Management Software for the Elaboration of an Electronic File in the Pharmaceutical Industry Following Mexican Regulations

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Abstract—For certification, certain goods of public interest, such as medicines and food, it is required the preparation and delivery of a dossier. For its elaboration, legal and administrative knowledge must be taken, as well as organization of the documents of the process, and an order that allows the file verification. Therefore, a virtual platform was developed to support the process of management and elaboration of the dossier, providing accessibility to the information and interfaces that allow the user to know the status of projects. The development of dossier system on the cloud allows the inclusion of the technical requirements for the software management, including the validation and the manufacturing in the field industry. The platform guides and facilitates the dossier elaboration (report, file or history), considering Mexican legislation and regulations, it also has auxiliary tools for its management. This technological alternative provides organization support for documents and accessibility to the information required to specify the successful development of a dossier. The platform divides into the following modules: System control, catalog, dossier and enterprise management. The modules are designed per the structure required in a dossier in those areas. However, the structure allows for flexibility, as its goal is to become a tool that facilitates and does not obstruct processes. The architecture and development of the software allows flexibility for future work expansion to other fields, this would imply feeding the system with new regulations.

Keywords—Electronic dossier, technologies for management, web software, dossier elaboration, pharmaceutical industry.

I. Introduction

THE project was presented with the aim of designing and building a platform based on cloud computing for the management of technical and normative information, as well as validation and manufacturing within the pharmaceutical and food industry.

A definition of what a dossier is required to describe how the software management for an electronic file is built. We start with the idea that a report is a record or history on a specific area [1]. In practical terms, it could be understood as the set of documented and structured information that covers a specific topic. The structuring of the information that it contains, depends totally on the subject treated. However, the assessment of the information to be included or excluded in it, depends on the purpose for which the dossier is made.

This article shows how the management software was

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validated with AM Dynamic Service, a Mexican company certified by the Federal Commission for the Protection against Sanitary Risks "COFEPRIS" as the Authorized Third Party (Verification Unit) to carry out Technical Predictions for Medicines And Medical Devices that require Health Records in Mexico (TA-01-15) to pharmacies, drugstores and establishments dedicated to the manufacture of medicines and drugs both domestic and foreign, to distributors of medicines, to conditioners Medicines, warehouses, and sterile mixing centers, this company specializes in the next two issuances:

- The issuance of pre-reports and technical recommendations to obtain the sanitary registration of allopathic, biological, vitamin, herbal and homeopathic medicines; as well as administrative modifications, technical modifications and extensions of health records suitable for what is established by the General Health Law, the Health Supplies Regulation and other applicable legal provisions.
- The issuance of pre-reports for medical records of Class I, Class II and Class III medical devices and their respective administrative and technical modifications.

To make the diagnoses, a dossier is requested from the user. However, 100% of the dossiers that the company receives contain errors in the presentation or content. All of them also lack the documentation required to obtain their health records. For this, it was found that the platform needed to have the necessary information on the health regulations in force in Mexico, as well as the capacity to manage the requirements that these establish. The elaboration of the electronic dossier and its administration allows the pharmaceutical and food industry to manage the governmental certifications of its products in a more accessible way [2].

To be submitted to the certifying authorities, the dossier must comply with certain requirements established by laws, regulations and health regulations [3]. However, the lack of experience and information in the field of management in these instances translates into absence of familiarity with legal language and making mistakes that impede successful registration [4]. This also implies an expenditure of resources that are not consolidated as added value to the company. Therefore, the developed platform guides and facilitates the preparation of a dossier, including and considering Mexican legislation and regulations, and which has auxiliary tools for its management.

II. EXPLANATORY FRAMEWORK

In search of these general results through the stated objective, certain technical characteristics were identified that gave the pattern to design the software:

- Cloud computing service
- Real-time information on the status of the dossier.
- System of alerts and calendar of relevant dates of the process.
- The system is a WEB application, allows entering and working from any browser, while maintaining the security and integrity of the data.
- The system was programmed in ASP (Active Server Pages), a technology made by Microsoft of the "server side" type.
- The system has a database in SQL Server (Structured Query Language) that functions as the database handler.

