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Drug Serialization And Traceability:

A focused overview of validation and qualification.

Elaborated in 2021/august, version 2

Drug Serialization And Traceability:

Be aware of the deadlines and main challenges for validation professionals

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In general, the serialization and traceability projects consist of obtaining information from each commercial drug unit in its entire chain (manufacture/import, storage, distribution and dispensation). In this way, it is possible to check the regulation of the drug, that is, if it is a registered product that was produced or imported by an authorized company and all its movement in the logistic chain until it reaches the consumer or health unit.

It is important to highlight that the SNCM (National Drug Control System) does not address the fiscal movement of drugs, focusing on the physical movement process, so it does not need to be communicated when there has been no physical movement or change/handling of cargo that can modify its sanitary conditions.

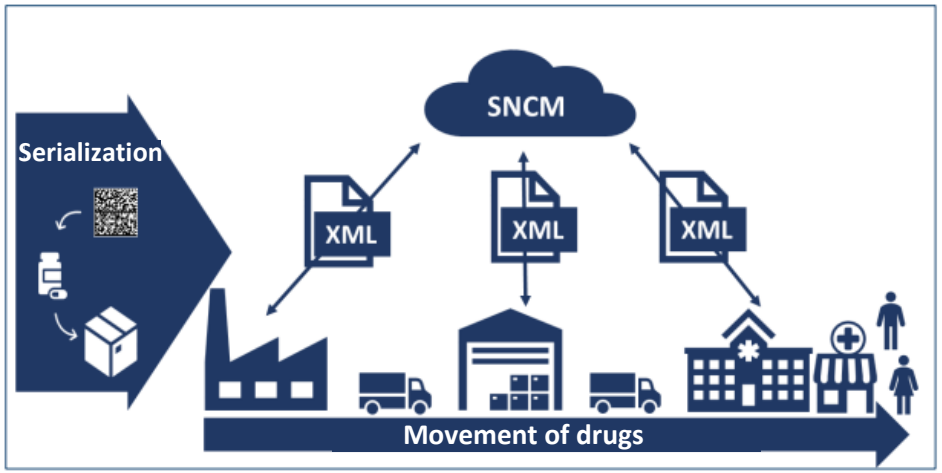


Figure 1: Serialized drug movement chain integrated into the SNCM (adapt. ANVISA, 2020)

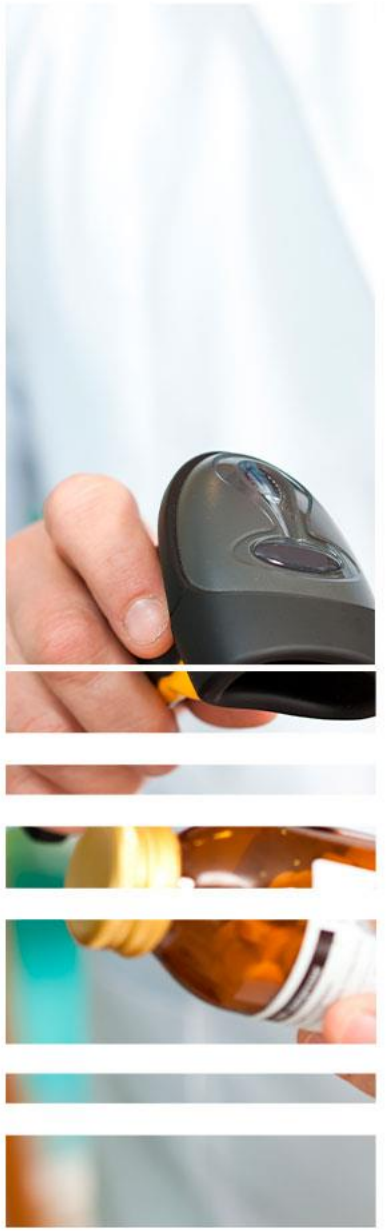
History

History

The drug traceability is a topic that has been discussed for almost 20 years, with the first legal proposition created in 2002 (Nº6.672/2002). Since then, several legal proposition, RDC's (Resolution of the Collegiate Board) and IN's (Normative Instruction) have been discussed and the Law nº 13.410/2016 is currently in force.

The Law nº 13.410/2016 provides for the National Drug Control System (SNCM) and, according to Art 1, aims to control the production, distribution, marketing, dispensation, and medical and dental prescriptions and, if it contains drug for human use, veterinary, as well as other types of movement provided by sanitary controls.

ANVISA working together with the Automation and IT Management Group (Gaesi) of the University of São Paulo carried out an experimental phase that simulated the transmission and validation of traceability data.

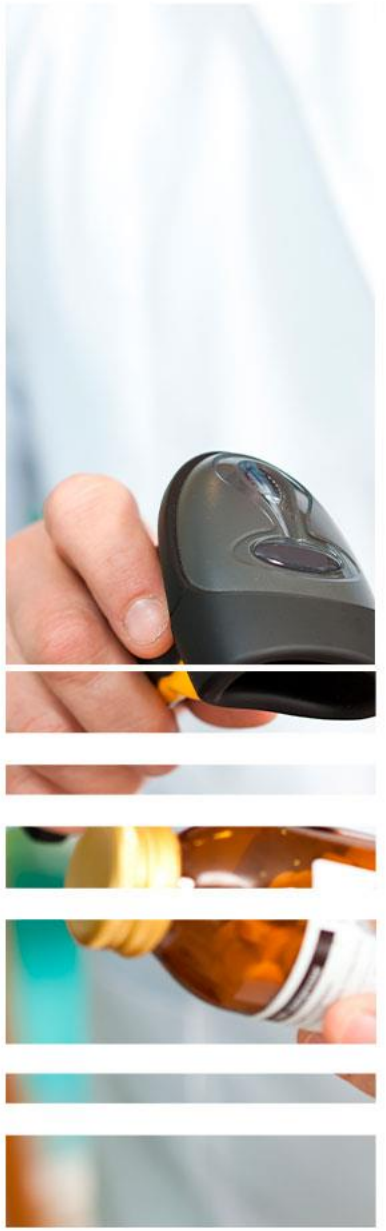


After one year of testing with the participation of several companies, including industries, distributors, pharmacies, and hospitals, ANVISA completed the experimental phase of the SNCM, which helped to mitigate risks and improve the system.

