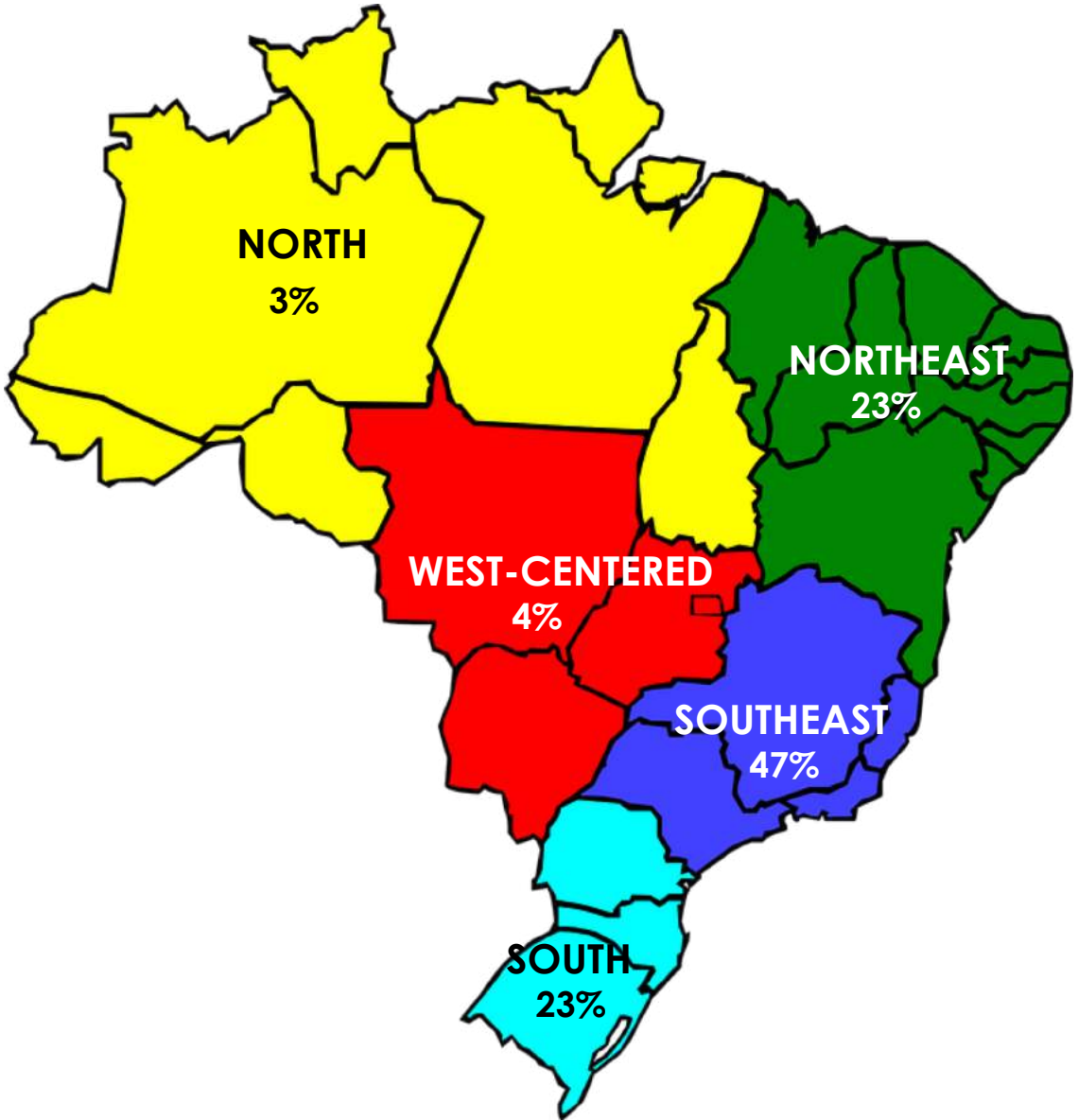
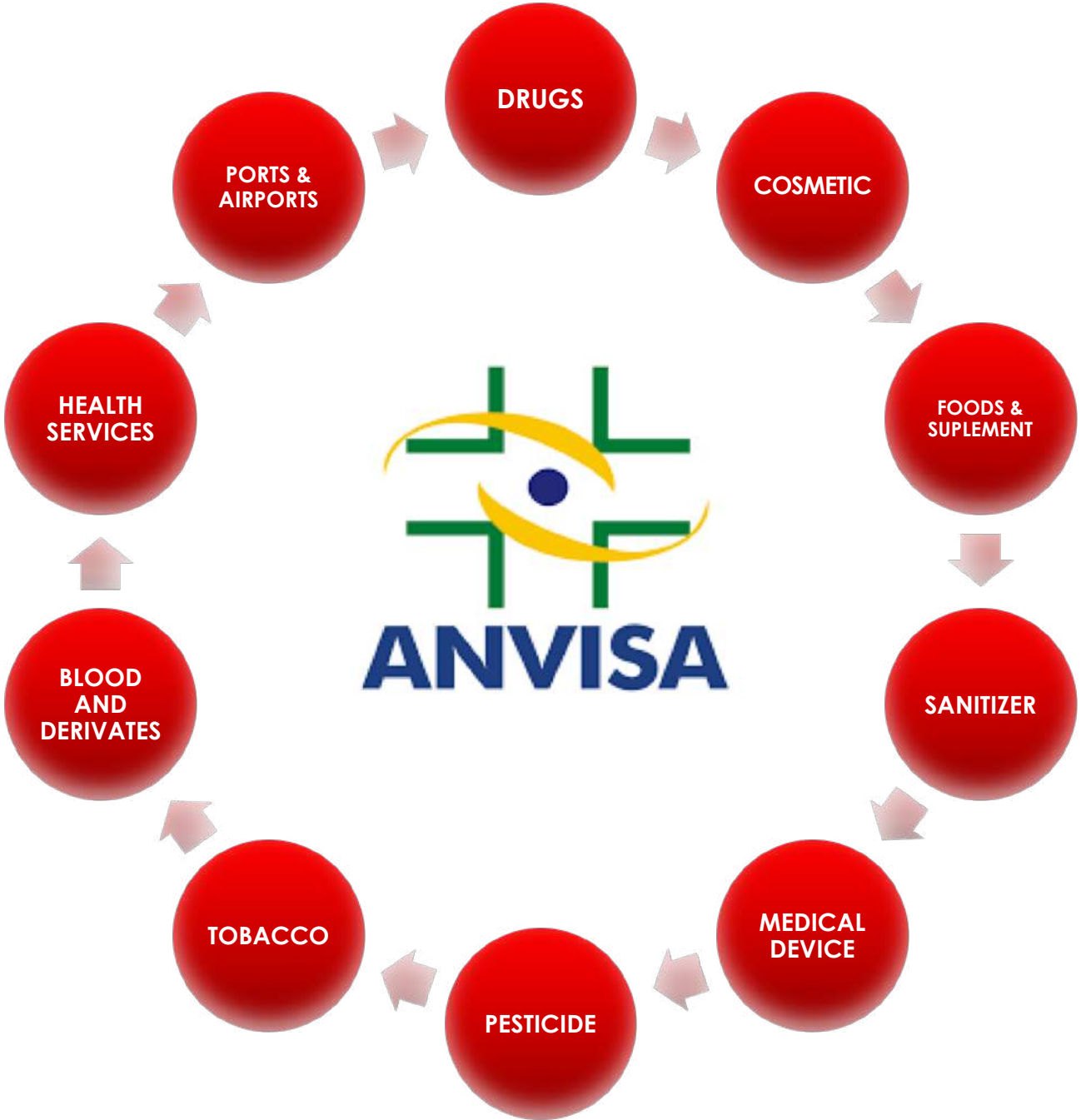
BRAZIL – a continental country



ANVISA
BRAZILIAN REGULATORY HEALTH AUTHORITY

- ANVISA – National Agency of Sanitary Vigilance was established in 1999.
- It is an autarchy, directed by the 05 nominated members of it's directory board
- ANVISA's headquarter is located in Brasília, Brazilian capital.
- Currently ANVISA has approximately 2.200 employees.


