



# REFORMATING YOUR CTD INFORMATION FOR YOUR BRAZILIAN REGISTRATION DOSSIER

DECEMBER 2014



THOMSON REUTERS™

# 1. INTRODUCTION

---

The European Union, United States, and Japan—all International Conference on Harmonization (ICH) country members—remain the biggest and highest potential yield markets for medicinal products worldwide. However, in the last few years global pharmaceutical companies have recognized other regions—including Latin America, Middle East/Africa, and Asia—as increasingly important and interest-worthy for strategic marketing purposes.

In most countries, pharmaceutical legislations and regulatory requirements are well established and implemented to describe the marketing authorization (MA) procedures for medicinal products. The objective of the pharmaceutical companies is to identify ways and factors that impede the efficient registration of new medicinal products and their timely access to patients.

To be able to submit a marketing authorization application (MAA) in all countries of interest, applicants need to know exactly in advance the pharmaceutical legislation (regulations, directives, and guidelines) and other regulatory requirements, in order to plan an efficient registration process.

This white paper aims at providing some insights to face such challenges, and focuses on Brazil's dossier requirements for new chemical entities (NCEs) and generics. It outlines the regional specificities of the Brazilian dossier and the similarities to the Common Technical Document (CTD)—applicable standard format in ICH countries—to help companies reformat the information for submission to the Brazilian Medicines Agency (*Agência Nacional de Vigilância Sanitária*—ANVISA).

# 2. CTD REGISTRATION DOSSIER

---

ICH is a joint initiative involving both regulators and research-based industry representatives of the European Union, Japan and the USA in scientific and technical discussions of the testing procedures required to assess and ensure the safety, quality and efficacy of medicines.

In the early 2000, the common registration format—CTD—revolutionized the regulatory registration processes in ICH country members. This harmonization led to implementing electronic submission and, in turn, facilitated the Good Review Practices by the different authorities. From the industry perspective, it eliminated the need to reformat the information

for submission. In addition, to meet a global registration approach, pharmaceutical companies generally use CTD dossier components as basis for registration dossiers in other countries. Regulatory reviews and communication with the applicant are facilitated by a standard document of common elements. Moreover, exchange of regulatory information between different Regulatory Authorities becomes simplified.

The CTD is organized into five modules. Module 1 is region specific and consists of administrative information, Modules 2–5 are intended to be common for all regions.

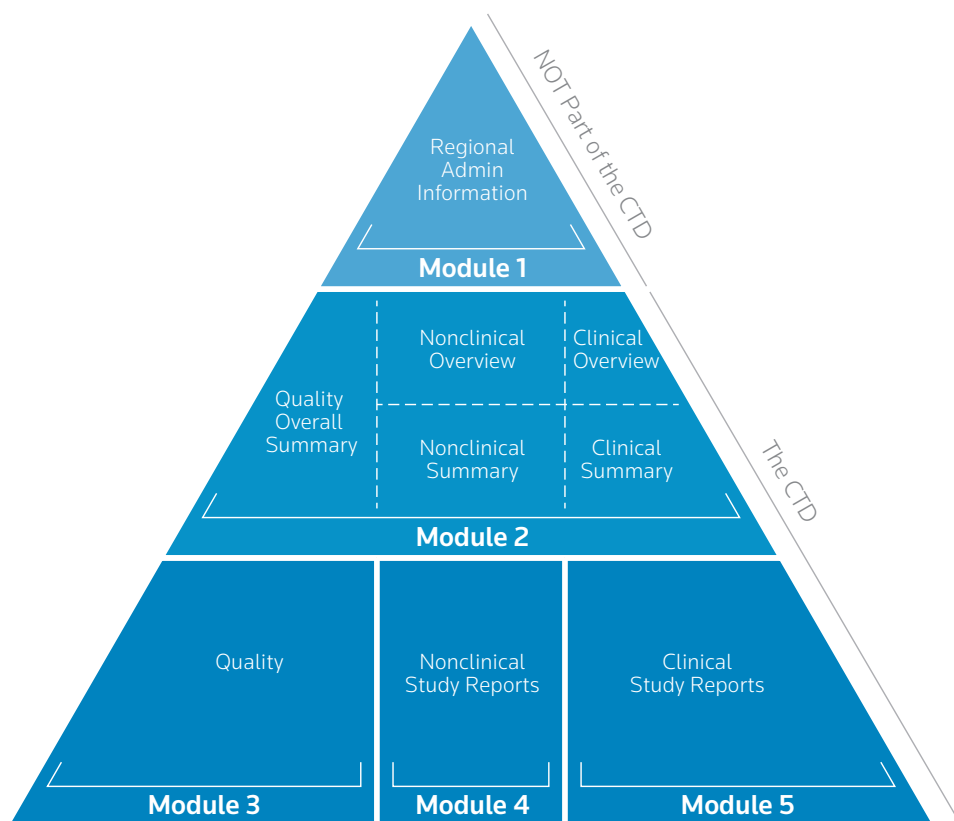
Module 2 contains summaries on quality, non clinical and clinical information, with references to appropriate sections of Modules 3, 4, and 5.

