DIVISION OF TECHNICAL SHEETS AND PATIENT INFORMATION LEAFLETS WITH WORD ADD-IN

Technical manual for the division of technical sheets and patient information leaflets

Version 5.0

Spanish Agency of Medicines and Medical Devices

MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

agencia española de medicamentos y productos sanitarios

Sede Electrónica

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IT Systems Division

ÍNDICE

INTRODUCTION OF NEW SYSTEM FOR DIVIDING TECHNICAL SHEETS AND PATIENT INFORMATION LEAFLET WITH WORD ADD-IN

New application for electronically sending variations of technical sheets and patient information leaflets by sections permits the generation of documents guaranteeing their accessibility in accordance with Legislation (Law 51/2003).

As opposed to the first version of the web-based document division application with text editor, with the limitations of this in relation to format and style, this new version with a Word add-in has the functionality of the Word text editor; therefore its use is much more accessible and simple.

All the requests for division of documents (medicines and variations) can be managed using the new application for dividing technical sheets and patient information leaflets.

Below follows a brief summary of the different options which will be explained in more detail in the manual.

1. INSTALLATION OF THE APPLICATION

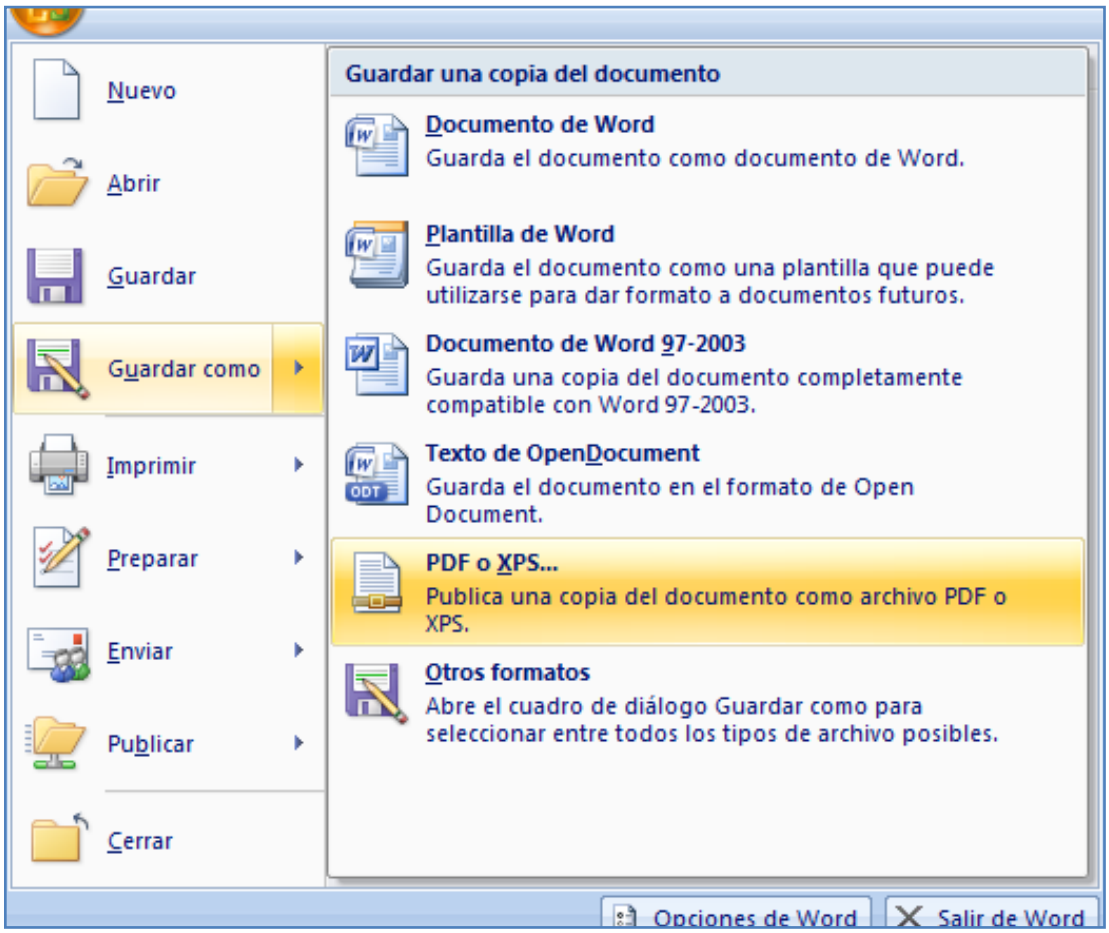
1.1. Application requirements

The installation of the application requires some previously installed requirements on the system as well as two Office add-ins.

- Requirements installed on the system (automatically installed if not found):
  - Windows Installer 3.1
  - NET Framework 3.5 SP1
  - Microsoft Office 2007 primary interoperability assemblies
  - Microsoft Visual Studio 2010 Tools for Office Language Pack Runtime (x86 and x64) - ESN
- Requirements with MANUAL INSTALLATION if not found in Office 2007:
  - Microsoft Office 2007 add-in to Save as PDF or XPS
    http://www.microsoft.com/es-es/download/details.aspx?id=7

The requirements previously installed on the system will automatically detect the installation package and will attempt to download them online for installation if they are not found on the computer.

Only for Office 2007, and if not already installed on the computer (this can checked to see whether the option "PDF o XPS" appears in Save as):



If this option does not appear, manually install the Microsoft Office 2007 add-in to Save as PDF or XPS, in order to be able to export the Word to PDF using the application's preview button.

Until these previous requirements are installed, neither the application nor the Office add-ins will be installed.

- Office Add-ins: Technical Sheet Editor and Patient Information Leaflet Editor

For the laboratory profile it is essential that the Office Add-ins are installed for the Technical Sheet Editor and Patient Information Leaflet Editor. The application will only request the installation of these packages the first time it is run.

Every time a session is started the application will check that the necessary add-ins are installed on the computer, as well as check for possible updates containing new functionalities or improvements. In the case of finding any updates, the application will request the user's permission to install them and the application will open after any updates have been installed.

For the laboratory profile it is essential that the Office Add-ins are installed for the Technical Sheet Editor and Patient Information Leaflet Editor. The application will only request the installation of these packages the first time it is run.

Every time a session is started the application will check that the necessary add-ins are installed on the computer, as well as check for possible updates containing new functionalities or improvements. In the case of finding any updates, the application will request the user's permission to install them and the application will open after any updates have been installed.

1.2. Instructions for initial installation

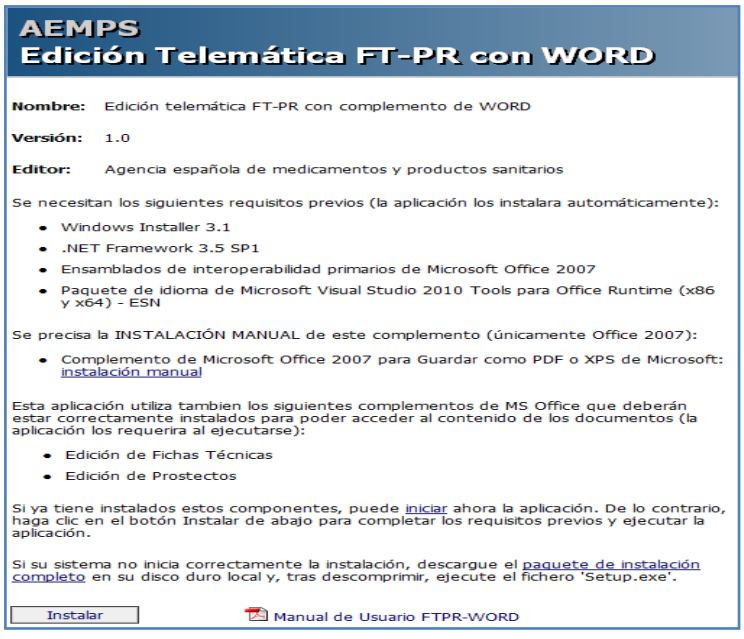
The application may be installed by:

- Directly accessing this link:

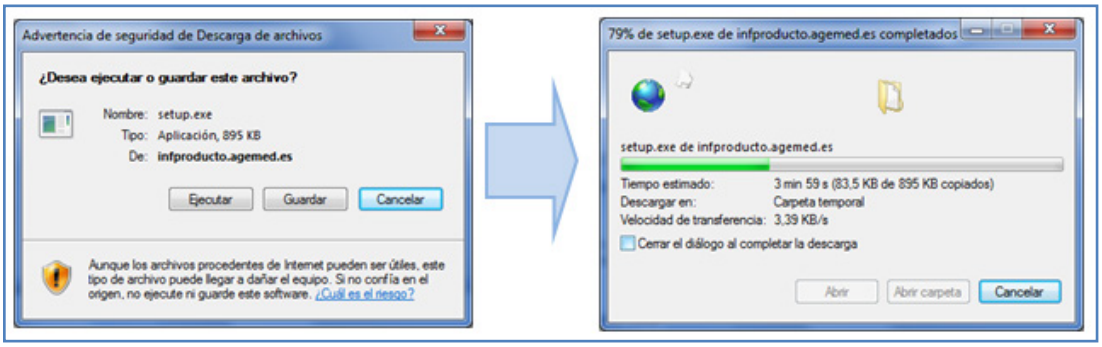
  http://infproducto.agemed.es/webdownloadftpr/apliftpr/

- (Start by clicking the install button at the bottom of the page)

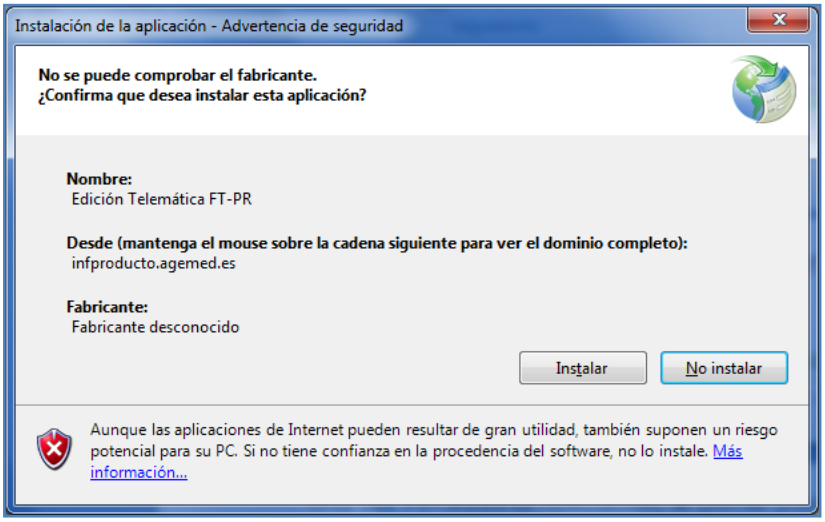
Click the INSTALL button located at the bottom of the page and follow the steps indicated for the installation process.



After the previous requirements are installed (if required), click the run or save button.

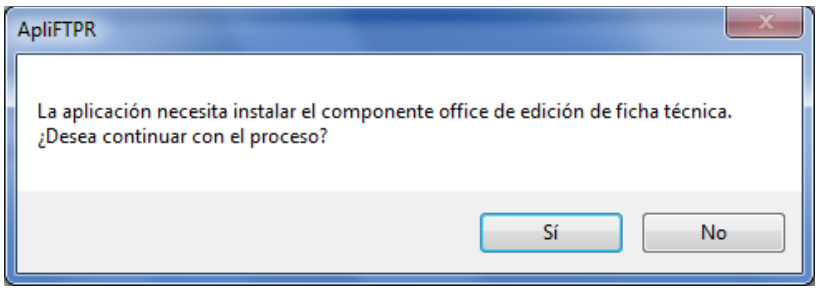


Once downloaded, the application can then be installed:



When running the application for the first time, it will ask the user to log on with their user name and password, using the same log-on credentials for RAEFAR.

When logging on for the first time to divide a Technical Sheet or Patient Information Leaflet, the relevant packages will be installed for each one of the documents.



By clicking 'Yes', it will download and install the Office add-in.

1.3. Important : configuring exceptions on the computer

The application requires continuous access to the AEMPS website:

http://infproducto.agemed.es/WebServicesFTPR/

This URL must be added as an exception any firewalls, proxies and antivirus for the correct functioning of the application and communication with the agency.

2. MANAGING REQUESTS TO EXTRACT SECTIONS

Once the application is installed, the first step is to enter the username and password on the authentication screen, using the same credentials used to access RAEFAR.

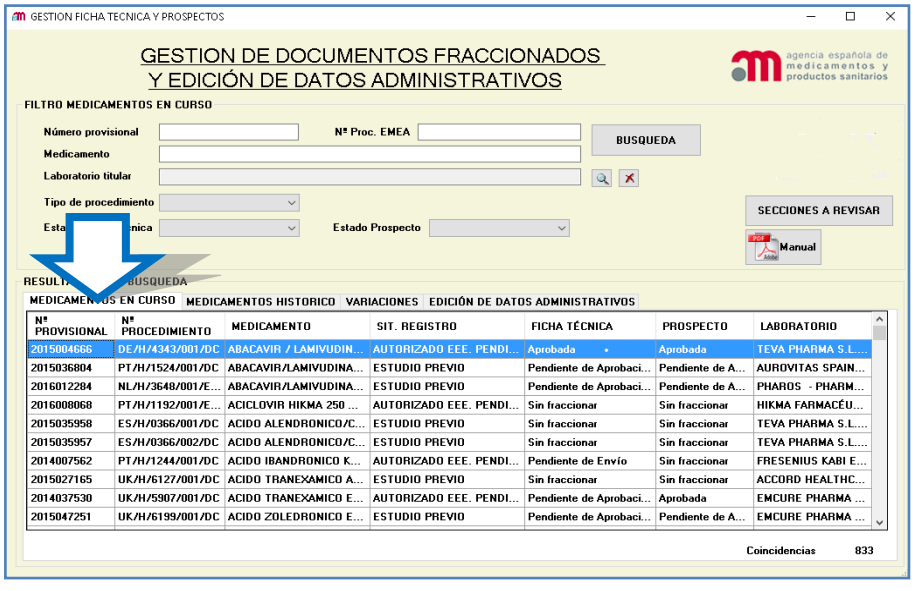
After the user is validated, the main screen will appear where all the requests to extract sections received from the laboratories assigned to the user are managed.

The main screen is divided into four tabs which contain all the requests that have sections that can be extracted, with extracted sections in progress or extracted sections approved, namely:

- **Medicines in the Process of being Registered** (new requests in process and authorised in the EEA, pending Spain)
- **Medicines in the History Log** (authorised/suspended)
- **Variations in Process that affect the Technical Sheet and/or Patient Information Leaflet**
- **Edition of Administrative Data** (Confirmation of changes caused by Variations that affect Administrative Data)

By default, the requests from the laboratory that the user has indicated as 'main' will be loaded. Using the magnifying glass of the main laboratory, this can be changed to any of the assigned secondary laboratories.

The search can be filtered according to several fields such as the name of the medicine, provisional number, status of the technical sheet/patient information leaflet.



3. TECHNICAL SHEET/PATIENT INFORMATION LEAFLET BY MEDICINE SECTIONS

The user will have access to requests to extract sections for both medicines in process (New requests) or medicines already authorised/suspended in the history log.