DRUGS
COSMETIC
FOODS & SUPLEMENT
SANITIZER
MEDICAL DEVICE
PESTICIDE
TOBACCO
BLOOD AND DERIVATES
HEALTH SERVICES
PORTS & AIRPORTS
ANVISA

DRUG PRODUCT

REGULATORY CLASSIFICATION

REGULATORY CLASSIFICATION – TYPE OF API

SYNTHETIC & SEMISYNTHETIC

- RDC 200/2017

Applicable to:
- NCE
- INNOVATORS
- GENERICS
- BRANDED GENERICS

BIOLOGIC PRODUCTS

- RDC 55/2010

Applicable to:
- NEW BIOLOGIC
- BIOSSIMILARS

SPECIFIC PRODUCTS

- RDC 24/2011

Applicable to:
- VITAMINS
- ANTIACIDS
- PHYTOCHEMICALS
- OPOTHERAPY
- PARENTERAL
- DEHYDRATION
- CAMPHOR
- OTHERS

HERBAL MEDICINES

- RDC 26/2014

Applicable to:
- HERBAL MEDICINES
- EXTRACTS
- HERBAL DRUG
- DERIVATIVES

DINAMIZE MEDICATION

- RDC 26/2007

Applicable to:
- DYNAMIZED
- HOMEOPATHIC
- ANTHROPOSOPHICS
- ANTOHOMOTOXIC

ALLERGEN

- RDC 233/2005

Applicable to:
- DIAGNOSIS (TESTS)
- TREATMENT (VACCINES)

PROBIOTICS

- RDC 323/2003

Applicable to:
- LIVE MICROSGANISM
- INACTIVATED MICRORGANISM

RADIOFARMS

- RDC 64/2009

Applicable to:
- RFU RADIOPHARMS
- NON-RADIOACTIVE COMPONENTS
- RADIONUCLIDES

NOTIFIED

- RDC 166/2006
- RDC 107/2016

Applicable to:
- LOW RISK MEDICATION(IN 03/09)
- TRADITIONAL USE HERBAL MEDICINES
- LOW POTENCY DYNAMIZES (IN 05/07)

MEDICAL GASES

- RDC 70/2008

SYNTHETIC & SEMISYNTHETIC DRUGS

REGULATORY PATHWAY
SYNTHETIC AND SEMI-SYNTHETIC DRUG PRODUCTS

NCEs

- New chemical entities (radical innovation)
- Complete package of non-clinical and clinical data
- Pre-approval required by regulatory agency
- About 3 years to register
- Premium price for patented drugs and new therapeutic areas
- Generally, they are listed as RLD (reference medicine)

INNOVATORS

- Incremental Innovation
- Reduced package of non-clinical data
- Bridge studies and Phase III clinical trial required
- Approximately 3 years for registration approval
- Price approval consisting of:
  - cost of the API,
  - sale price in other countries
  - maximum therapeutic cost in the country

GENERICS & BRANDED

- Comparative trials (PE / BE) against RLD
- About 2 years for registration (prioritized) and 5 years (commodities)
- Priority granted to the first 3 of the market
- Pre-set price
  - 35% below the approved price for the RLD if generic
  - Average cost of existing competitors plus RLD price if similar

CLONES

- No regulatory dossier submission required
- Exclusive packaging (clone holder brand)
- From 1 to 3 months for registration
- Predefined price (even from matrix drug)

RDC 200/17 SYNTHETIC & SEMISYNTHETIC

PRE-SUBMISSION

- DCB: RDC 63/2012 IN 05/2012
- RLD: RDC 35/2012

APIs

- STARTING MATERIAL: NT 06-001/2015
- DMF: NI 01/2015 NI 02/2015
- AMV: RE 166/2019
- FORCED DEGRADATION: RDC 53/2015
- MIX OF SOLVENTS: NT 01/2016
- STABILITY: RDC 45/2012
- NOTIFICATION: RDC 30/2008
- REGISTER: RDC 57/2009 IN 15/2009 IN 03/2013

PRODUCTION

- GMP: RDC 361/2019
- BIOBATCH, EXHIBIT BATCH: RDC 73/2016 NT 37/2016
- OUTSOURCING: RDC 234/2018
- PROCESS VALIDATION: GUIA 01/2015

QUALITY CONTROL

- STABILITY & PHOTOSTABILITY RE 01/2005
- OUTSOURCING: RDC 234/2018
- AMV: RDC 166/2017
- EET: RDC 213/2002 RDC 214/2002
- DISSO PROFILE: RDC 31/2010 NT 03/2013
- FORCED DEGRADATION: RDC 53/2015

SAFETY & EFFICACY

- NON-CLINICAL: GUIDES AVAILABLE AT ANVISA PORTAL
- CLINICAL TRIALS: RDC 09/2015
- PV: RDC 04/2009 IN 14/2009 GUIDES AT ANVISA PORTAL
- FIXED DOSE COMBINATIONS: NT 09/2015 GUIDES AT ANVISA PORTAL
- PE: RDC 31/2010 IN 01/2013 NT 03/2013
- BE/BD: RDC 1170/2006 RDC 37/2011 RDC 27/2012 IN 10/2016

LABELLING

- BRAND NAME: RDC 59/2014 LEI 63060/1976 OS 43/2017
- PIL: RDC 47/2009 RDC 200/2017
- LABEL: RDC 71/2009 RDC 137/2003 RDC 200/2017 DECRETO 8077/2013

SUBMISSION

- ELETRONIC APPLICATION: RDC 86/2016
- PETITION FORMS: ONLINE - ANVISA WEBSYSTEM
- FEES: PORTARIA INTERMINISTERIAL FAZENDA SAÚDE 45/2017
- ORPHAN DISEASES RDC 205/2017
- PROTOCOL: RDC 25/2011; LEI 9784/1999