The tests evaluated the concepts in controlled scenarios of data transmission of regular drug movement operations, being possible to evaluate scenarios, such as reception prior to activation/dispatch, event communication after the deadline defined in the regulation and divergence in IUM (Unique Medicine Identifier) information, among others.

The result of the experimental phase proved to be satisfactory, despite needing adjustments.

According to data from ANVISA (process nº 25351.048778/2012-10), the project depends on thousands of agents to be carried out, with 221 companies producing and/or importing medicines; more than 250 distributors; 87,000 pharmacies; 4,600 private hospitals, plus the public sector, which will also have to minimally communicate the data through the states and municipalities.



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Which Drugs Will Be Subject To SNCM Control?

Which drugs will be subject to SNCM control?

As required by law, the competent federal health surveillance agency will determine the categories of drugs that will be subject to control.

On August 23rd, 2021, ANVISA consolidated the Normative Instruction - IN No. 100, which establishes the drugs subject to the National Drug Control System (SNCM) and the deadlines for serialization and for starting the communication of records of instances of events.

According to the Normative Instruction (article 4), all medicines registered with ANVISA are subject to the National Drug Control System - SNCM, however it is optional the following categories of medicines.

I. OTC or nonprescription medicine;

II. specific, herbal and dynamized;

III. radiopharmaceuticals;

IV. injectable contrast media;

V. medicinal gases;

VI. parenteral solutions from 50ml;

VII. serums, vaccines, and medicines with institutional destination; and

VIII. free samples.

Phases And Deadlines Of The Serialization And Traceability Project

Phases and deadlines of the serialization and traceability project

All regularized drugs, with the exception of the one highlighted in Art 4, must be mandatorily serialized for the purpose of reporting the instance record of events in the movement chain to the National Drug Control System (SNCM) by April 28, 2022. Therefore, there seems to be no longer the concept of a module “implementation SNCM” and “definitive SNCM”, and it is not clear how the L5 tests (see layer definition on page 16) with the ANVISA server will be. Perhaps the first tests can be carried out with a real product.

In general, there is no doubt, but it is clearly highlighted in Article 5 that the manufacturing and importing companies must plan the acquisition, qualification, validation and logistical integration of equipment and serialization solutions for all medicines regulated under the terms of the article 4th. The established actions must be arranged in a Serialization Plan, which must:

I cover all production lines, medicines and deadlines referred to in art. 4th;

II - be formally documented and approved by the Pharmaceutical Quality Management System and ratified by the company's management;

III - be permanently updated and adapted according to its execution;

IV - possess information and data relating to the drugs, sites, production lines and steps involved;

V - be available via the SNCM portal; within 30 days after the platform is made available; and

VI - have partial percentages until the complete serialization of the production lines of the products referred to in art. 4th.

Therefore, although it is not subdivided into two phases and contains defined stages and percentages until its completion, the partial percentages must be provided in accordance with the serialization plan defined by the company. Thus, the issuance of partial reports to prove the service, as well as to verify that 'what was foreseen' was 'actually delivered,' and the validation of this data.

The deadlines are challenging and according to article 4, until April 28, 2022, 100% of the batches must carry out the appropriate communication of events in the SNCM system. Validation, in addition to being a regulatory requirement, can support proof of these percentages to the regulatory body.

The fact that the serialization plan must be made available within 30 days after the platform is made is highlighted, that is, the sooner companies prepare, the easier the availability and planning will be. Do not leave the planning and quotation of activities to the last minute.

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Implementation Of The Serialization And Traceability Project

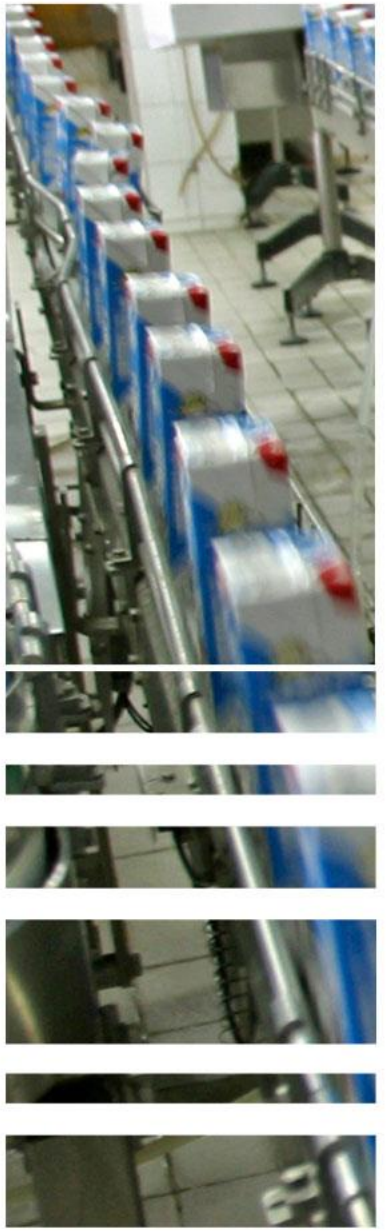
Implementation of the serialization and traceability project