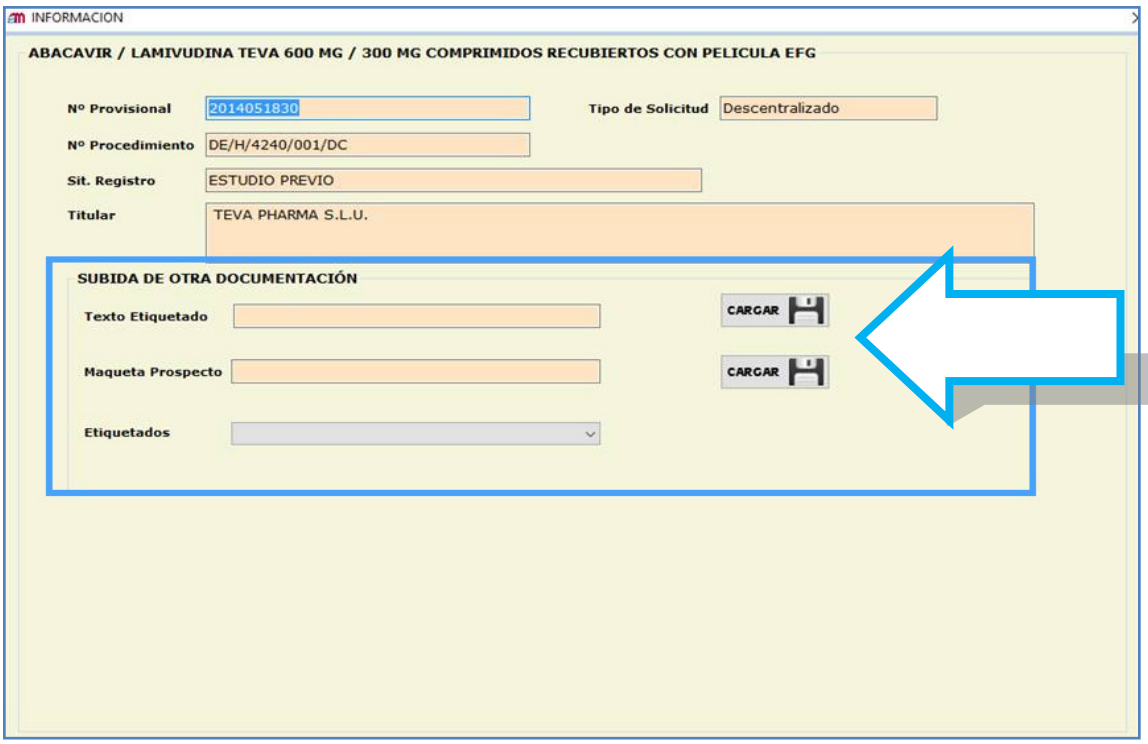
3.1. Medicines in Process

The first tab, Medicines in Process, details all the requests for New Records **and highlighted in yellow are those that meet the following conditions (and are therefore suitable for carrying out the document division request)**:

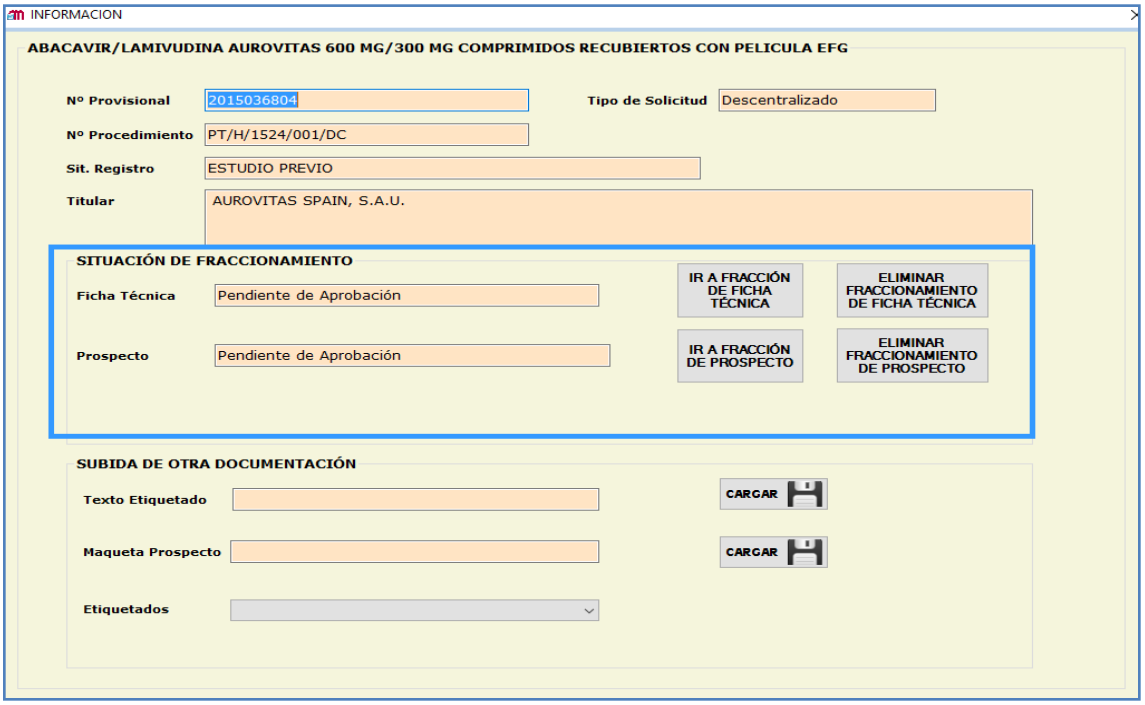
- New DC/MRP records, the section extraction phase will begin when the translation phase begins, day 210 in the case of the DC and day 90 in the case of the MRP.
- New national records, the extraction will commence after the first CODEM.

The query returns all the medicines in process thereby permitting the upload of labelled text files, patient information leaflet layout and labels in all the records.

When double-clicking on a record without permission for extracting sections (blank records) a screen appears where we can upload the aforementioned files. The last document Labelled is a drop-down list because there are six possible documents that can be uploaded.



When double-clicking on a record WITH permission to extract sections (records in yellow), in addition to being able to upload the files, the user can extract sections from the medicine document.



Using each of the buttons for the technical sheet and patient information leaflet, the user can access the edit/management template for the selected document.

3.1.1. Status of the Extraction of Sections for Medicines in Process

There are different statuses that determine the enabled editing options.

- **Not extracted**

  The original status of the document, prior to the commencement of the editing of the extracted section of the document.

  This status offers the option to copy an already approved technical sheet or patient information leaflet (buttons to copy existing document) (see section 4.6) so as not to start from zero, such as for example for different doses of the same medicine whose document has sections in common that are already completed.

- **Pending creation**

  The editing of the extracted section of the document has already begun, the structure of the sections has been created (minimum of 10 sections on the technical sheet and all the sections of the patient information leaflet).

- **Pending release**

  Step prior to the release of the document for approval.

- **Pending approval**

  Document already sent for approval This is the status in which the communication phase with AEMPS begins. The revision of the document by sections is enabled from the SECTIONS TO REVIEW button on the filter (which indicates the sections that AEMPS have referenced with comments or changes).