POST-APPROVAL

- POST-APPROVAL: RDC 73/2016
- HMP/APR: RDC 73/2016
- RENEWAL: RDC 200/17
- CONDITIONAL APPROVAL RDC 219/18

Brainlike
estratégia regulatória

CMC REQUIREMENTS

- ✓ **DEVELOPMENT REPORT**
  - FORCED DEGRADATION STUDIES – API AND FINISHED PRODUCT
  - DISSOLUTION MEDIA – DEVELOPMENT AND VALIDATION
  - RESIDUAL SOLVENTS
  - PILOT STUDIES AGAINST BRAZIL RLD
- ✓ **PROCESS VALIDATION AND BATCH MANUFACTURING RECORD FOR EACH STRENGHT, PHARMACEUTICAL FORM AND PACKING**
- ✓ **ANALYTICAL METHOD VALIDATION**
  - API AND FINISHED PRODUCT
  - PERFORMED AT ALL INVOLVED MANUFACTURER SITES (API AND FINISHED PRODUCT)
  - TEST PROCEDURE, VALIDATION PROTOCOL + REPORT AND RAW DATA MANDATORY
  - FOR PHARMACOPOEIC METHODS: METHOD VERIFICATION ON SAME BASE
- ✓ **STABILITY STUDIES**
  - ZONE IVB STABLITY IN 03 BATCHES
  - API STABLITY (FOR THE FP MANUFACTURER COUNTRY CLIMATIC ZONE)
  - ADITIONAL STUDIES (PHOTOSTABILITY, AFER RECONSTITUTION, OTHERS)
  - 6 MONTHS ACCELERATE AND PARTIAL LONG TERM FOR SUBMISSION
  - +36 MONTHS OF SHELF-LIFE ONLY WITH LONG TERM STABILITY REPORT
- ✓ **CoA FOR THE API AND FINISHED PRODUCT**

ICH versus ANVISA

ICH

ANALYTICAL METHOD VALIDATION
- summary of results

PROCESS VALIDATION
- declaration of process validation performance

BATCH MANUFACTURING RECORD
- not required

STABILITY STUDY
- table of results

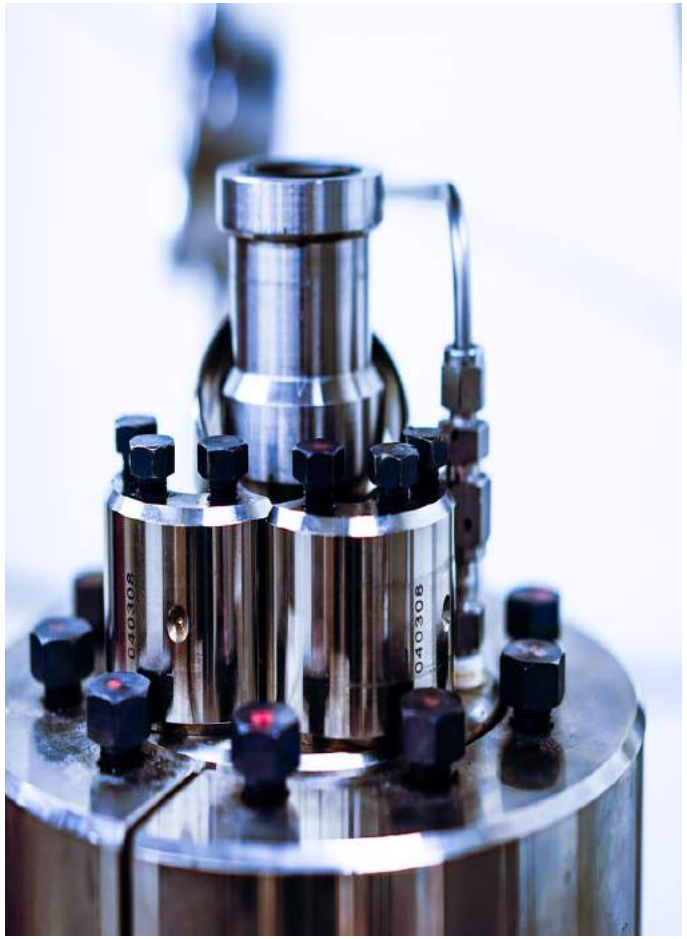
ANVISA

ANALYTICAL METHOD VALIDATION
- protocol
- report
- chromatograms

PROCESS VALIDATION
- summary of process validation (as per Anvisa's guideline)

BATCH MANUFACTURING RECORD
- required to present excuted batch record of higher and lower dose

STABILITY STUDY
- protocol
- report
- forced degradation studies



PROCESS VALIDATION

AT ANVISA...

The summary report of the validation of the manufacturing process is the compilation of information obtained during the process validation of the drug product subject to registration or post-registration. The purpose of the validation summary report is to know the product and its production process before submitting it for registration, thereby reducing the number of post-registration petitions, such as moderate and larger process changes, as per Post-Registration specific guidelines.

GUIDE FOR PREPARING THE SUMMARY REPORTVALIDATION OF DRUG PRODUCTS MANUFACTURING PROCESS

GUIA nº 01, versão 02, de 30 de junho 2017

VALIDATION SUMMARY AND PATE

The **PURPOSE** of the validation summary report is to **KNOW** the product and its production process before submitting it for registration, thereby reducing the number of post-registration petitions, such as moderate and larger process changes.

In situations where pilot batch registration is allowed, full process validation data is not available. In such cases, the information from the first stage of process validation - process design shall be provided. **This step is performed during product development and production scheduling, and should be included in the Master Validation Plan**.

It is the definition of the critical parameters for the product quality and the controls in process to be used in the validation of the industrial lots.

EXAMPLES

Etapas	Parâmetros Críticos	Comentários
WEIGHT	Weighing Check	To be monitored
WET GRANULATION & DRYING	Amount and speed of addition of granulating agent, mixing speed, time, order of addition	To be monitored Drying uniformity (humidity)
DRY GRANULATION	Compression Parameters	Monitored or sampled for IPQC
MIX	Mixing Speed, Time	To be monitored Uniformity of the mixture should be checked
COMPRESSION	Setup parameters, speed, pressure	To be monitored Sampling and IPQC
FLUIDIZED BED	Spray Speed, Jet Temperature, and Pump Pressure Product	To be monitored Appearance, weight, release tests
PRIMARY PACKING	Sealing Temperature, Speed	To be monitored Sealig test

ANALYTICAL METHOD VALIDATION

RDC 166’17 x RE 899’03 x ICH

RDC 166*	RE 899	ICH
Establishes criteria for validation of analytical methods.	Guide for analytical methods validation	Presents a discussion of the characteristics for consideration during the validation and does not necessarily seek to cover the testing that may be required for registration in and is not intended to provide direction on how to accomplish validation.
Applies to analytical methods used in pharmaceutical ingredients (including excipients)	Not discussed	Not discussed
Applied to the investigational products used in clinical trials	Not discussed	Not discussed
Additional documentation and tests may be requested at any time by Anvisa	Used to be requested by queries after evaluation	Not discussed
All relevant data obtained during the performance of the analytical validation, as well as the formulas used for calculation, must be filed, together with the request of interest, for Anvisa's evaluation.	Used to be requested by queries after evaluation	Summary is accepted
It will be accepted characterized standard, but not of working standard;	It was accepted only compendial standards, if they are available	Not discussed
Protocol, analytical procedures, parameters, acceptance criteria, report, raw data (chromatograms) should be presented;	Used to be requested by queries after evaluation	Summary is accepted

ANALYTICAL METHOD VALIDATION

WHAT HAS TO BE VALIDATED ?

- In case of analytical methodology not described in pharmacopoeias or official forms, duly recognized by ANVISA, it should be validated.

- The analytical methodology shall be revalidated:
  - Changes in the synthesis of the active substance;
  - Changes in the composition of the finished product;
  - Changes in the analytical procedure.

SOME OTHER CHANGES MIGHT REQUIRED A NEW VALIDATION. DECISION TREE BASED ON RISK ASSESSMENT SHALL BE APPLIED.

ANALYTICAL METHOD VALIDATION

In the case of analytical methodology not described in official pharmacopoeias or compendiums.