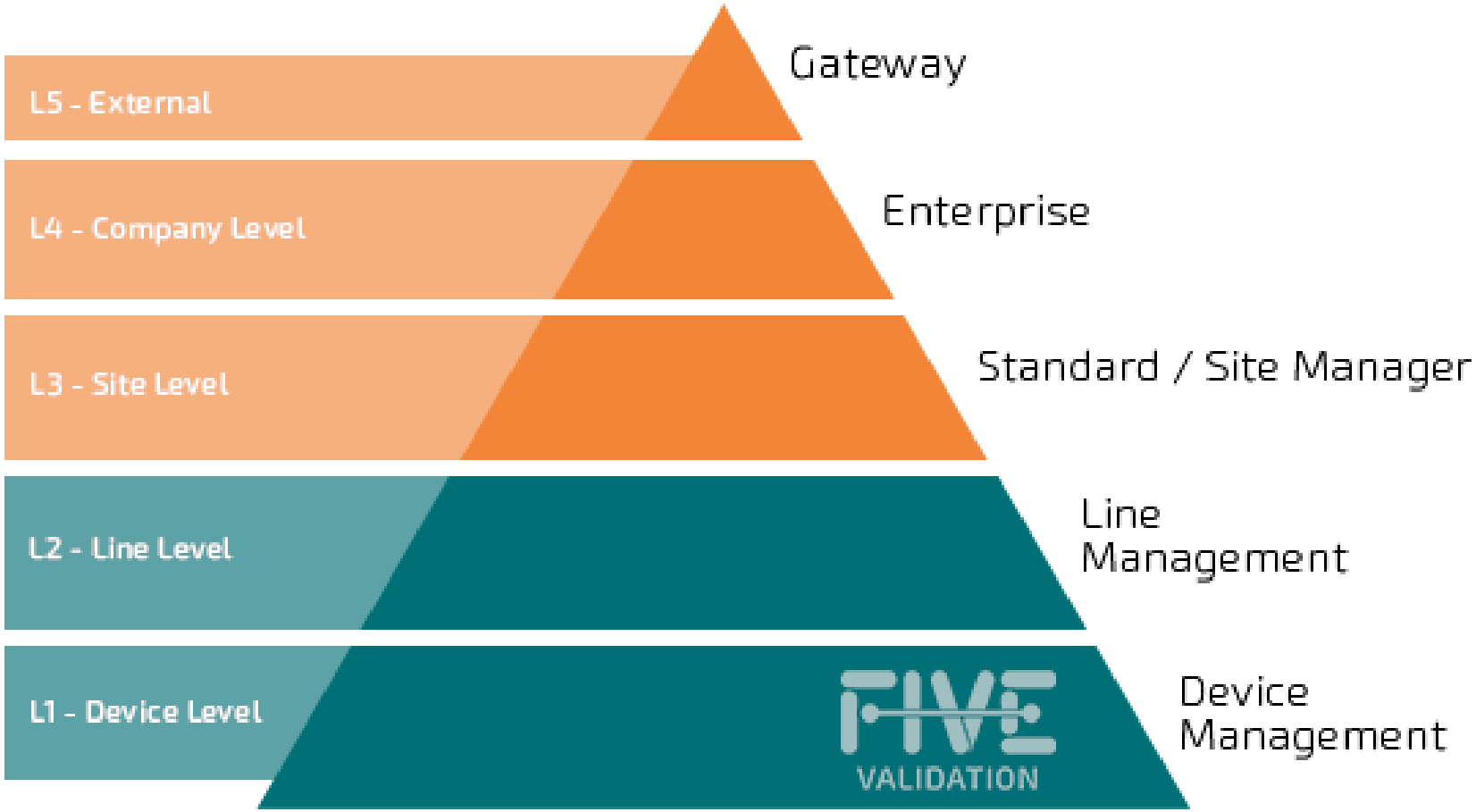
Manufacturers and importers must establish a Serialization Plan to schedule the acquisition, qualification, validation and logistics integration of the serialization equipment and solutions.

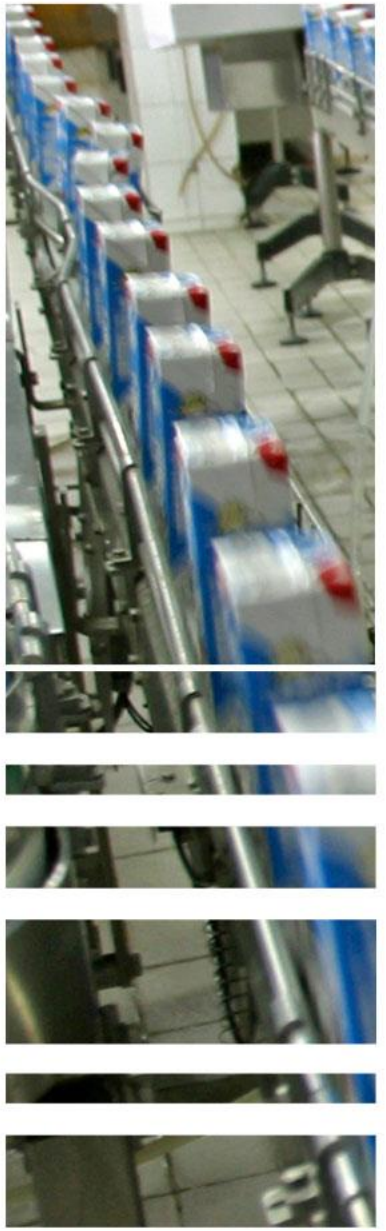
The implementation of traceability takes place through the serialization and aggregation of products. Depending on the automation of the line and its complexity, the project can be ‘more or less’ challenging.

The first step in carrying out the project is to provide the necessary people for discussion, implementation, and management, by creating a multidisciplinary traceability group or committee. Given that, the GxP impact and risk of sanctions, it is extremely important to evaluate the suppliers involved as a way of complying with the rules of RDC 301/2019 IN 43 art 11, which apply to suppliers and service providers that are used to supply, install, configure, integrate, validate, maintain, modify or store a computer system.

The traceability project is composed of several levels, which is the hardware and software architecture necessary for this relevant information of drugs, are intact, complete and traceable. Try to identify which layer(s) will be needed and which equipment, devices, packaging lines and software will be involved.



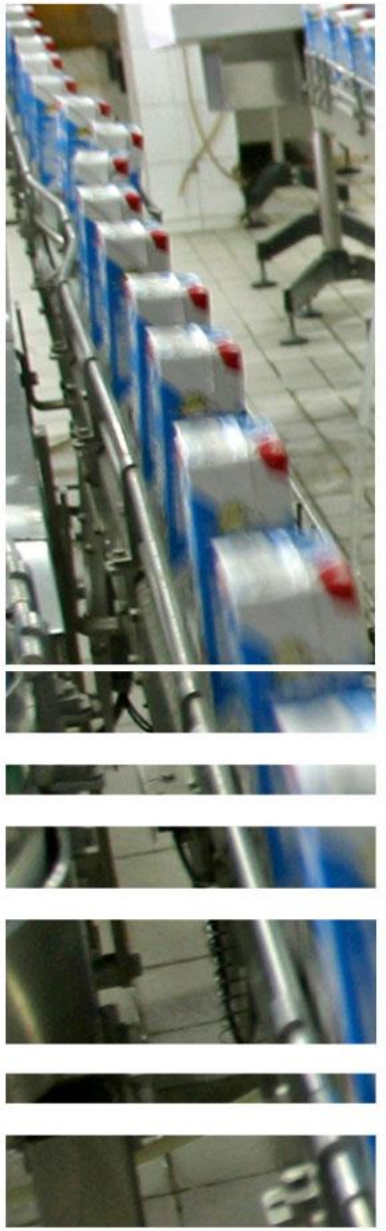

L5 - External
Gateway
L4 - Company Level
Enterprise
L3 - Site Level
Standard / Site Manager
L2 - Line Level
Line Management
L1 - Device Level
Device Management
FIVE VALIDATION



L1 – “Device Management” - management of physical equipment and devices used for serialization, such as data matrix encoders, vision cameras, printers, scanners, readers, among others. In this layer, for example, equipment qualification, compliance of the Unique Medicine Identifier (IUM) and Transport Packaging Identifier (IET) must be verified, and these can be performed at the L2 level, depending on the solution.