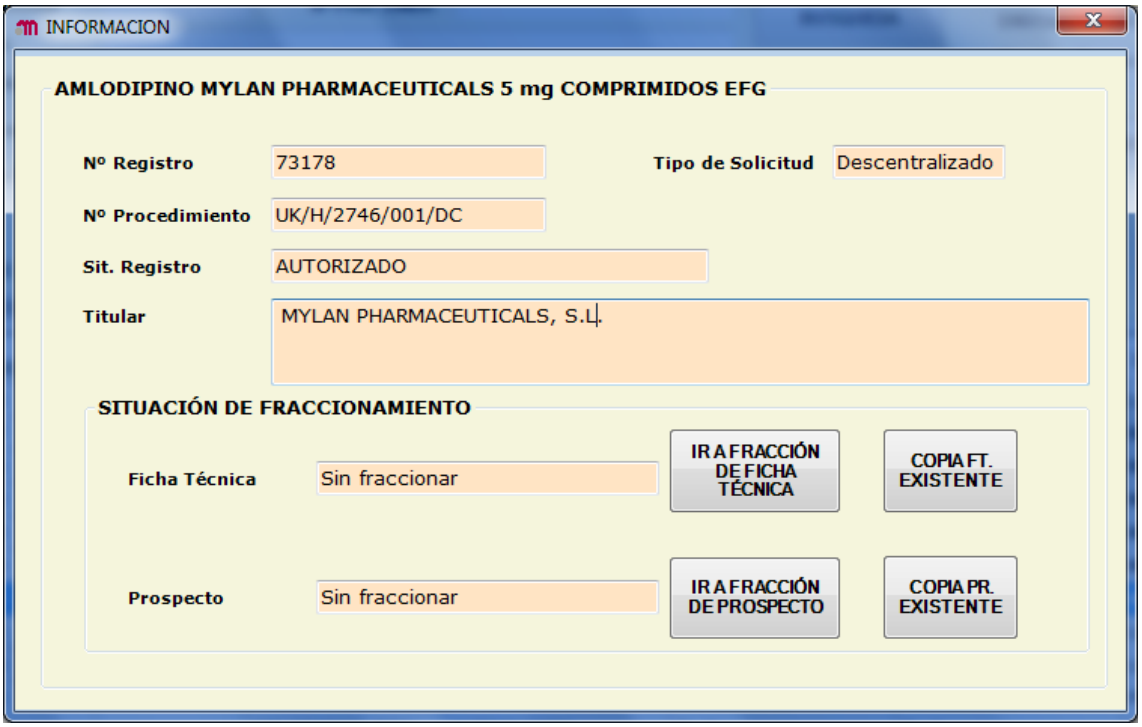
- **Approved**

  Document approved by the AEMPS, the document cannot be edited. The approved version of the document is the one that will appear in the approved medicine when this is in the history log phase, as well as in CIMA.

3.2. Medicines in history log

The second tab, medicines in history log, contains all the requests of authorised and suspended medicines, with the details of the status of the extracted sections for each one of them.

By clicking on each of the medicines, we can access the details of the status of the medicine as well as the situation of the extracted section thereof.



Using each of the buttons for the technical sheet and patient information leaflet, the user can access the edit/management template for the selected document.

3.2.1. Status of extracted sections of medicines in the history log

There are different statuses that determine the enabled editing options.

- **Not extracted**

  The original status of the document, prior to the commencement of the editing of the extracted section of the document.

  This section also provides the option to copy an already approved technical sheet or patient information leaflet (buttons to copy existing document) (see section 3.6).

- **Pending release**

  Step prior to releasing the document for review.

- **Under review**

  Document already sent for approval For medicines in the history log there is no communication phase with AEMPS.

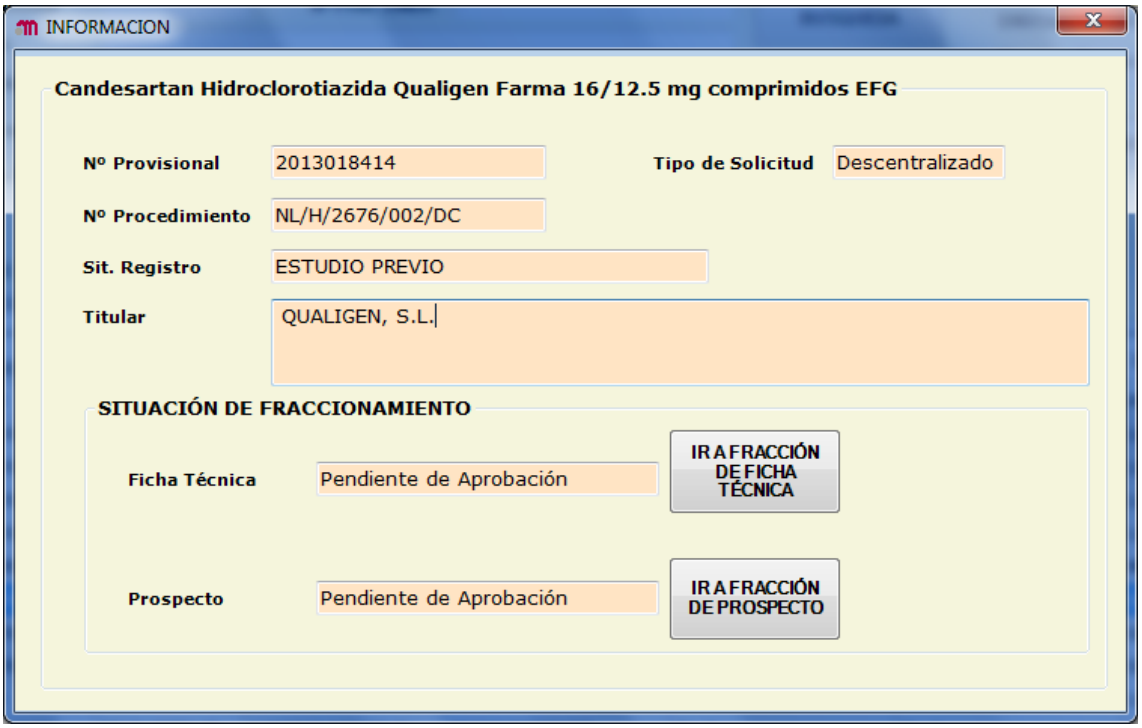
  The document will change to approved or pending release, should the laboratory need to make any change to the application.

- **Approved**

  Document approved by the AEMPS, the document cannot be edited. The approved version of the document is the one that appears in the approved medicine, as well as in CIMA.

4. USE OF THE WORD APPLICATION TO EDIT DOCUMENTS FOR SECTIONS OF MEDICINES

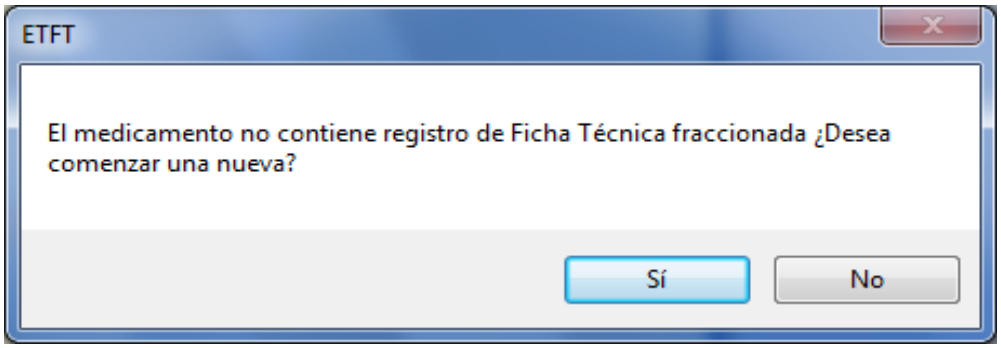
When instantiating the extraction of sections from the technical sheet or patient information leaflet using the buttons “GO TO SECTION”, the application opens Microsoft Word as an editor so that we can work with the same functionalities offered by this text editor (including track changes).



4.1. Technical sheet/patient information leaflet. Not extracted

When editing a document that has not any sections extracted using Word for the first time, the application will ask:

“The medicine does not contain a technical sheet log of extracted sections. Do you want to start a new one?”