- **Specificity & Selectivity**
- **Linearity**
- **Interval**
- **Accuracy**
- **Precision**
  - **Repetibility**
  - **Intermediate precision**
  - **Reproductibility**
- **LOQ & LOD**
- **Robustness**

According to the test classification according to its purpose.

ANALYTICAL METHOD VALIDATION

WHAT IS METHOD VARIFICATION ?

Documented evidence that a previously validated method performs as intended in the environment in which it is being applied.

In case of transfer of validated methodology from national companies to pharmaceutical equivalence centers. Or between companies of same group:

- **Specificity & Selectivity**
- **Accuracy**
- **Precision**

Copy of all original documentation of methodology validation should be attached.

#TIP

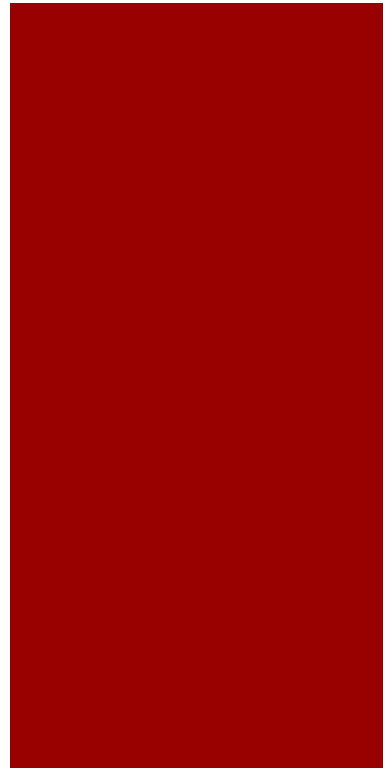
- Specificity (selectivity): In chromatographic methods, the necessary precautions must be taken to ensure the purity of the chromatographic peaks, and the peak purity should be demonstrated. Chromatograms are MANDATORY for specificity and these records should be in a readable form and in a manner that preserves the content and meaning for a proper evaluation. Chromatograms records as screen shot lose the capability of show a more detailed viewing of baselines, peaks or retention times.

- The characterization report should contain the data obtained from applicable techniques to the characterization of each chemical substance, for example thermogravimetry, melting point, differential scanning calorimetry, IR-spectroscopy, mass spectrometry, nuclear magnetic resonance, elemental analysis (carbon/ hydrogen/ nitrogen), X-ray diffraction, optical rotation, chromatographic methods, among others. Besides characterization data, the following information should be included in the report: batch number and shelf life of the substance used in the characterization; common Brazilian designation or international non-proprietary name; CAS number; chemical name; synonymy; molecular and structural formula; molecular weight; physical form; physical-chemical properties; impurities profile; handling and conservation care; certificate of analysis proving the identity, content and validity of the characterized reference standard.

- Robustness: According to RDC 166, the following parameters should be changed: mobile phase pH, mobile phase composition, column, temperature and flow rate. Please, clarify if the other parameters were changed in Validation Report MVR/PAT/004/00 (not received).

- Linearity: According to RDC 166, the residue dispersion graphic, accompanied by its statistical evaluation, should be presented.

BIOLOGICAL PRODUCTS



REGULATORY PATHWAY
BIOLOGIC PRODUCTS

NEW BIOLOGICAL PRODUCT

- [ ] Radical innovation
- [ ] Complete package of non-clinical and clinical data
- [ ] Pre-approval required by regulatory agency
- [ ] Approximately 1-3 years for registration approval
- [ ] Might be subject to prioritization of analysis
- [ ] Premium price for patented drugs and new therapeutic areas

DEVELOPMENT BY COMPARABILITY

- [ ] Biossimilars
- [ ] Reduced package of non-clinical data
- [ ] Comparator must be pre-validated by Anvisa
- [ ] Approximately 1-3 years for registration approval
- [ ] Price approval subjected to comparator and therapy cost locally

INDIVIDUAL DEVELOPMENT

- [ ] Incremental Innovation
- [ ] Complete package of non-clinical and clinical data
- [ ] Comparator is not mandatory
- [ ] Approximately 1-3 years for registration approval
- [ ] Price approval subjected to comparator and therapy cost locally

DEVELOPMENT ROUTE
BIOLOGIC PRODUCTS

- ✓ DEVELOPMENT BY COMPARABILITY: it is the regulatory route that can be used by a biological product to obtain registration with the regulatory authority, in which the comparability exercise was used in terms of quality, efficacy and safety, between the product developed to be Comparative biological product;

- ✓ INDIVIDUAL DEVELOPMENT PATH: it is the regulatory route that can be used by a biological product to obtain registration with the regulatory authority, in which it is necessary to present total data on the development, production, quality control and non-clinical data and clinical trials to demonstrate the quality, efficacy and safety of the product, in accordance with the provisions of this Resolution.

BIOSSIMILAR CONCEPT AT BRAZIL

BIOLOGIC PRODUCTS

The products known internationally as "biossimilars" are those registered in Brazil by means of development by comparability, recommended by RDC 55/2010.

The development of these products is done through an exercise of comparability with respect to the comparative biological product (biological product registered with the submission of a complete dossier).

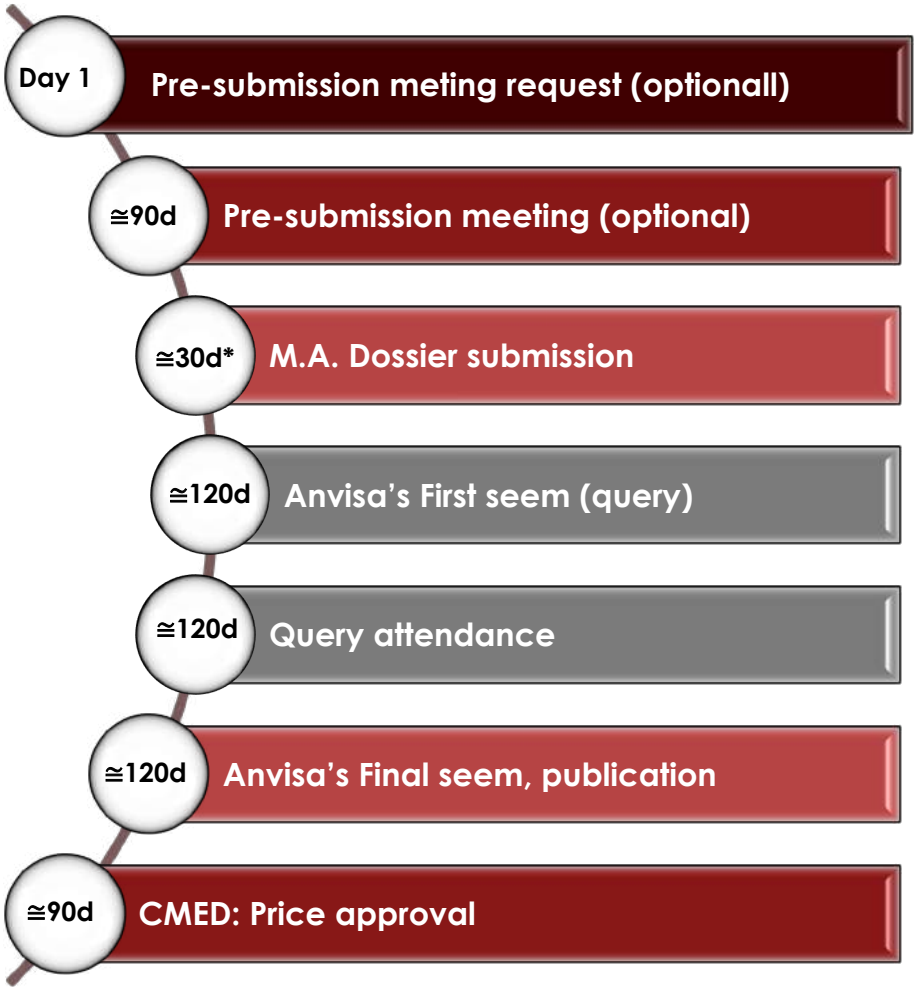
The main objective of comparability is to demonstrate that there are no significant differences in quality, efficacy and safety between the two products.