L2 – Line Management - software that controls the serialization and aggregation hardware present in a packaging line. It is necessary to understand whether the lines are automatic or manual, the number of lines that will be equipped with serialization and aggregation. At this level, the system involved applies and prints serial numbers on the packages, operates the aggregation of boxes and pallets, creates the 'parent-child' relationship between the box and all codes within it, packaging products for shipping and distribution. Label printing and verification can be done automatically, as well as rejection of non-conformable products. If the project is composed of a single line, level 3 may not be necessary.

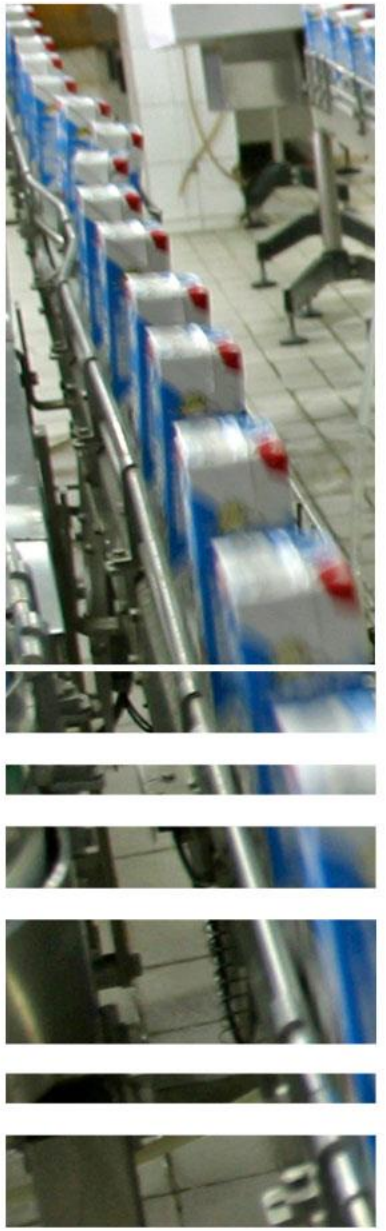
L3 – Standard/Site Manager - it is the system responsible for centralizing information from different production lines, and can be solved by a MES (Manufacturing Execution System) system.



L4 – Enterprise - traceability system: it is the corporate level of the solution, responsible for the generation and management of serial numbers to be used by the shop floor systems for L2/L3 in which it will interface with L5.

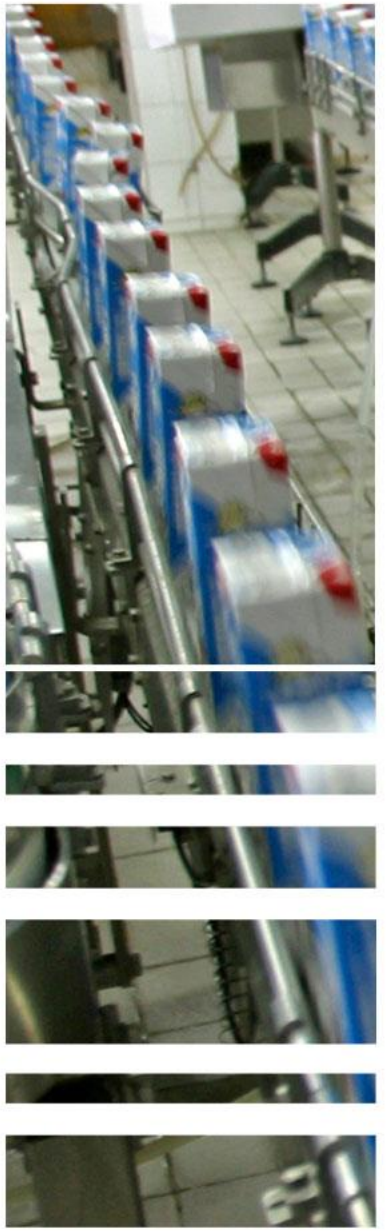
L5 – Gateway – external communication with the regulatory agency – ANVISA with the next link of the chain (and previous, if applicable), that is, communication must be vertical and horizontal. Connects the supply chain partner and regulatory authorities.

There are software solutions on the market that address more than one level described above. Thus, depending on the size of the company, it may be common to implement 2 different system solutions, from different suppliers that communicate: serialization, in the manufacturing area and traceability, to manage the IUMs and communicate the events to ANVISA.



In summary, to prepare the project, the following should be considered:

- creation of a serialization and traceability group/committee;
- creation of user requirements;
- supplier qualification;
- different scenarios (new and/or old machines);
- different processes (manual and/or automatic);
- expected events (activation, dispatch, receipt, completion, replacement and revocation);
- communication between links of the chain, i.e. vertical and horizontal communication;
- project dimension (different levels, equipment, interfaces and systems involved);
- equipment qualification;
- validation of computerized systems.



Validation Of Computerized Systems

Validation of computerized systems

Phased projects and partial reporting that are in line with paperless validation platforms. When it is done in the traditional way, on paper, they are difficult to be managed and elaborated, also making it difficult to monitor and control deviations that can happen in the project, bringing, in addition to bureaucracy and slowness, risks of delays and compliance.

The changes that will be made to the project, for example, change, addition of lines and equipment, and the systematics for these records and management, can have a significant impact on the success of the project. Using the flexibility of a Validation Lifecycle Management System - VLMS software means using a tool that is fully adapted to the needs of companies, with the compliance required by the regulatory agency and the facility to maintain the validation of the systems involved in the project.

According to Guideline n° 01/2020 of October 7, 2020 (Guideline of the National Drug Control System), they must submit the client system1 to computerized systems validation:

- Registration holder;
- Distributor;
- Dispenser.

If the communication is carried out by a third party, it is necessary to qualify the supplier and validate the horizontal and vertical communications. Carrying out the validation will minimize project risks and ensure application compliance, avoiding regulatory agency sanctions[2].