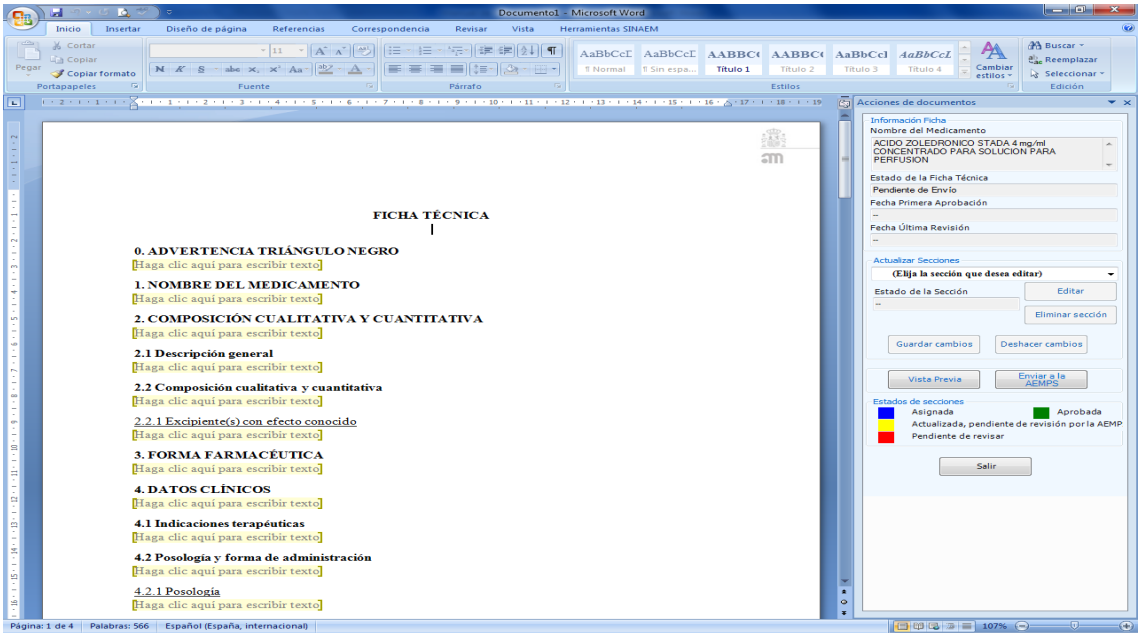


When starting a new one, it will load a blank technical sheet template and create the minimum structure of assigned sections (10 by default) in such a manner so that we can edit each one of them and then add those required afterwards. The status will change automatically to Pending creation.

If the option to start a new one is not selected, Word will close in order to be able to select another option from medicine details such as, for example, copy an existing document.

4.2. Technical sheet/patient information leaflet. Editing in progress

For the statuses pending creation, pending release and pending approval, it is possible to access the editing controls of the installed Word add-in.

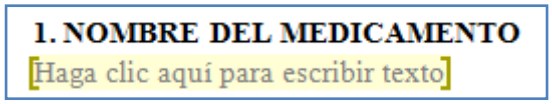


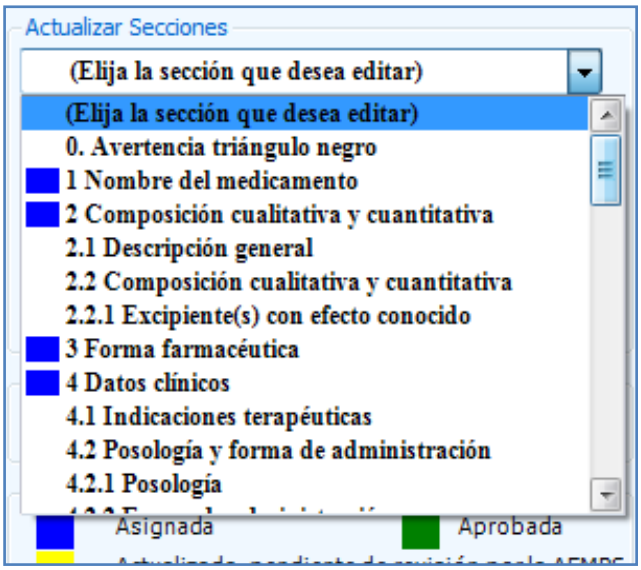
The document displays the template with all the sections of the technical sheet/patient information leaflet that can be edited.

Initially, there is a minimum number of assigned sections, by default these are 10 for the technical sheet and six for the patient information leaflet, which are obligatory.

Afterwards, the user may assign as many sections as required for the document being edited, to do so it is necessary to edit the content section by section.

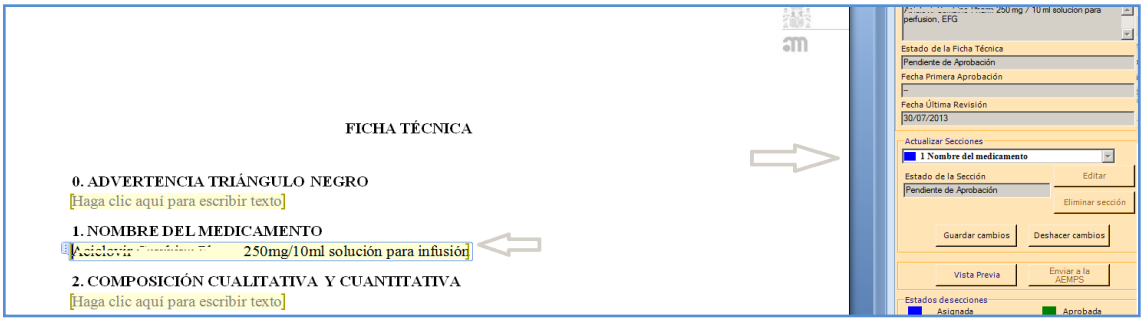
In order to edit the content, position the cursor on the section to be edited. There are two methods for positioning the cursor on the section to be edited: by clicking on the content of the section (clicking between the square brackets),





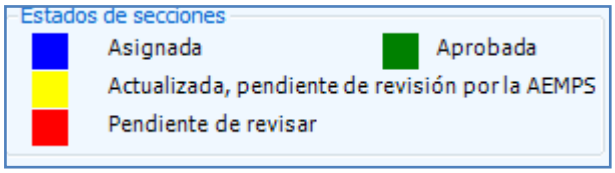
or, this by selecting the section from the "Update sections" drop-down list.

In both cases, whether from the document or from the drop-down list, the selected section will be indicated.



In each section of the drop-down list there is a colour that indicates the current status of that section.

On the panel itself, there is a key to the statuses of each section.



- **Assigned**

  Section that has already been assigned/edited and will therefore be assessed by AEMPS.

- **Updated, pending review by AEMPS**

  With the document already sent to AEMPS, this indicates that the section has been modified by the laboratory and is pending review by an AEMPS reviewer.

- **Pending review**

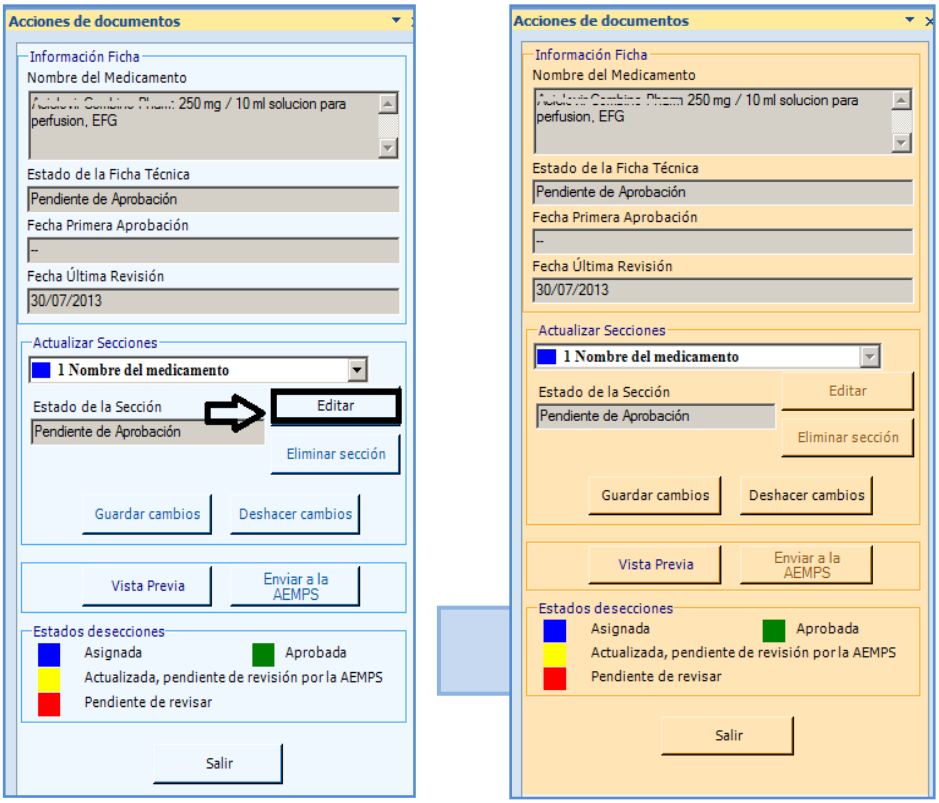
  With the document already sent to AEMPS, this indicates that the section has been modified by an AEMPS reviewer and needs to be reviewed by the laboratory.