Thus, the biossimilar product need not establish the efficacy and safety of the molecule, since these have already been established by the biological comparator product.

The performance of specific studies to demonstrate interchangeability, in turn, is not a regulatory requirement for the approval of a biossimilar.

Therefore, we consider that the definition on interchangeability at the time of sanitary registration of the product is not applicable. It is worth noting that the requirements of RDC 55/2010 for registration of biossimilar products are in line with the current recommendations of the World Health Organization (WHO) and internationally recognized Guides of other Regulatory Agencies, such as EMA, Health Canada and FDA.

BIOLOGICs:
REGULATORY PATHWAY (RDC 50'10)



≅18 months

✓ Phase II + Ongoing Phase III studies
✓ Comparability pathway
✓ Waiver for local (importer) QC analysis
✓ OS 45/2018, procedure of analysis

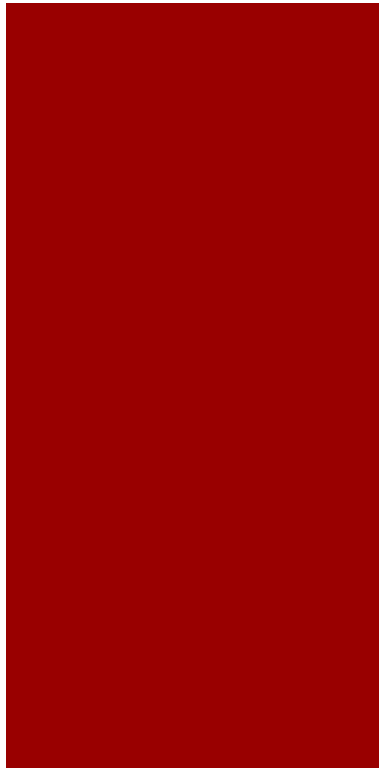
ITEMS FLEXIBILIZED

COMPULSORY ITEMS

✓ M.A. approval* (country of origin)
✓ GMP approved site
✓ Transport validation
✓ Complete quality data pack

** recommended*

ORPHAN DRUGS



RARE DISEASES
AS PER ANVISA'S CONCEPT (RDC 205'17)

"RARE DISEASE: ONE THAT AFFECTS UP TO SIXTY-FIVE PEOPLE OUT OF EVERY ONE HUNDRED THOUSAND INDIVIDUALS, AS DEFINED BY THE NATIONAL POLICY FOR COMPREHENSIVE CARE FOR PERSONS WITH RARE DISEASES, BASED ON NATIONAL OFFICIAL DATA OR, WHEN NONEXISTENT, DATA PUBLISHED IN TECHNICAL AND SCIENTIFIC DOCUMENTATION".

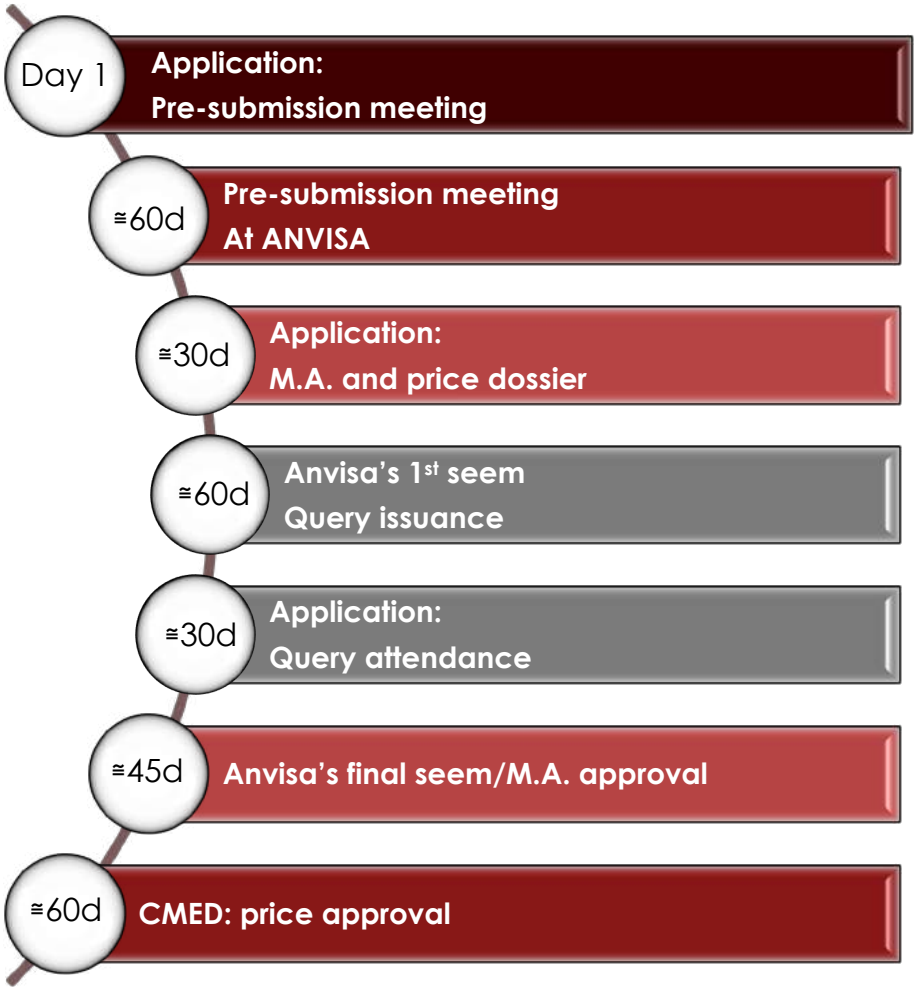
The rare disease pathway is applied for a new drug product that has the purpose of treating, diagnosing or preventing the rare disease and who:

I. **be used in a serious debilitating condition*; and**
II. **proposes to change in a clinically significant way the evolution or make possible the remission of the disease.**
III. **global and national data on the prevalence and incidence of the rare disease for which the drug will be indicated; and**
IV. **document proving the designation of a rare disease drug by another regulatory authority, when available.**

If the application for a new drug product for rare disease is not confirmed during the technical analysis of petitions for the approval of clinical trials and registration of a new drug, the application shall be rejected.

**serious debilitating condition*: disease or condition associated with irreversible morbidity or high probability of death, unless the course of the disease is discontinued.