The control of the system was fixed with the handling of users and permissions. That is, it depends on the different permissions they may have for the creation, editing or revision of the files contained in the system. The section was considered based on the requirements that the company provided for the project development. Another section that was found necessary was the catalogs where all the links to documents or institutions that serve as important tools for the projects development and the filling of files are presented. For example, the lists inclusion of auxiliary experts and notaries.

Due to the legal requirements for pre-opinions, it is necessary to add fields within the system that allow obtaining and collecting this type of information, as well as giving accessibility to these norms. Some of the standards that were included in the consultation are: Good practice guidelines for change of drug manufacturer or inclusion of alternate manufacturers for the use of distinctive drug names and guidelines for the good manufacturing practices validation.

For building a regulatory framework, we consider the following items before the identification of general characteristics, a revision of laws, norms and sanitary guidelines were made that were showing the necessary requirements for the elaboration of the dossier. The documents analyzed were:

1. Laws:
- General Law of Health [5].
2. Regulations COFEPRIS
- Regulation of inputs for health [6].
- Regulation of COFEPRIS (Federal Commission for protection against health risks [7].
- Regulation of the general health law on advertising [8].
- Regulation of the general health law on sanitary control of activities, establishments, products and services [8].
- Internal regulation of the committee of new molecules [9].
3. Standards
- NOM-059-SSA1-2013 deals with good drug manufacturing practices [10].
- NOM-072-SSA1-2012 on labeling of medicines and herbal remedies [11].
- NOM-073-SSA1-2005 on drug and drug stability [12].
- NOM-137-SSA1-2008 about Labeling of Medical Devices [13].
- NOM-164-SSA1-2013 about Good Manufacturing Practices for Drugs [14].
- NOM-176-SSA1-1998 on health requirements for manufacturers, distributors and suppliers of drugs used in the manufacture of medicinal products for human use [15].
- NOM-177-SSA1-1998 establishes tests and procedures to demonstrate that a drug is interchangeable [16].
- NOM-220-SSA1-2012 on the installation and operation of pharmacovigilance [17].
- NOM-249-SSA1-2010 about sterile mixtures: Nutritional and medicines, and facilities for their preparation [18].
- NOM-257-SSA1-2014 on biotechnological drugs [19].
4. Guidelines:
- Guidelines for the validation of Good Manufacturing Practices (GMP) [20]
- Guidelines for change of drug manufacturer or inclusion of alternate manufacturers [21].
- Guidelines for the use of distinctive drug names [22].
5. Agreements:
- Agreement by which modifies and adds the diverse by which the procedures and services are disclosed, as well as the formats applied by the health secretariat [23].
6. Reports:
- Report COFEPRIS 2015 [24].
- Pro-México 2015 Pharmaceutical Industry Report [25].
7. Instructions:
- Instruction of filling format of warning of operation, responsible sanitary and modification or low [26].
- Instruction of filling the format authorizations, certificates and visits [27].
8. Checklist and Formats:
- COFEPRIS 04-004-D (Foreign Medicines).
- COFEPRIS 04-004-B (National Medicines).
- Format Authorizations, certificates and visits.
- Form of warning of operation, sanitary responsible and modification.
9. Lists:
- Generic interchangeable.
- Auxiliary experts.
- Notary.

In addition to the documents already mentioned, the internal documents of the Mexican company (Authorized Third Party) are added:
1. Procedure for preparing a document.
2. Control of documents.
3. Execution and monitoring of corrective and preventive actions.
4. Monitoring and control of nonconformities.
5. Good documentation practices.
6. Development and control of formats.