- **Approved**

  Section approved, this cannot be edited nor deleted, this section will form part of the approved document in the history log.

Once positioned in the section, it may be edited or deleted from the document (provided it is not an obligatory section).

When pressing "Edit", the panel will change to the colour beige to indicate that the section is being worked on in edit mode.



In edit mode the selected section will be enabled so that it may be edited, as well as the buttons "Save changes" and "Undo changes".

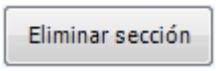
Whilst editing a section, it is not possible to access or edit another.

It is possible to modify the content of the selected section and save the changes entered using the save button, or undo any changes made to the section while in edit mode.

Edit mode ends when the content of the section is undone or saved, once again enabling the preview controls, send to AEMPS, and the appearance of the panel changes to blue.

4.3. Technical sheet/patient information leaflet. Word add-in additional buttons

In addition to the buttons enabled in edit mode (save and undo changes), the following are also available:



Eliminate the section from the document, so that it is not included in the final approved version.

Generate the resulting PDF of the document's content. When pressing the button, the final version of the document with the assigned sections is displayed.

To send the document to the Agency upon completion of the editing of the document's sections. The document will only be sent to AEMPS once, after this the document will change to pending approval and the communication period with AEMPS will commence.

4.4. Technical sheet/patient information leaflet. Communication period

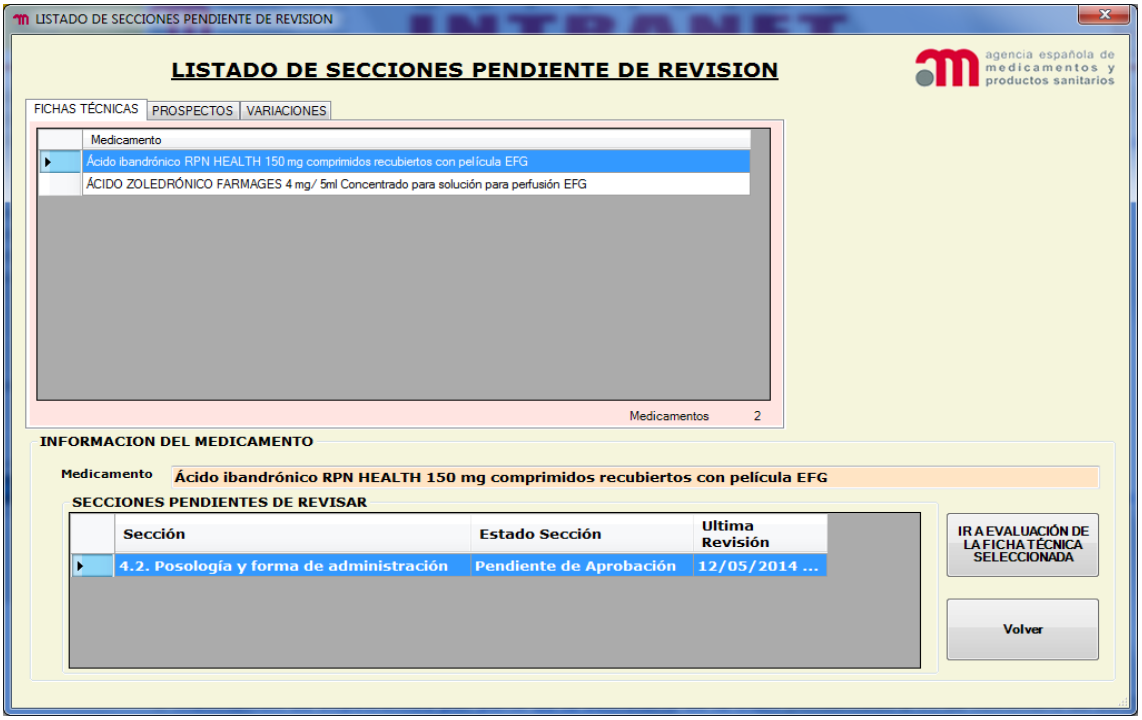
Once the request to split a document is sent to AEMPS, and this is already pending approval, both the laboratory as well as AEMPS can add content and/or comments to each one of the sections.

All the changes made to a section will be indicated in red so they may be easily identified from the content of the section originally sent. Each change made in this status will be marked as a section pending review by AEMPS. Similarly, any changes saved or modified by AEMPS in this status, will be marked as a section pending review by the laboratory.

It will not be possible to edit sections that AEMPS has already approved and which are therefore closed.

4.5. Technical sheet/patient information leaflet. Sections to review

On the main filter there is a button labelled “SECTIONS TO REVIEW” which lists all the documents, new records, as well as the variations part, that contain sections where AEMPS has changed the content (in other words, they were previously sent) or added a comment, which must be reviewed before its possible approval.



There are three tabs which contain all the documents for technical sheets, patient information leaflets and variations which already sent to AEMPS. Documents that contain sections where AEMPS has made changes or added a comment.

When clicking on each one of the documents, the list sections to be reviewed in the selected document appears.

When pressing the “Go to Evaluation” button, Word opens with the add-in loaded in order to edit the section in question.

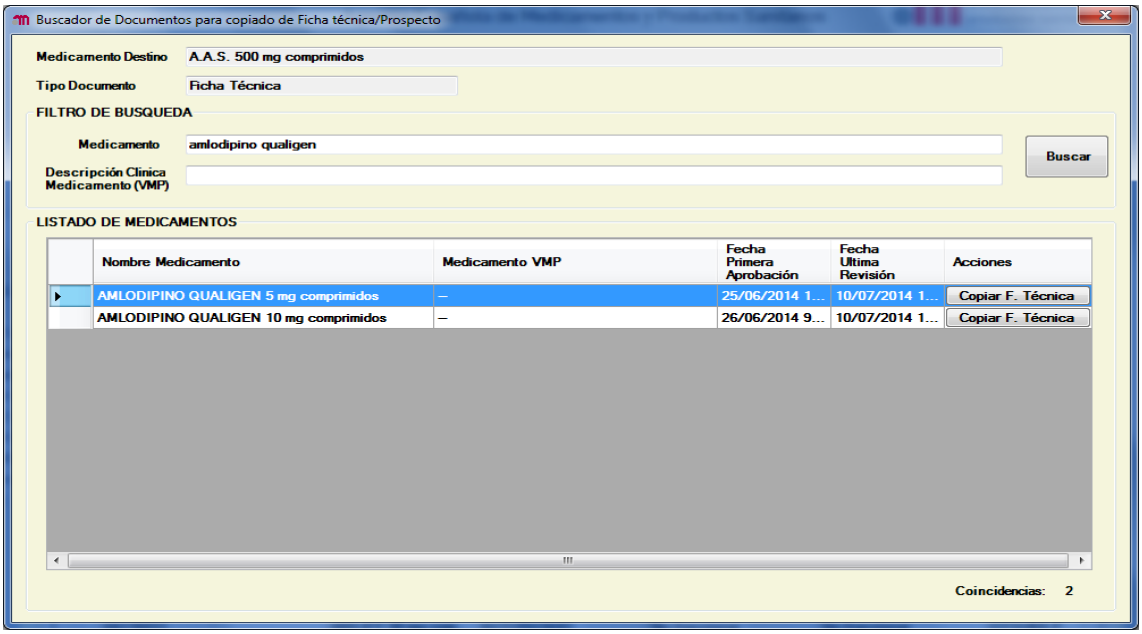
4.6. Technical sheet/patient information leaflet. Copy existing document filter

Before editing the document for the first time, there is the option to make a copy of the technical sheet/patient information leaflet, started if it is from the same owner or approved when it is from different owners.