The elaboration of a well-documented User Requirement Specification (URS) considering the mandatory requirements efficiently assists in the choice of suppliers and equalization of proposals.

[1]According to Guideline nº 01/2020 of October 7, 2020 (Guideline of the National Drug Control System), the client system is characterized by the technological environment that must be operated by the member of the drug movement chain or respective attorney, with the purpose to perform this communication.

[2]According to Law nº 13,410, Art. 3: the establishment that fails to communicate any information regarding the movement of drugs commits a sanitary infraction.

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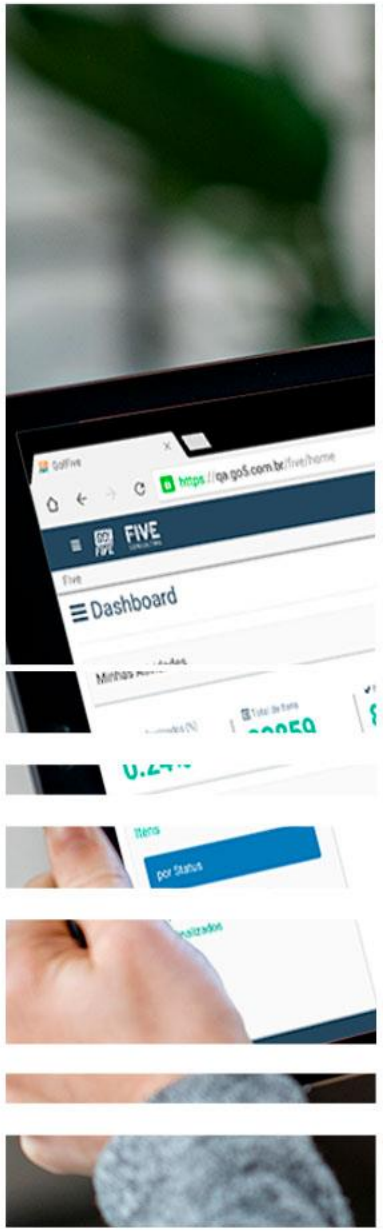
Use Of Paperless Validation In The Serialization And Traceability Projects

Use of paperless validation in the serialization and traceability projects

The serialization and traceability project involves a lot of technology; however, many companies still choose to carry it out in the traditional way, on paper, which makes the process time-consuming and bureaucratic.

This project has different characteristics, because it has several stages and partial validation releases for the use of the traceability system, since there are communications with different links in the supply chain and respective validations that can occur at different times in the project. The completion of this project will only take place in 2024 when all lines are serialized. Paperless validation is the best solution and strategy. Validation should not be the “bottleneck” in the innovation and technology chain, but rather an ally to ensure compliance at each stage and application.

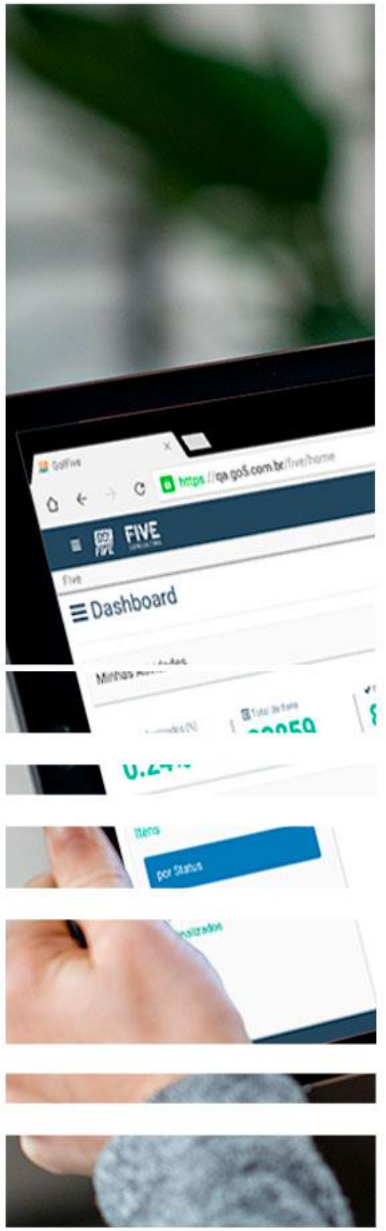
Briefly, each line that will be inserted may eventually include new equipment and systems, have other players in the chain, different business rules, new links in the chain and communication with CMOs (Contract Manufacturing Organizations), that is, outsourced companies for the drug manufacturing.



When serializing different batches, we must assess whether there was an impact or not, which will depend, for example, on the type of product, its presentation, whether all or part of the manufacturing is outsourced, among several other factors that may or may not modify the validation already performed.

This behavior is typical of a project that requires releases in phases, and multiple validation reports at different times.

GO!FIVE™ has a partial release function to facilitate projects that have a single Validation Plan, a single strategy, but distinct release phases.



And Why Is Validation Required?

And why is validation required?

To avoid risks to the patient or consumer, regulatory agencies such as the FDA, EMA and WHO require the pharmaceutical, medical products and the entire supply chain to prepare documents that prove the proper functioning of processes, systems, and equipment.

Traditionally, validation is documented on paper and is contained in many folders, as well as being costly, bureaucratic, subject to failure and slow. Some of the risks are production interruption, delay in product registration and fines, which can cause recall and affect brand image.

To solve this problem, we created GO!FIVE™, a scalable SaaS platform, where it is possible to validate 3x faster following agile methodology. It has over 13 years of consultancy knowledge within the software, with pre-formatted validations built into it. Electronic workflow review and approval allows for remote validations most of the time.

GO!FIVE™ is designed so that each item has its own version control, it is not necessary to version the entire document.

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Why Using GO!FIVE™ Can Be Interesting In The Traceability Project?

Why using GO!FIVE™ can be interesting in the Traceability project?