Modules 3, 4, and 5 are detailed studies and reports on quality, non clinical and clinical topics, respectively.

However, until now, no harmonization in the organization of registration documents has

occurred. Each region has its own requirements for the organization of the technical reports to be submitted and for the preparation of the summaries and tables.

For example, in Japan, applicants must prepare the GAIYO, which organizes and presents a summary of the technical information. In Europe, Expert Reports and tabulated summaries are required, and written summaries are recommended.



**Figure 1:** Organization of the CTD dossier

# 3. ANVISA'S SUBMISSION: PRODUCT REGISTRATION DOSSIER

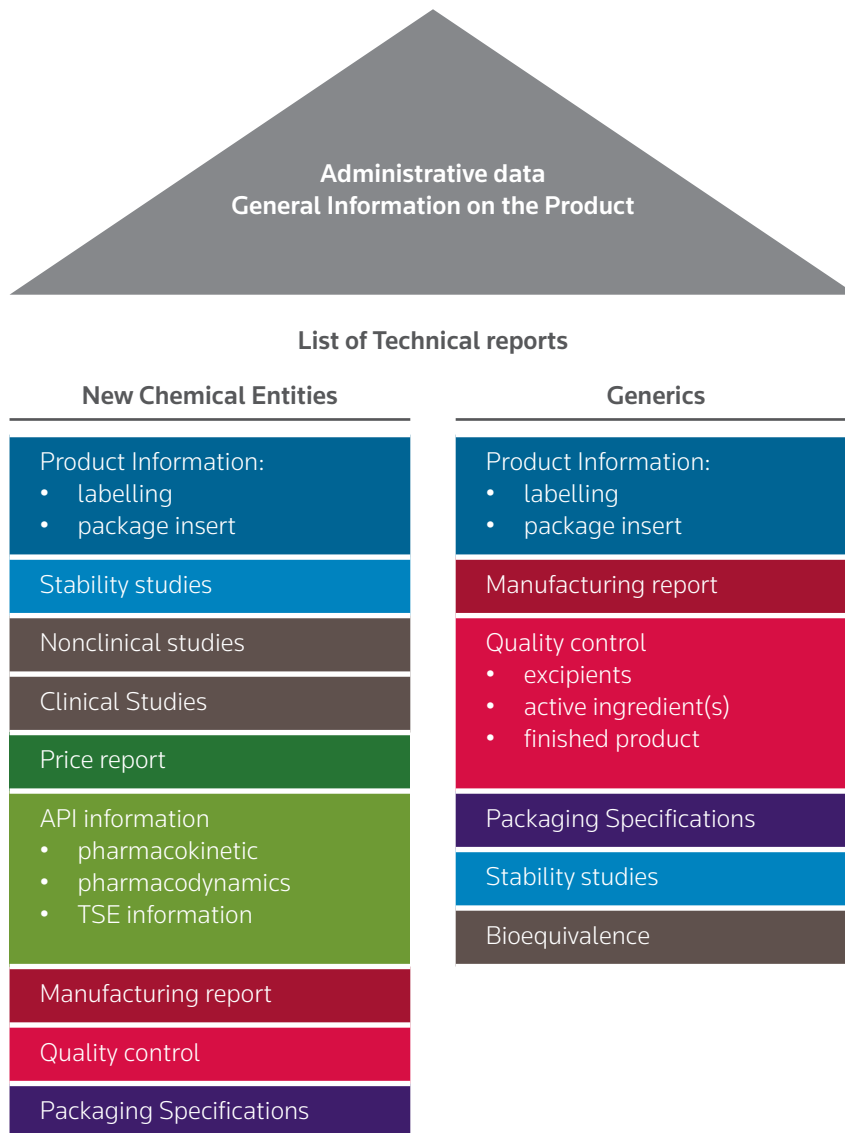
The marketing authorization dossier of a medicinal product—Product Registration Dossier (PRD) — should be submitted to the Brazilian Health Authority in Portuguese.