Access to the copy will be possible provided that the status of the document of the medicine to be copied is “Not extracted”. In this case the buttons which give access to the selection filter for the document which will be copied to the selected medicine will be enabled.

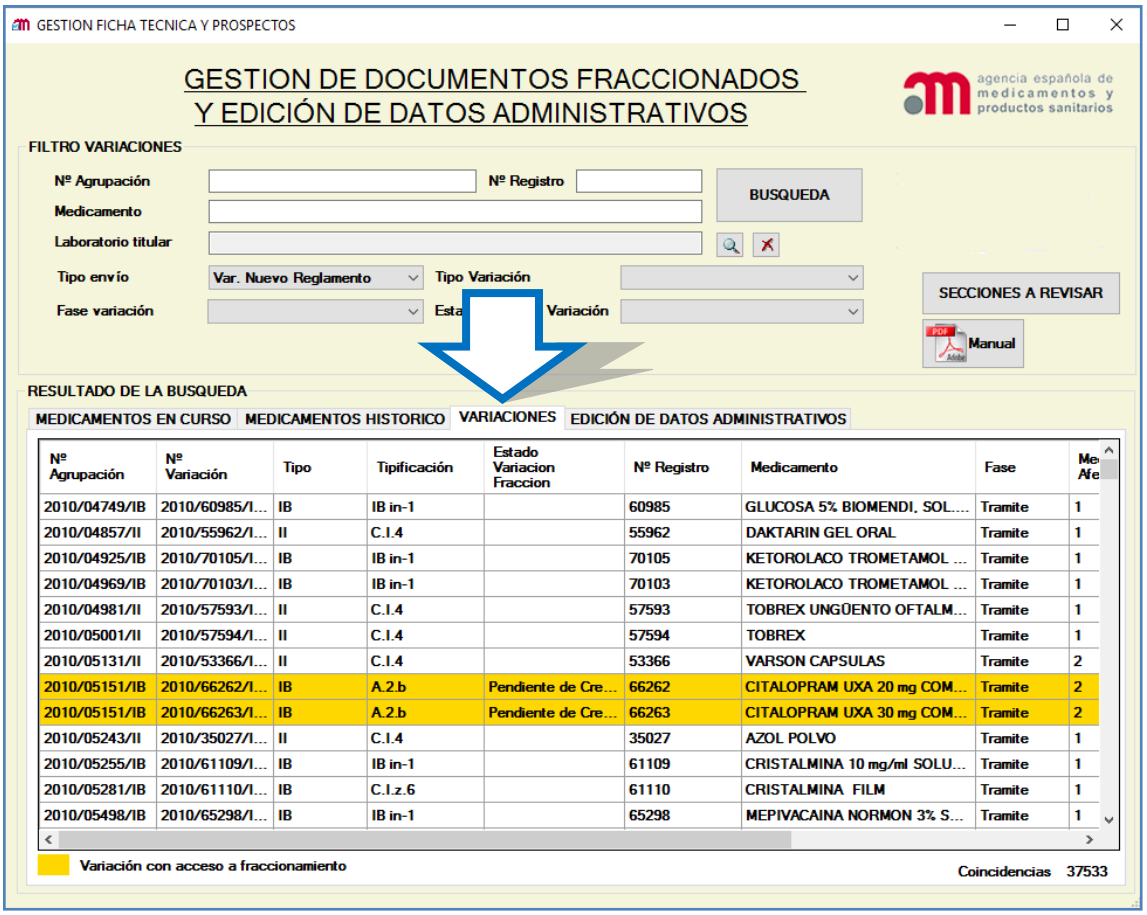
Using the copy existing document filter it is possible to search for the medicine by name or by clinical description.

In the final column of the results there is a copy document button which will make an exact copy of the document of the medicine searched for in the target medicine selected from the previous filter.



5. VARIATIONS OF A TECHNICAL SHEET/PATIENT INFORMATION LEAFLET BY SECTIONS

The third tab of the main filter displays the data of the variations that affect the technical sheet and the patient information leaflet that have medicines edited using the new Word add-in, with details of the rules, group numbers and status of the extracted section of the variation.



The query returns all the variations (previously it only allowed those that permitted sections to be extracted), and allows the labelled text files, patient information leaflet layout and labelled files.

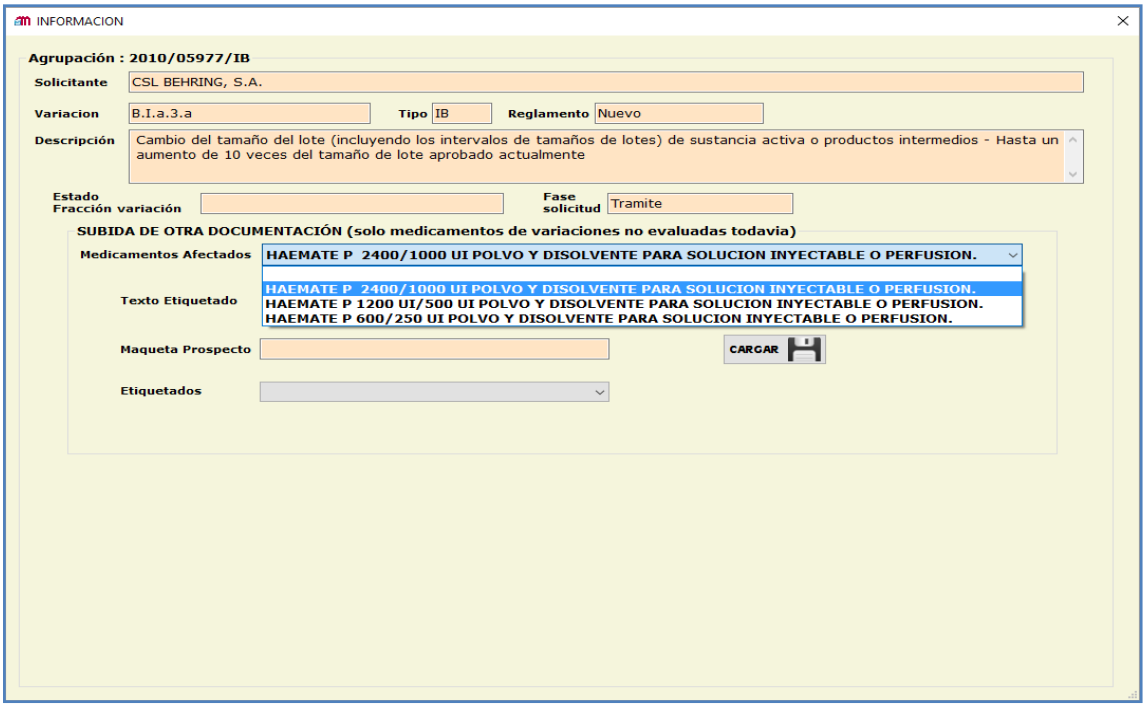
The variations that allow files to be uploaded are those that still have not been evaluated yet, in other words, those that do not have a final status (authorised, denied, withdrawn), all have extracted sections from the technical sheet/patient information leaflet or not.

As with the case of medicines, only the records highlighted in yellow may be selected in order to edit the extracted section of the technical sheet and patient information leaflet of the variation.