III. METHODS AND MATERIALS

Many documents were analyzed to design the dossier, the followings are the most important:

A. System Control Modules

In this module, the users and capacities of each were defined. The system has 3 preconfigured user roles:

- Administrator: User who manages and manages the other accounts of different users.
- Editor: User with permission and authorization to edit and modify the texts, documents and progress status of the Dossier.
- Observers: Users who will only have the option to get access to the dossier to see without being able to modify any item.
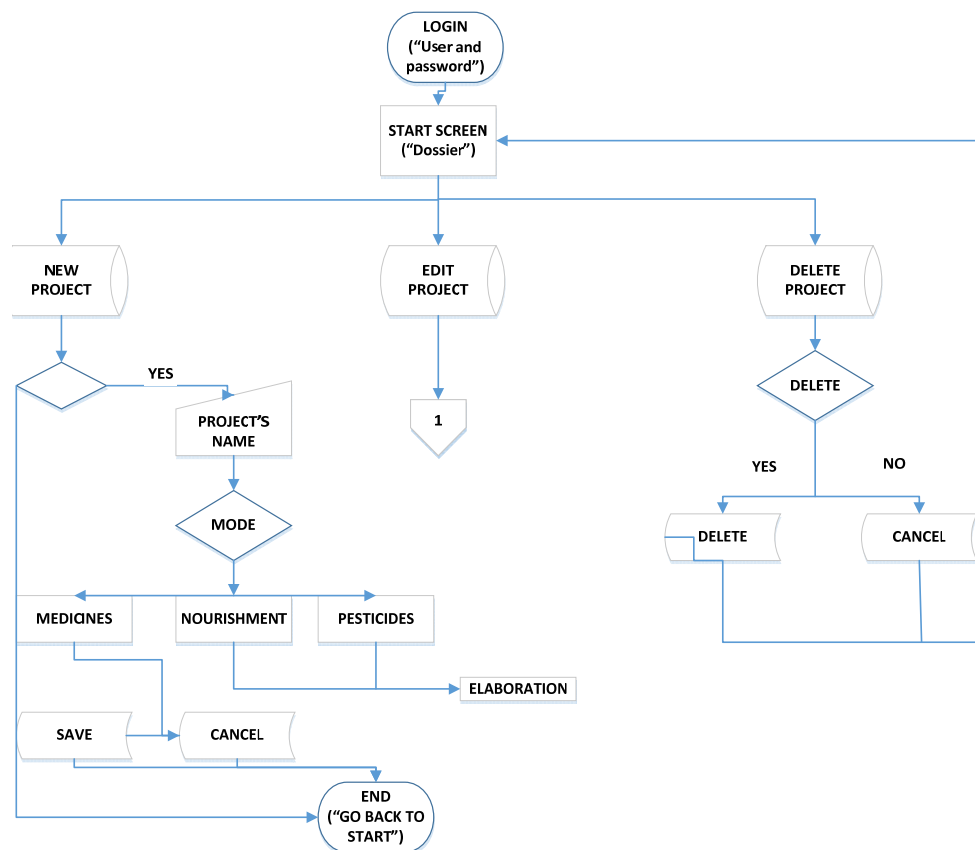

Fig. 1 Home screen flowchart

B. Catalog Modules

The dossier catalog module includes:

- Pharmacopoeia: Book that includes the general and specific information of the medicines existing in the national market.
- Experts Translators: List with the experts in charge of all the translation from Spanish to English as well as from English to Spanish.
- Notaries.
- GNP Certificates: List where one of the GNPs is selected or the data entered manually per the country of origin of the medicine.
- Sanitary License: The user manually enters the health license number and the system valid for the duration of the license or the option of uploading the license by scanning.
1. Maquiladora (make the product)
2. Conditioner (adapts the product for use)
3. Distributor (packs and distributes)

C. Dossier Modules

The dossier construction comprises three main modules: Administrative and legal documentation, quality information and interchangeability information.