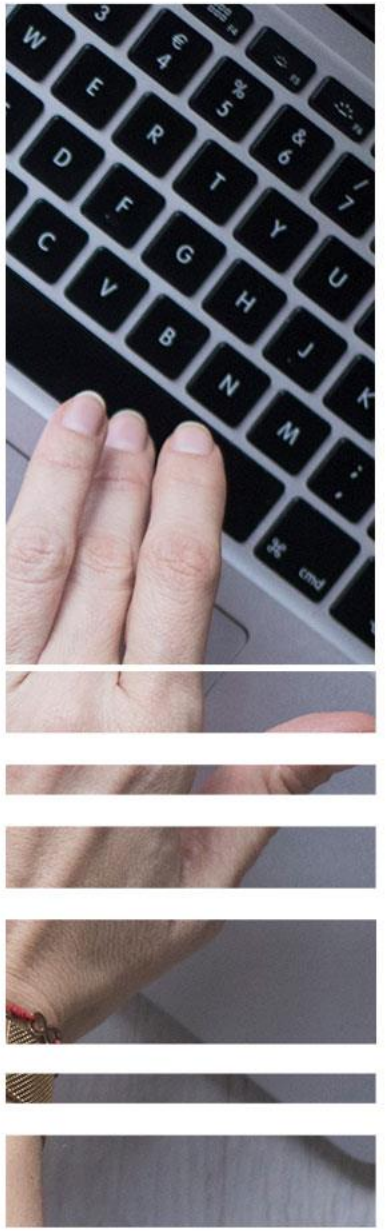
The project became more audacious in terms of the time for its completion. There are several advantages in carrying out the project digitally, with each need for change and design change, gaining flexibility and agility. Reports of these deliveries can be issued, in addition to ensuring all traceability by requirement, risk and test items that are part of the validation documentation.

Some advantages

GO!FIVE™ is a scalable SaaS platform, where it is possible to validate 3x faster following agile methodology. It has over 13 years of consultancy knowledge within the software with pre-formatted validations built into it. Electronic workflow review and approval allows for remote validations most of the time.

- ✓ Save time and increase compliance

GO!FIVE™ drastically reduces the risk of non-compliance, in addition to being designed to allow not only the management, but the preparation of documents with greater agility and security, from the beginning of the project to the Final Validation Report.



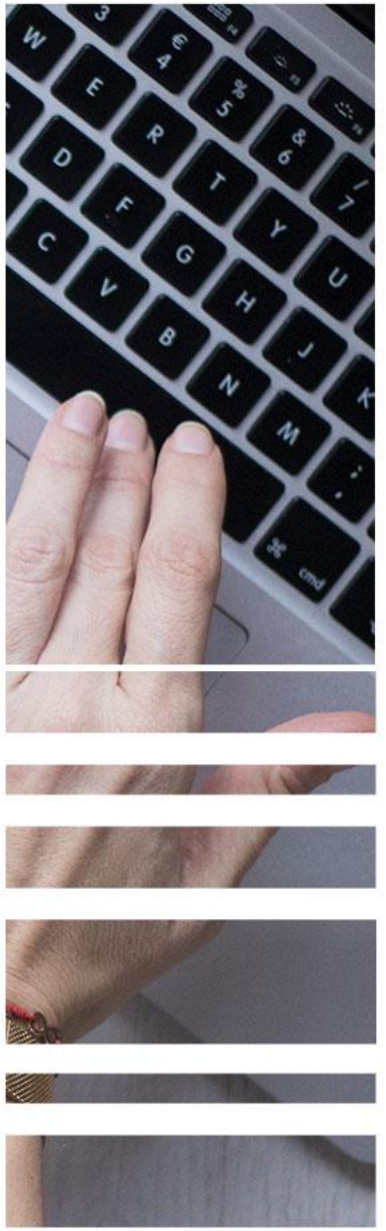
✓ Greater compliance with digital data management

The data generated on GO!FIVE™ is stored on a cloud server, with international certifications, which confirm the commitment to high levels of security, confidentiality and availability of the service. You can also define roles for users and limit access according to project responsibility and expand the platform's capacity to accommodate large-scale concurrent access with stability.

✓ Greater agility with Parallel Flow and Validation per Item

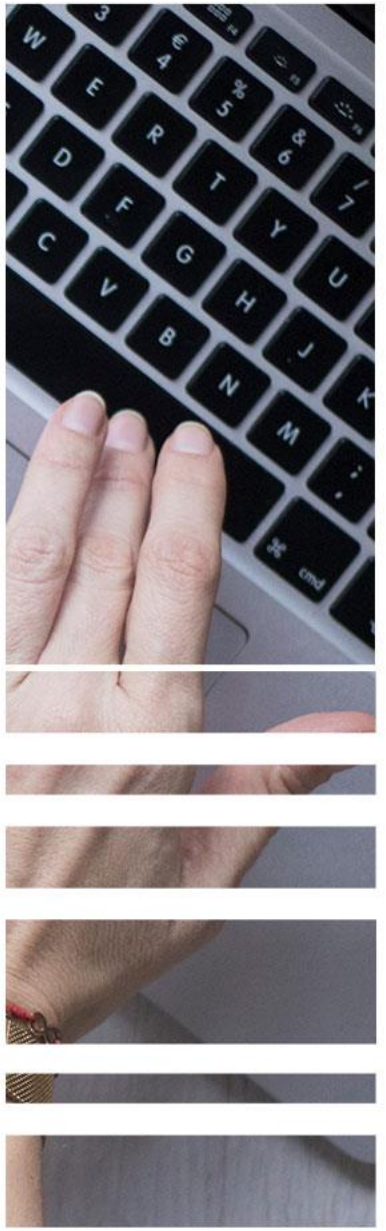
GO!FIVE™ eliminates the need to complete the review and approval of an entire document, before starting the next one. It is also possible to create packages of items of the same type and send them for review and approval in a parallel flow, i.e., sending the package items to all those responsible at the same time.

In serial flow, the items to be evaluated are available for each analyst one at a time. These are resources dedicated to reducing the time for reviewing and approving documents and, consequently, reducing the time it takes to issue Validation Reports.



Below we highlight the top 10 reasons to consider paperless validation:

- ✓ 1.) More compliance: decrease regulatory risks to businesses and data integrity.
- ✓ 2.) Faster time to market: with no validation, biopharma and medical device industries cannot register or produce their products.
- ✓ 3.) More efficient work: 'right the first time;' decrease the time to compliance, make projects agile, and possess 'a knowledge database'.
- ✓ 4.) Decrease validation costs: faster work, avoid paper work, no printers, no physical space to store documents, no documentation scanning.
- ✓ 5.) Remote work: healthier staff and quality of life, online management, connect teams between several countries.
- ✓ 6.) Easier validation status maintenance: decrease the time to keep validation status with constant update and periodic inspections.
- ✓ 7.) Easier audits: immediate availability of data.
- ✓ 8.) Standard documents: maintaining good documentation practices according to GMP guidelines, GAMP5, for example.
- ✓ 9.) Easier management: immediate availability of data (online management).
- ✓ 10.) Sustainable: no use of paper, no printers, no cartridge disposal.