RARE DISEASES: REGULATORY PATHWAY (RDC 205'18)



≅9 months

- ✓ Anvisa's GMP protocol
- ✓ Ongoing Zone IVb stability
- ✓ Phase II + Ongoing Phase III studies
- ✓ Shifting validation OR Importer QC
- ✓ Priority Review is now submitted with the MAA application

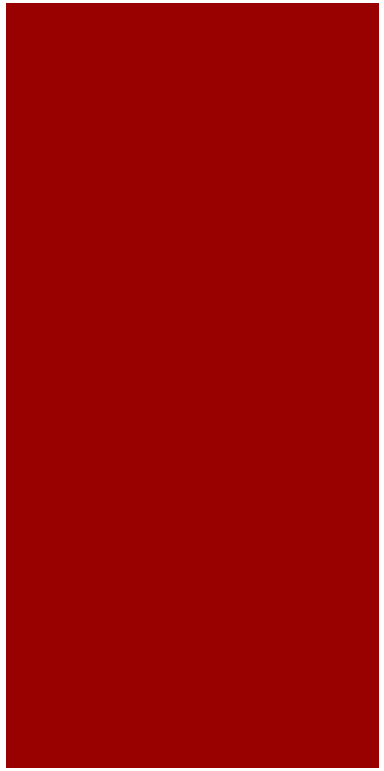
ITEMS FLEXIBILIZED

COMPULSORY ITEMS

- ✓ M.A. approval* (country of origin)
- ✓ Orphan disease status
- ✓ GMP approved site
- ✓ Complete quality data pack

** recommended*

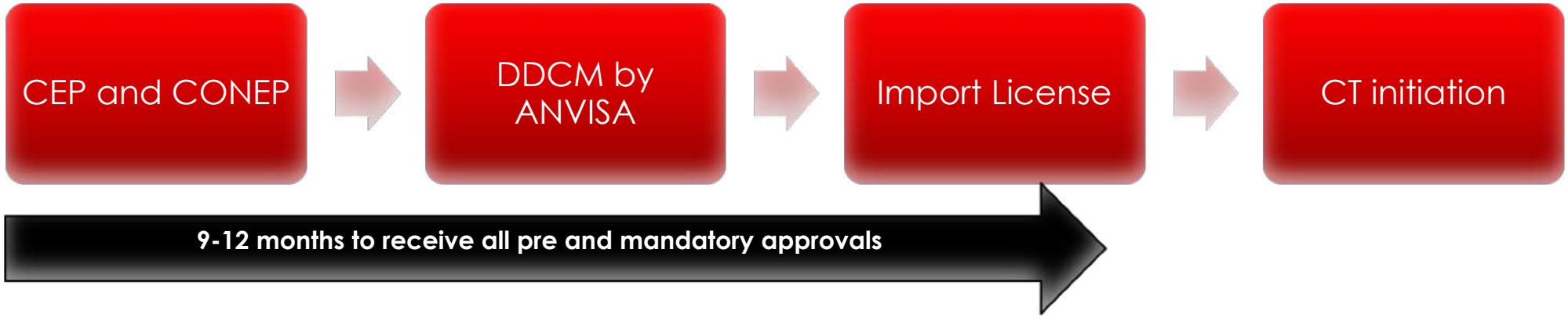
SAFETY & EFFICACY PROOFS



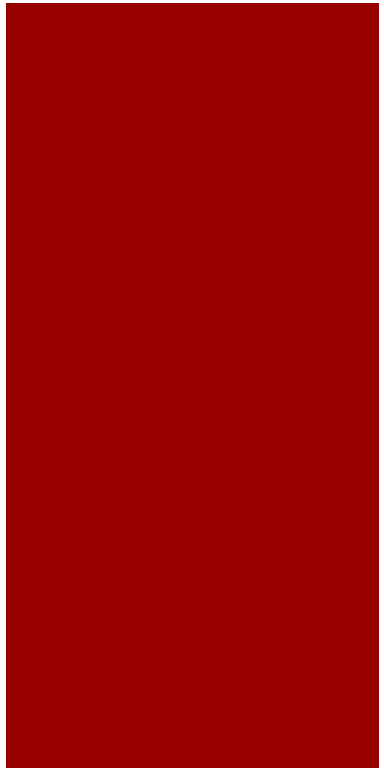
PE (Pharmaceutical Equivalence)	BE (Bioequivalence study)
General Concepts	
▪ Mandatory: same batch for PE+BE and Zone IVB stability studies. ▪ The innovator must be a Brazilian RLD, locally acquired. ▪ Only REBLAS centers are allowed to acquire RLD samples for PE+BE conduction.	
Samples	
01 batch of each strength for PE (except NS /MDIs/DPIs = 03 batches)	01 batch of higher strength for BE (same batch from PE study)
Leadtime	
45-90 days	in average 04-06 months
Specific Requirements	
Bio exemption based on BSC is accepted if proved at a REBLAS center	FAST+FED for modified release oral solids and some specific active drugs

CLINICAL TRIALS

Conduction of clinical trials with drugs in Brazil requires prior approval by Committees for Ethics in Research (CEPs), in certain cases, by the National Commission for Ethics in Research (CONEP) and, except for Bioequivalence, Bioavailability and Phase IV studies the prior approval by the National Health Surveillance Agency (ANVISA), through an application named DDCM (Drug Product Clinical Development Dossier).



CTD APPLICATIONS



ANVISA CTD GUIDE

Published on August 14th 2019

M1

- ✓ **Index / ToC**
- ✓ **Justification**
- ✓ **Copy of Technical Requirement**
- ✓ **Company operating license**
- ✓ **Certificate of Technical Responsibility**
- ✓ **Good Manufacturing Practice (GMP)**
- ✓ **Communications with the Agency**
- ✓ **Prioritization**
- ✓ **Global Regulatory Situation**
- ✓ **Evaluation report of other agencies**
- ✓ **Package Leaflet and Labeling**
- ✓ **Literature data (hyperlink)**
- ✓ **Justification for Bioisention**
- ✓ **BD / BE Study Identification**
- ✓ **List of National Researchers**
- ✓ **API, Anvisa Registration (CADIFA)**
- ✓ **API, Good Manufacturing Practices**
- ✓ **API, Labeling**
- ✓ **Last Modifications (variations)**
- ✓ **Conditional Approval (if any)**
- ✓ **Electronic media**

M3

API QC

3.2.**S**.4.1 Specification of Drug Substance

API & DRUG PRODUCT MANUFACTURERS QC

→COMPARATIVE TABLE WITH SPECS OF THE API AND DP MANUFACTURERS

API QC

3.2.**S**.4.1 Specification of Drug Substance
3.2.**S**.4.2 Analytical Procedures
3.2.**S**.4.5 Justification of Specification
3.2.**S**.4.3 Validation of Analytical Procedures
3.2.**S**.4.4 Batch Analyses

API & DRUG PRODUCT MANUFACTURERS QC

- → **SPECIFICATION**
- → **ANALYTICAL PROCEDURE**
- → **SPECS JUSTIFICATION**
- → **AMV**
- → **CoA**

M3

EXCIPIENTS QC

3.2.**P**.4.1 Specifications
3.2.**P**.4.4 Justification of Specifications
3.2.**P**.4.2 Analytical Procedures
3.2.**P**.4.3 Validation of Analytical Procedures

Not provided in CTD

EXCIPIENTS QC BY THE DP & EXCIPIENT MANUFACTURERS

→ **REQUIRED DATA FROM BOTH**

→ **CoA FROM BOTH**

M3

DP MANUFACTURING PROCESS

3.2.P.3.3 Description of Manufacturing Process and Process Controls

→**PRODUCTION & QC REPORTS IN ACCORDANCE TO RDC 200’17**

PRODUCTION ORDERS (EBR)