Module I. Administrative-Legal Documentary Requirements

Within this module are administrative-legal requirements that give off additional fields and divisions, such as:

- Request format: This field provides a format that requires the capture of necessary information.
- Payment of rights: To continue with the process is necessary to make the payment of rights to get authorizations, permits, applications and records that involve analysis and management of health risks in public health.
- Sanitary License: This is a document to load (attach), within this field there are three more divisions that must also be loaded.
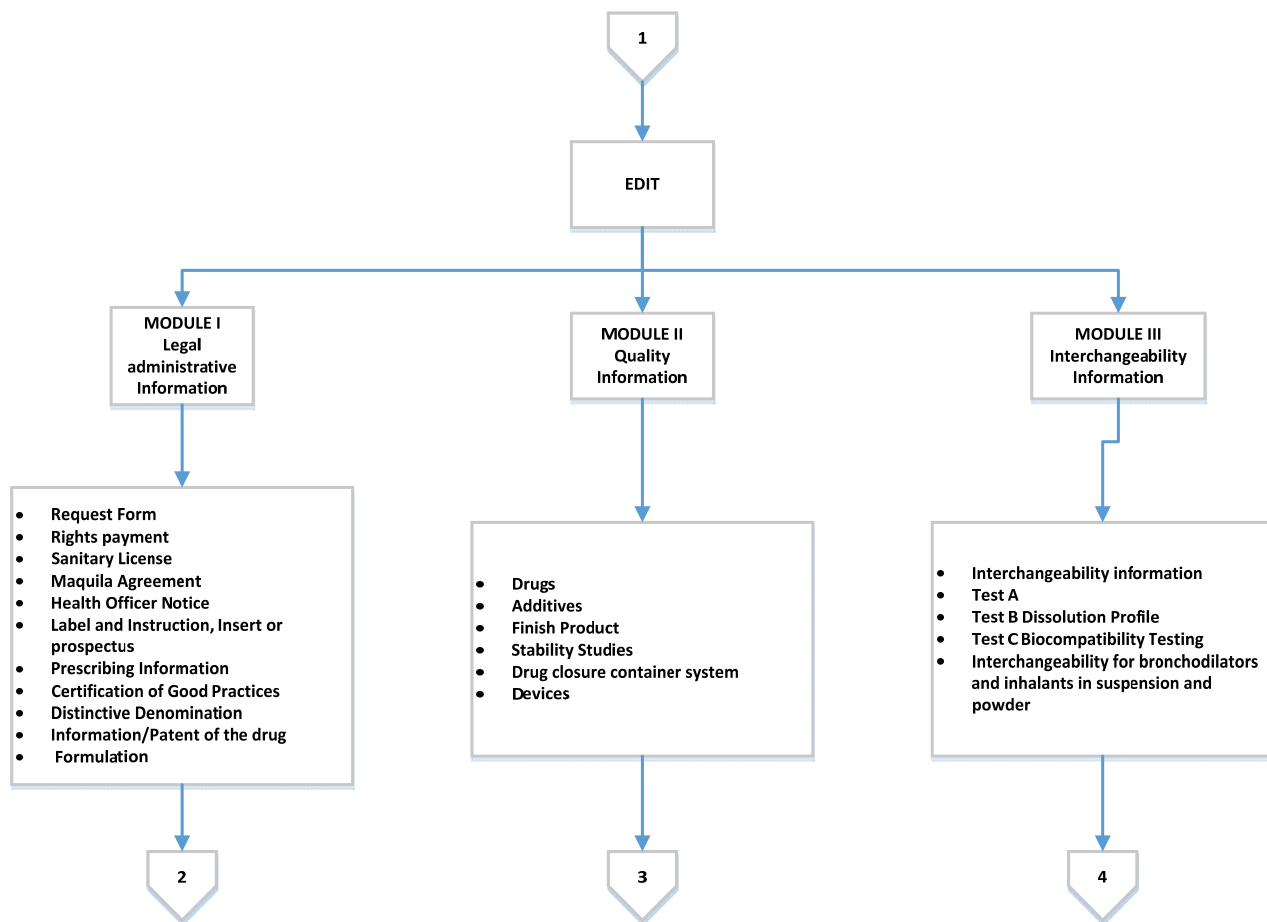
Fig. 2 Modules structure