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Why The Partial Releases Function Of GO!FIVE™ Is Important For Serialization And Traceability Project

Why the Partial Releases function of GO!FIVE™ is important for serialization and traceability project

Releases are used by GO!FIVE™ to indicate the completion of a validation lifecycle. This functionality also makes partial releases flexible, allowing the user to partially use the system or equipment, in compliance. In addition, releases are also used to maintain the validated status, allowing the user to handle new items separately from existing ones.

For a partial release, the analyst must segregate the items referring to the part (e.g., equipment, lines, and systems) that will be released in one or more specific Review and Approval Packages identified by the title.

The management of these deliverables and partial releases is simpler and more robust using a platform like GO!FIVE™, since with just a few clicks, it is possible to generate an updated document of the entire project, or documents, and partial reports: referring to the validated parts; browsing through items; and treating them individually.

✓ Maintenance of validated status

While new lines, equipment and systems are being changed or included, the control of these changes is necessary.

The severity of the change must determine the extent and verification of activities and necessary updates, with an approach based on Risk Analysis and the complexity of the change to be implemented.

In GO!FIVE™, it is not necessary to control the version of the entire document to maintain the validated status. It is possible to treat new items separately from existing ones, and generate a new version individually for those impacted, furthermore ensuring the complete traceability of the project.

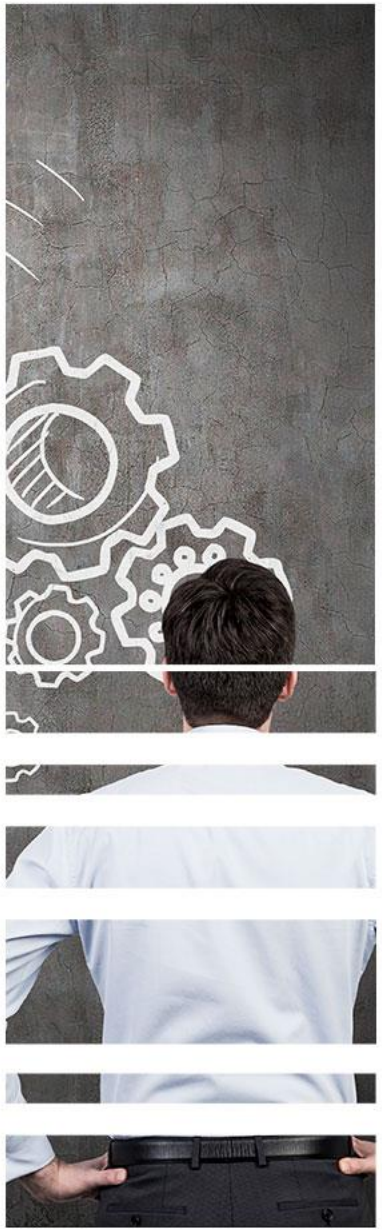
✓ Test replication

GO!FIVE™ has a functionality for test replication, in those cases where it is necessary to repeat the same procedure to check different system components. For example, in this project several tests can be common for different lines and the analyst can use the function to automate the creation.

Important!

The validation cycle must be concurrent with the project implementation. “Don't leave it to the last minute,” get in touch with one of our specialists via e-mail: contact@fivevalidation.com.

We hope that the content expressed in this article has been useful for you!



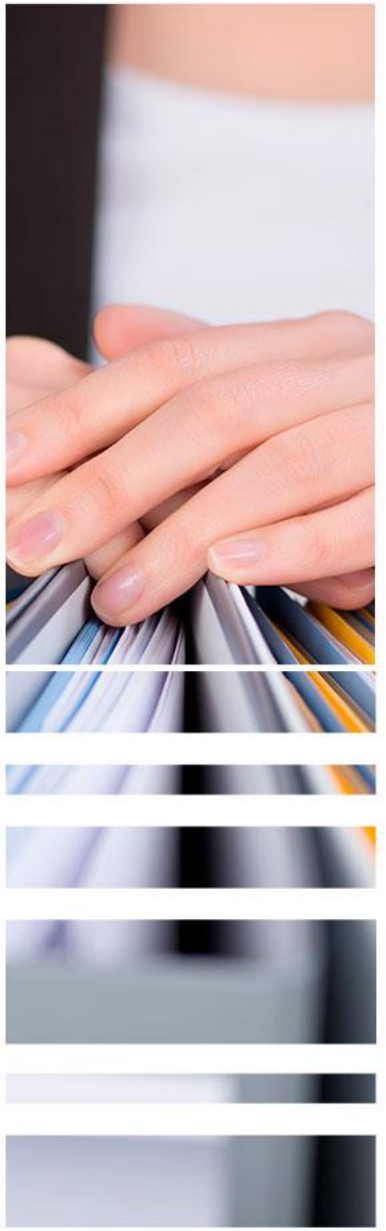
References:

ANVISA. RDC 319/2019 of November 12th, 2019, provides for the implementation phase of the National Drug Control System.

ANVISA. Analysis of the results of the experimental phase and validation of the information technology solution. April 29, 2019.

ANVISA. GUIDELINE Nº 01/2020. Guide to the National Drug Control System. Accessed on March 2nd, 2021 at: https://www.gov.br/anvisa/pt-br/assuntos/fiscalizacao-e-monitoramento/rastreabilidade/guia_sncm_ver_1_0_0_publicacao.pdf

ANVISA. Process N° 25351.048778/2012-10. It analyzes the Normative Instruction that establishes the drugs subject to the National Drug Control System, the deadlines for starting the communication of records of instances of events and other definitions related to the implementation stage. Accessed on March 2nd, 2021 at: <http://antigo.anvisa.gov.br/documents/33760/6098354/Item+2.4.3_ROP+20_+Voto+235.2020.DIRE5.pdf/a1cccf54-8875-40cd-bca9-a64a444cb593>.