The main current regulations in Brazil, Resolutions of the Collegiate Board of Directors (*Resoluções da Diretoria Colegiada—RDC*), describe the exact content of the application dossier, for each type of product. In addition, different check lists are available on ANVISA's website, for applicants to ensure their documentation is complete and submitted in an orderly fashion.

A brief overview of the Brazilian regulations shows that the dossier is structured in two main parts:

- Compilation of all administrative data, including specific requirements for imported products
- Technical reports, including quality, non-clinical and clinical information, presenting similarities to the Modules 2, 3, 4, and 5 of the CTD dossier

**Figure 2:** Organization of the Brazilian Product Registration Dossier (PRD) for New Chemical Entities (NCEs) and Generics



## 4. HOW TO BUILD A PRD USING A PREVIOUSLY SUBMITTED CTD?

Generally, the full dossier requirements for new medicinal products in Brazil are quite similar to those of ICH countries. The content of the technical dossier (pharmaceutical/chemical, preclinical, and clinical documentation) is generally similar to the ICH region.

Special attention should be paid to the order of submission. It is crucial the documentation be arranged in the same order as the one described in the procedure-related checklist.

The information should be submitted with a similar approach, with the first part on administrative data, followed by a succession of technical reports.

However when looking closely at the documentation, the general approach remains different: “summaries” as such are not required; documents submitted in the “Administrative” section of the CTD are part of the Technical report in the PRD, whereas specific documents not part of the CTD are essential to the PRD submission.

As far as Administrative information is concerned, based on practical experience, some administrative documents (like Certificates of Pharmaceutical Product, Powers of Attorney, Good Manufacturing Practices certificates, manufacturing authorizations, etc.) are required for new medicinal products which are imported to Brazil.

Most of the documents must be submitted in Portuguese, meaning additional time (and associated costs) is necessary. A global registration strategy should take into account such specificities and plan resources accordingly.

The approach for the submission of technical reports is more complicated and must be included from the beginning when assembling a global

ADMINISTRATIVE

### Specificities of the PRD

- CPP issued from the Health Authority of the manufacturing country or country of origin
- Legalization of the documents
- GMP certificate granted by ANVISA upon inspection
- For imported products only: local repetition of release product labelling once a product is approved and during commercialization

TECHNICAL REPORT

### Specificities of the PRD

- Inspection of the manufacturing sites by ANVISA for product approval. An inspection request (separate application from the MA application), needs to be built from site master files (SMFs) and other manufacturing site specific documentation and filed prior to the MA application.
- Specific conditions applicable to Stability Studies—climate zone IV b
- Labelling requirements: in Portuguese, mock-ups required for submission. Pursuing serialised two-dimensional codes
- Generics: Biostudies have to be performed against a reference product marketed in Brazil
- Economic information (price report)

**Figure 3:** Main specificities of the PRD

registration strategy. Several specificities stand out, such as requesting manufacturing batch records for finished products. In addition, as Brazil belongs to the climatic zone IV b, the dossier must contain stability data performed at 30°C/75% RH for long term stability.

One document is specific to all Brazilian applications: a price report must be included as part of the dossier's technical report. This price report will help the Authorities fix a price for the finished product, taking into account the manufacturing price in Brazil and the costs for the patients. This report must be submitted as part of the application dossier, therefore should be prepared in advance.