1. Maquila agreement. A document with the name of the owner (company) and the business name of the maquiladora must be loaded.
2. Conditioner. An official document is required with: the name and address of the conditioner, another official document with the license number of the conditioner and choice of the type of conditioning.
3. Distributor. Per the sanitary license an official document with the company name and address of the distributor must be loaded.
• Notice of health officer: The name of the health officer is entered and a responsible warning is filled out.
• Projects of label: A form with the label information and the logo of the same, in duplicate is filled.
• Instructive, Insert or leaflet: A writing must be typed with the instructions and measures of use of the drug or as a second option to load the instructions in a document.
• Information to prescribe.
• Certificate of GMP of the manufacturer of the drugs.
• GMP certificate of the manufacturer of the diluents.
• Distinctive name.
• Patented drug/ formulation information.

Module II. Quality Information
• Drug. It is the module classification that includes the basic and detailed information of the drug already in its final product, inside this are more fields to fill and specify.
• Additives.
• Finished product.
• Container system closing the medication.
• Device

Module III. Information Interchangeability

The interchangeability information module 3 has a menu which selects which kind of drug is available and from that choice one of the different tests is accessed, in each one of them is a different menu for loading the document that Certify the required information.

D. Module of Management of the Company

The management module of the company has two different sub-modules: The customer module and the general information module.

In the sub-module of clients, you will find a list of all the clients and their general information registered by the company, from this list you can reach the more specific

information.

In the second sub-module is general information, which displays a menu with fields to fill about the general information of the company, including points such as: Logo, name, R.F.C. Address and contact information.

E. Validation

After the design and development of these modules, the Institution of Higher Education was transferred to the validation stage with which a link was made. The software test plan was developed to specify which elements or components are to be tested so that the work group can do the Validation and Verification process of the functional requirements. These tests are documented in a format (Fig. 1).

When developing the test plan, you can get information about the errors, defects or flaws that have the prototype, so make the proper corrections to assure the quality of the product. Through these documents was intended to take back information directly related to the tests, to make sure the quality of these and the product. In addition, this allows the person responsible for the tests to know exactly the criteria that must be considered to test each element of the system.

IV. RESULTS

The results show some of the main screens of the software. In them you can see the options to generate users, create projects and manage them through the three modules.

In the first access to the system (Fig. 3), it is necessary to enter the general information of the laboratory, as well as the data of the user who will be administrator of the company in the system. This first user administrator will can create, edit and delete both projects and users with different access permissions.

When you try to create an account, the system requests the necessary information about the user and company data that will be registered (Fig. 4).

After you have created the user and an email confirmation, you can start creating new projects (Fig. 5). This process allows the user to create a "new drug" from which you can control the filling of all the necessary requirements to give the guarantee of your entry to Mexico.