M3

DP QC – DRUG PRODUCT MANUFACTURER

3.2.P.5.1 Specification(s) of Drug Product	→**COMPARATIVE TABLE OF DP SPECS: SHELF-LIFE AND RELEASE**
3.2.P.5.3 Validation of Analytical Procedures	→**AMV PROTOCOL AND REPORT**

DP QC – DRUG PRODUCT IMPORTER (BRAZIL MA HOLDER)

Not provided in CTD	→**QC REPORT AND CoA PERFORMED BY THE IMPORTER**

M3

COMPARATIVE TABLES

Not provided in CTD

→**MASTER FORMULA (POST-APPROVALS)**

→**MANUFACTURING PROCESSES (POST-APPROVALS)**

→**BATCH SIZE (POST-APPROVALS)**

→**COMPARATIVE STUDIES (COMPARATIVE IMPURITY PROFILE, DIFFERENCES OF ANALYTICAL PROCEDURES, COMPARATIVE DISSOLUTION PROFILE)**

TRANSITION

IS THE DOSSIER MIGRATION ALREADY APPROVED BY ANVISA FOR CTD FORMAT COMPULSORY?

No, but it is encouraged that the quality part (Module 3) be reformatted to facilitate change management throughout the product life cycle.

It is recommended that the reformatting company make a statement that the quality information is exactly the same as that already approved.It is the company's choice to migrate to CTD format, but once the new format is adopted, all subsequent petitions must follow the format, including the Product Change History protocol, as described in 3.2.R.

TRANSITION

IS IT POSSIBLE TO MAKE A POST-REGISTRATION IN CTD FORMAT NOW AND REFER TO THE OLD FORMAT DOSSIER?

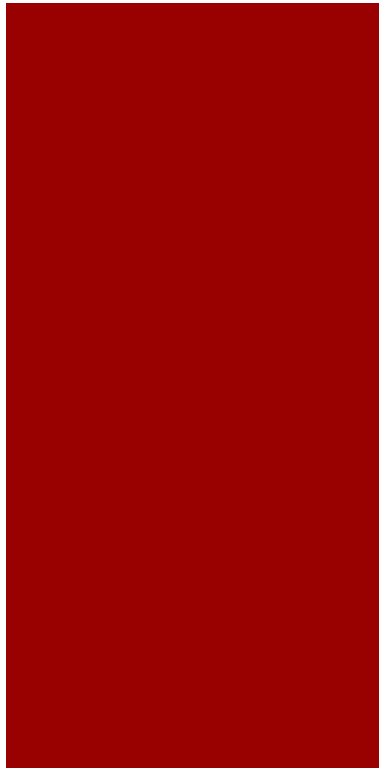
YES, it is possible to indicate the checklist item where the approved information is in the old dossier.

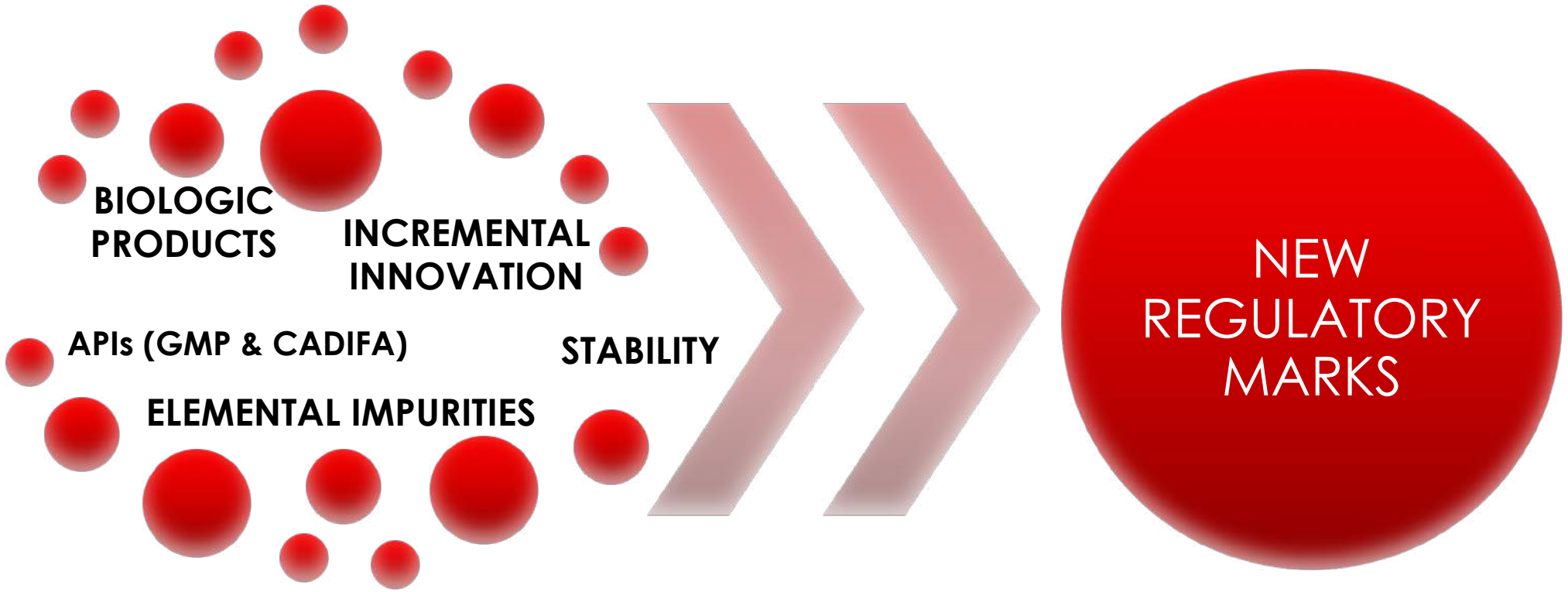
IF DOES THE COMPANY CHANGE THE DOCUMENT WHEN IT MUST SUBMIT TO ANVISA?

Preferably in a post approval change petition.