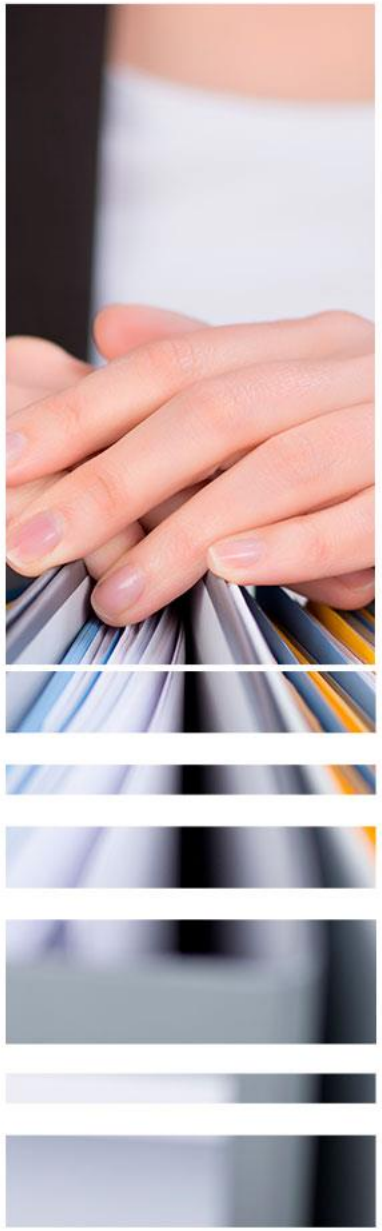
ANVISA. Management Committee Meeting, May 14th, 2020.

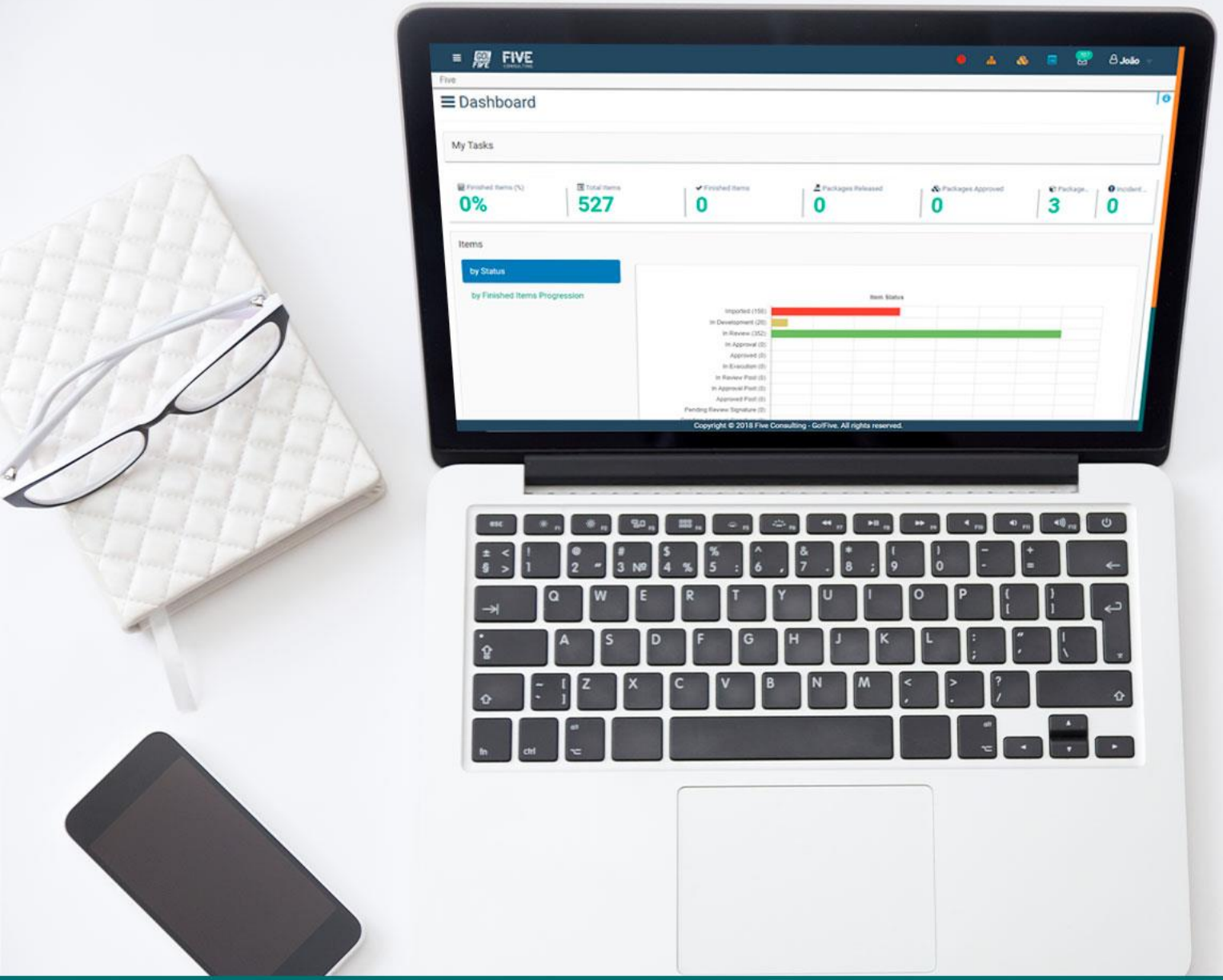
BRAZIL. Law N° 13,410, of December 28, 2016. Provides for the National Drug Control System.

OPTELGROUP. Como implementar a rastreabilidade de medicamentos. Accessed on March 2nd, 2021 at: <https://www.optelgroup.com.br/blog/como-implementar-a-rastreabilidade-de-medicamentos/>.

OPTELGROUP. Rastreabilidade de Medicamentos. Accessed on March 2nd, 2021 at: <https://www.optelgroup.com.br/rastreabilidade-de-medicamentos/perguntas-e-respostas/#:~:text=A%20implementa%C3%A7%C3%A3o%20da%20rastreabilidade%20ocorre,de%20Medicamentos%E2%80%9D%20(IUM)>.

R&B RASTREABILIDADE. Rastreabilidade: empresas fornecem soluções para adequação das linhas de produção. Accessed on March 2nd, 2021 at: <http://rbrastreabilidade.com.br/empresas-fornecem-solucoes-para-adequacao-das-linhas-de-producao/#:~:text=O%20n%C3%ADvel%204%2C%20segundo%20Cardozo,sistemas%20de%20ch%C3%A3o%20de%20f%C3%A1brica>.





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