When you have created a project, it is managed through the modules described. The screen that marks the percentage of progress in each of the items in the file is shown in Fig. 6. From this menu (Fig. 6), you can deploy the multiple options of each module, upload or consult the necessary files and record the progress. This process allows the user to edit a project in Module I "Administrative-Legal Information" of a project already created in the consecutive of existing projects; to complete the necessary requirements of the legal and administrative information necessary to give the certificate of the medicine (Fig. 7). This process allows the user to edit a project in module II "Quality Information" of a project already created in the consecutive of existing projects; To complete diligence, the quality information of the drugs, additives, finished product, stability studies, among others.
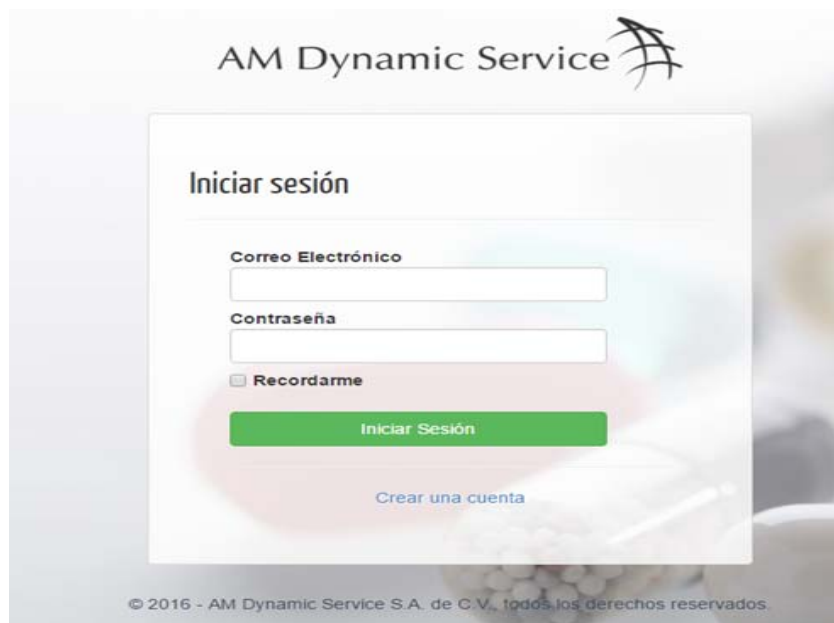

Fig. 3 "Login" system access screen

Fig. 4 "Customer Registration" screen

Fig. 5 "Create new project" screen
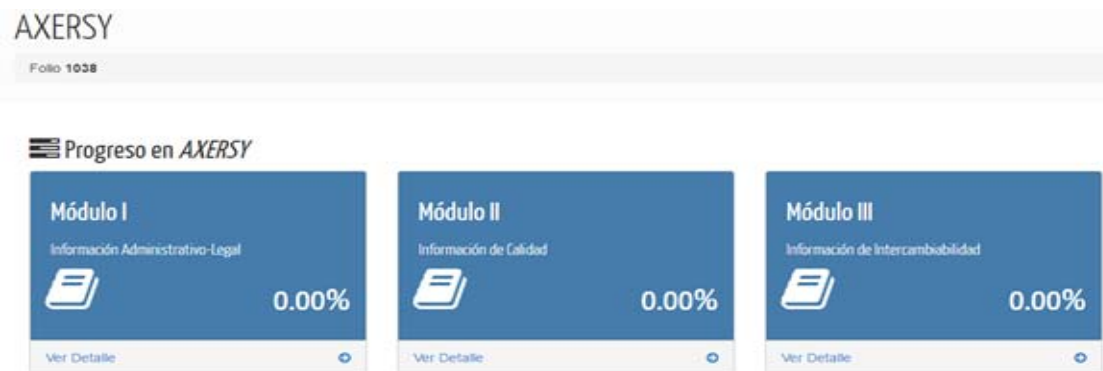
Fig. 6 "Progress in AXERSY" screen

Fig. 7 Project editing screen "Module I"

It can be observed that in modules II and III they have a section of file management, where they can be downloaded by the user (see Fig. 9).

V. CONCLUSIONS

Identifying the management problem impacting directly on the results of a company, a technological alternative was proposed that will support the organization of documents, the order of the necessary items and accessibility to the information required to specify the successful elaboration of a dossier.

The modules were designed per the structure required in a dossier in the areas mentioned. However, the structure allows flexibility, since its aim is to be a tool that facilitates and does not obstruct processes. This same flexibility, allows to consider as future work the expansion of the platform in other topics.

Updates of the system can be made as needed including the new regulations. The structure can be applied in different areas, taking advantage of the architecture and software development to different fields.

Fig. 8 Project editing screen

Fig. 9 Project editing screen "Module III"

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