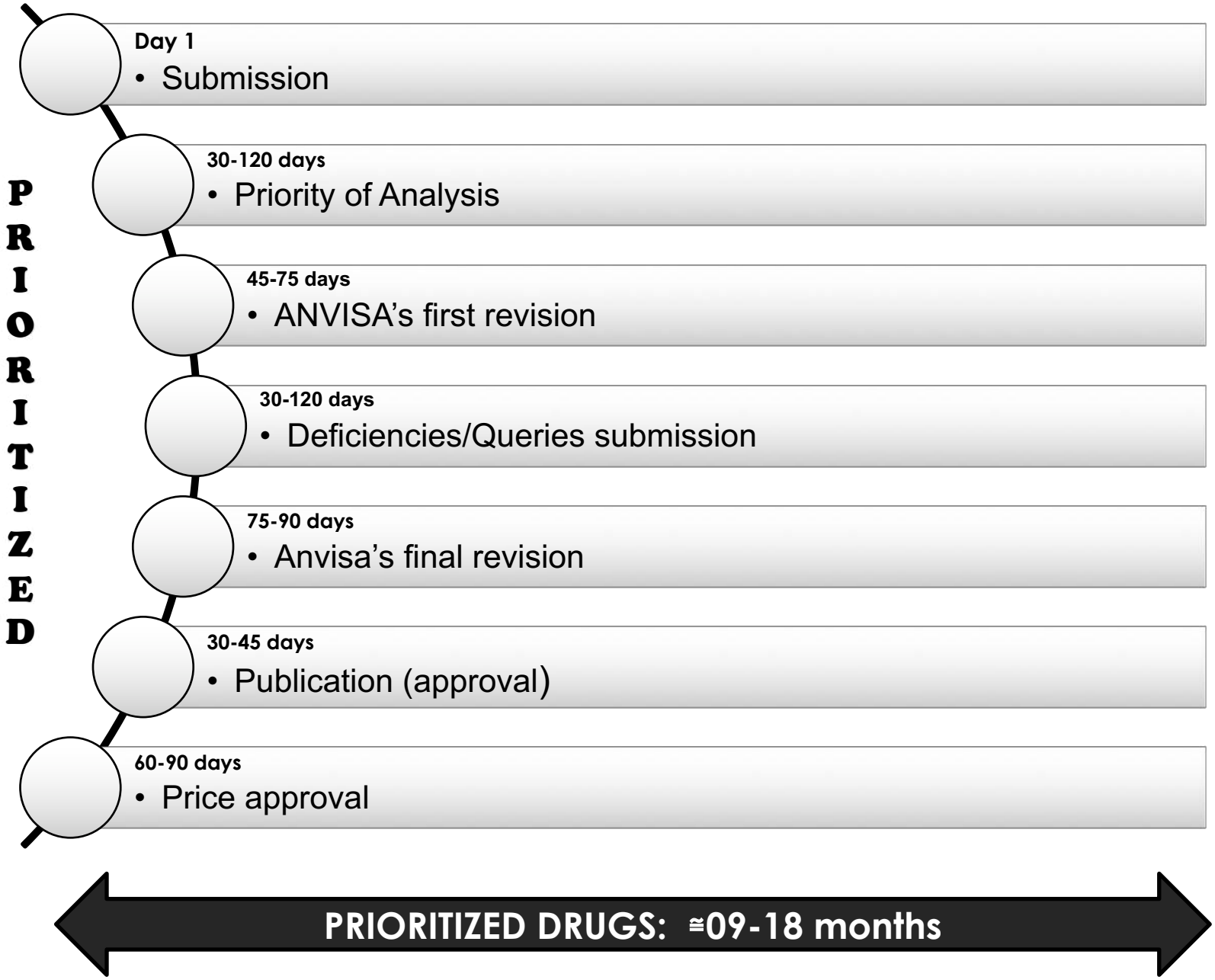
Ideally, it should be presented separately from the change so that changes can be verified between the original dossier and the petition dossier.

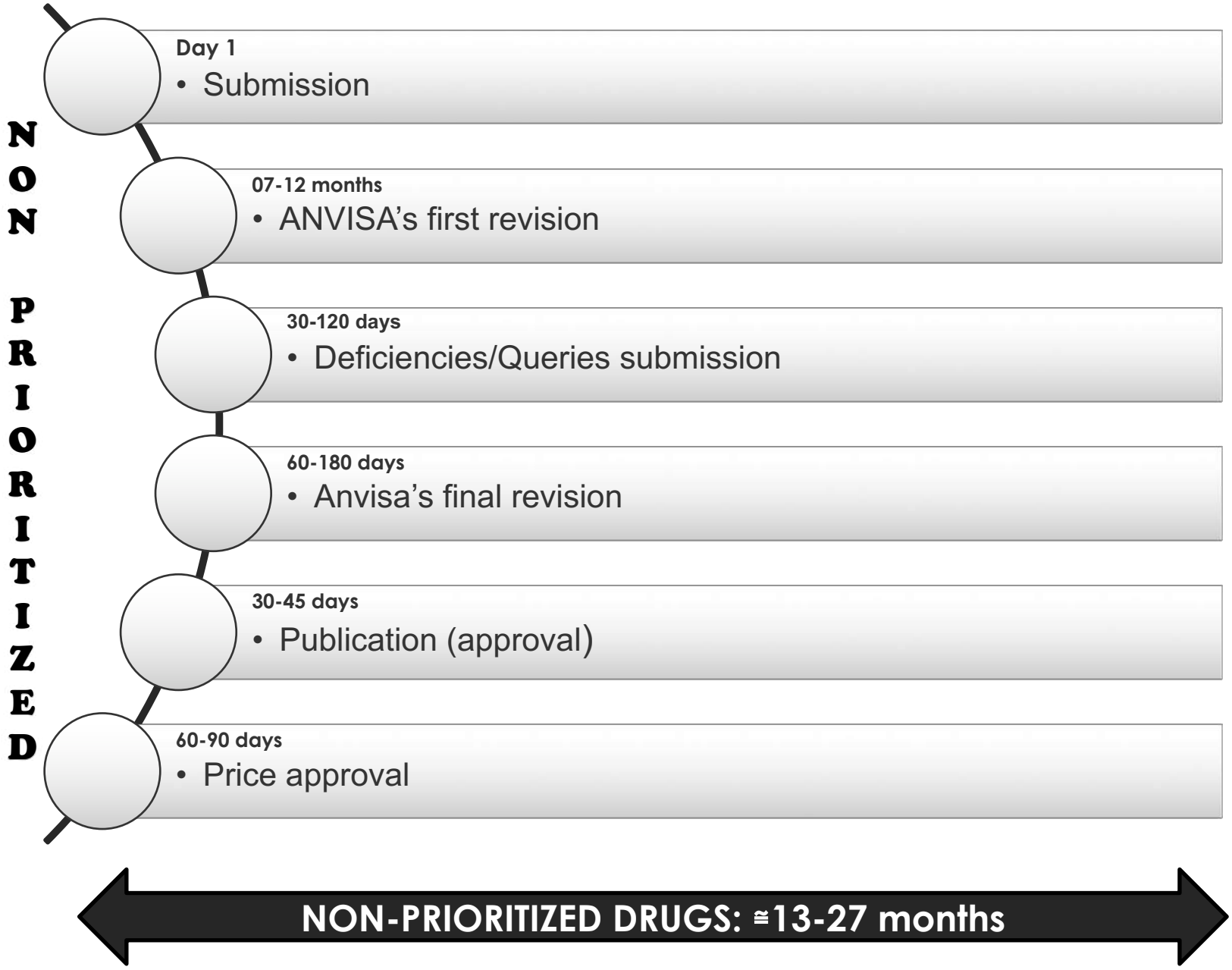
REGULATORY TRENDS
public consultations




BIOLOGIC PRODUCTS
INCREMENTAL INNOVATION
APIs (GMP & CADIFA)
STABILITY
ELEMENTAL IMPURITIES
NEW REGULATORY MARKS

APPROVALS


PRIORITIZED
Day 1
• Submission
30-120 days
• Priority of Analysis
45-75 days
• ANVISA's first revision
30-120 days
• Deficiencies/Queries submission
75-90 days
• Anvisa's final revision
30-45 days
• Publication (approval)
60-90 days
• Price approval
PRIORITIZED DRUGS: ≅09-18 months


NON PRIORITIZED
Day 1
• Submission
07-12 months
• ANVISA's first revision
30-120 days
• Deficiencies/Queries submission
60-180 days
• Anvisa's final revision
30-45 days
• Publication (approval)
60-90 days
• Price approval
NON-PRIORITIZED DRUGS: ≅13-27 months