Transparency in documentation and decision outcomes is a hot topic and access to regulatory information has been facilitated over the last few years in Brazil. However, due to regular organizational changes at ANVISA and to the Medicines Agency's website, information readily available on the Internet may not be the most up to date. In addition, the regulations have been developed on a text by text basis, through the publication of multiple Resolutions (Resoluções), giving form to a regulatory layer cake. Previous rules have been enhanced by adding new layers. As such, finding the appropriate regulation on a specific topic might be a big challenge.

Confirmation with local experts or affiliates is strongly recommended.

## 5. CONCLUSION

---

In 2013, ANVISA adopted a set of measures to modernize and expedite the marketing approval review process for new products. The goal is to improve the operational capacity of the agency, modernize the regulatory framework, debureaucratize processes, focus on actions such as health risk management, and expand cooperation with international agencies to avoid duplication of inspections (for instance in the GMP certification, with the publication of [Resolution RDC 39/2013 \(IDRAC 168782\)](#)). This could reduce the 600 inspections conducted annually by ANVISA in other countries by 70 percent, without compromising public health in Brazil. Another goal is to reduce review and approval time to six months from the current nine month average for technological innovation and priority medications for hypertension, diabetes, and cancer.

Updates to regulations are therefore frequent to reinforce the implementation of legislation. Public consultations are regularly issued by the Agency, but it is difficult to forecast when a new legislation will be officially published. Changes are constant; consequently it is critical to remain up to date with the latest regulatory updates. In parallel, the services of regulatory professionals, with the appropriate local experience, knowledge of the country's language, and the Medicines Agency's culture might be helpful to orient strategy in the preparation of the dossier.

Knowledge of the drug registration processes and submission content is key for effective planning and execution of global regulatory strategy. But a step by step approach is essential to make any global submission successful.

## 6. WHERE TO FIND MORE INFORMATION

---

Information related to the Brazilian Registration dossier and to the comparison of the PRD with the CTD format described in this paper, is available in Cortellis Regulatory Intelligence : "[How to reformat your CTD information for your local registration dossiers](#)". Thomson Reuters has recently increased the coverage of Regulatory Intelligence Reports with the addition of detailed table to provide clear insight to the pharmaceutical industry on how to reuse the information initially contained in the CTD, in order to adapt it for local registration dossiers.

For any specific inquiries about Thomson Reuters offerings please contact:

### EMEA

Riccardo Sciabica, PharmD  
Solutions Specialist, Cortellis  
Regulatory Intelligence  
O: +33 1 5306 2031  
M: +33 6 8998 0437  
E: [riccardo.sciabica@thomsonreuters.com](mailto:riccardo.sciabica@thomsonreuters.com)

### JAPAN

Shiho Yoshitomi  
Solutions Specialist, Cortellis  
Regulatory Intelligence  
O: +81 3 4589 3179  
E: [shiho.yoshitomi@thomsonreuters.com](mailto:shiho.yoshitomi@thomsonreuters.com)

### LATIN AMERICA

Antero Macedo, PhD  
Solutions Specialist, Life Sciences  
O: +5511 2159 0552  
M: +5511 98556 8849  
E: [antero.macedo@thomsonreuters.com](mailto:antero.macedo@thomsonreuters.com)

### NORTH AMERICA

Ilan McNamara, PhD  
Solutions Specialist, Cortellis  
Regulatory Intelligence  
O: +1 215 823 5369  
M: +1 267 402 0897  
E: [ilan.mcnamara@thomsonreuters.com](mailto:ilan.mcnamara@thomsonreuters.com)

## 7. REFERENCES

---

1. [ANVISA—Homepage](#)
2. [Thomson Reuters Cortellis Regulatory Intelligence](#)
3. [EMA—Dossier Format: Regulatory and procedural guidance](#)
4. [ICH—M4: The Common Technical Document](#)

### THOMSON REUTERS REGIONAL OFFICES

#### Americas

+1 800 333 4656  
+ 1 651 244 5375

#### Europe, Middle East, Africa

+ 44 20 7433 4000

#### Asia Pacific

+ 65 6775 5088 (Singapore)  
+ 813 4589 3101 (Tokyo)

Copyright © 2014 Thomson Reuters



THOMSON REUTERS™