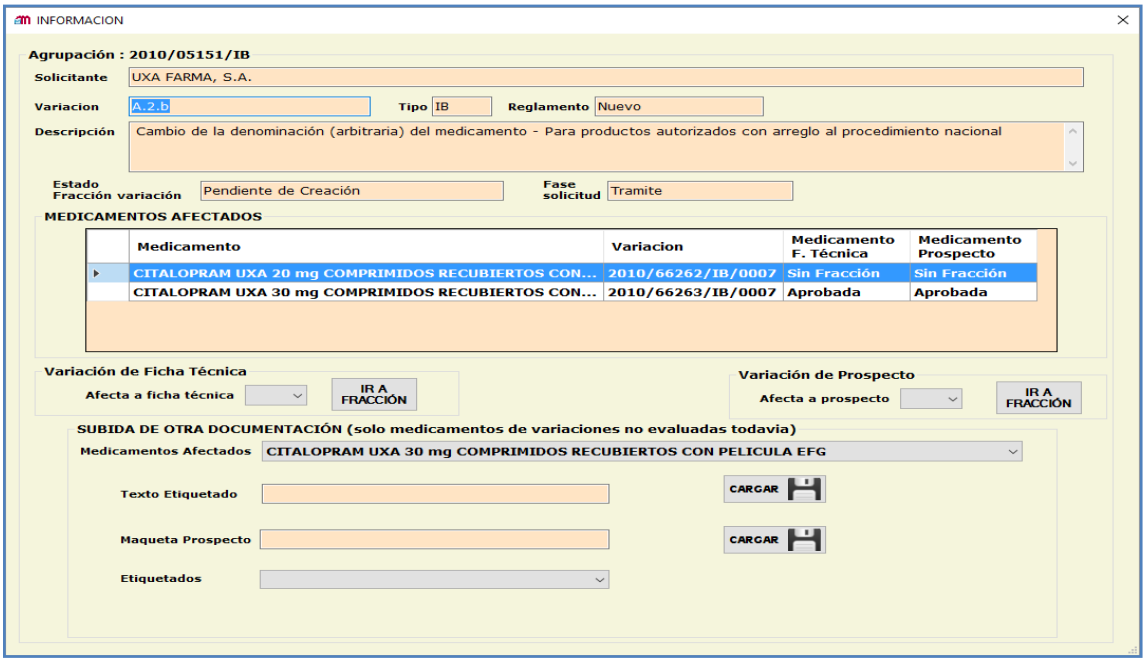
When double-clicking on a record WITHOUT permission to extract sections (blank), a screen appears where we can upload the aforementioned files.

For variations it is possible to upload each file to each of the medicines affected by the selected variation. Therefore, each medicine of the variation yet to be assessed will appear on the drop-down list.

Every time one of these is selected, an upload panel appears with three possible types of documents to upload.

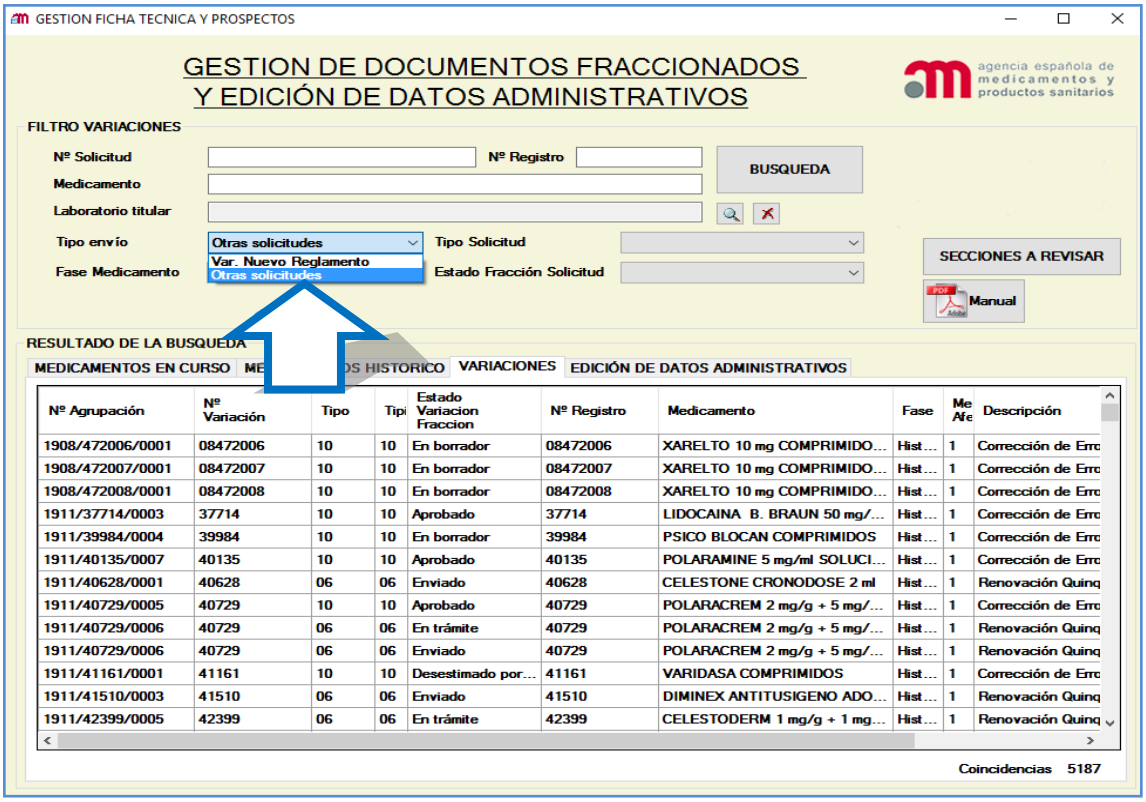


When double-clicking on a record WITH permission to extract sections, in addition to being able to upload the files, we can access the splitting of the variation.



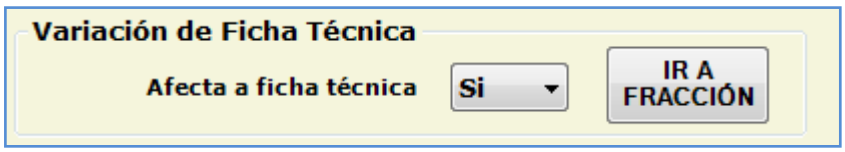
This information screen displays the phase of the variation on RAEFAR, as well as the status of the extracted section of the variation, description, type of variation, rule.

Using the same variations filter, there is also the option to access other types of requests (revalidations, error corrections, transfers of ownership, notifications concerning article 61.3, change of representatives).

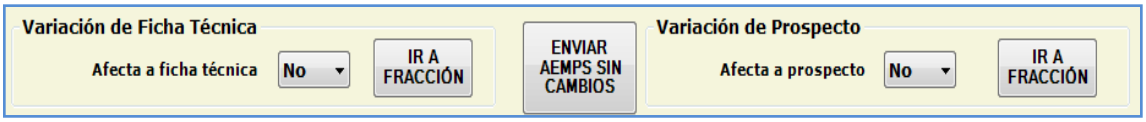


Below follows the breakdown of the medicines affected by the variation or other request, and the status of the extracted section of both the technical sheet and Patient Information Leaflet documents. Editing in Word is only permitted for those medicines where the extracted section status is 'approved'.

For both the technical sheet and the patient information leaflet, we can select whether the variation or other request affects the document or not, simply by changing the option in the drop-down list for each one of the documents.



If the variation does not affect either of the documents, the 'send to agency without changes' button will become available:



If the variation does affect the documents, by clicking on each of the "Go to section" buttons, the edit/manage screen of the variation template for the selected document will appear.

5.1. Status of extracted sections of variations

There are different statuses of extracted sections that determine the enabled editing options.

- **Pending creation**

  Extracted section of the open variation with or without changes but still not sent.

- **In Process**

  Variation already sent to AEMPS. This is the status in which the communication phase with AEMPS begins. The revision of the document by sections is enabled from the SECTIONS TO REVIEW button on the filter (which indicates the sections that AEMPS have referenced with comments or changes).

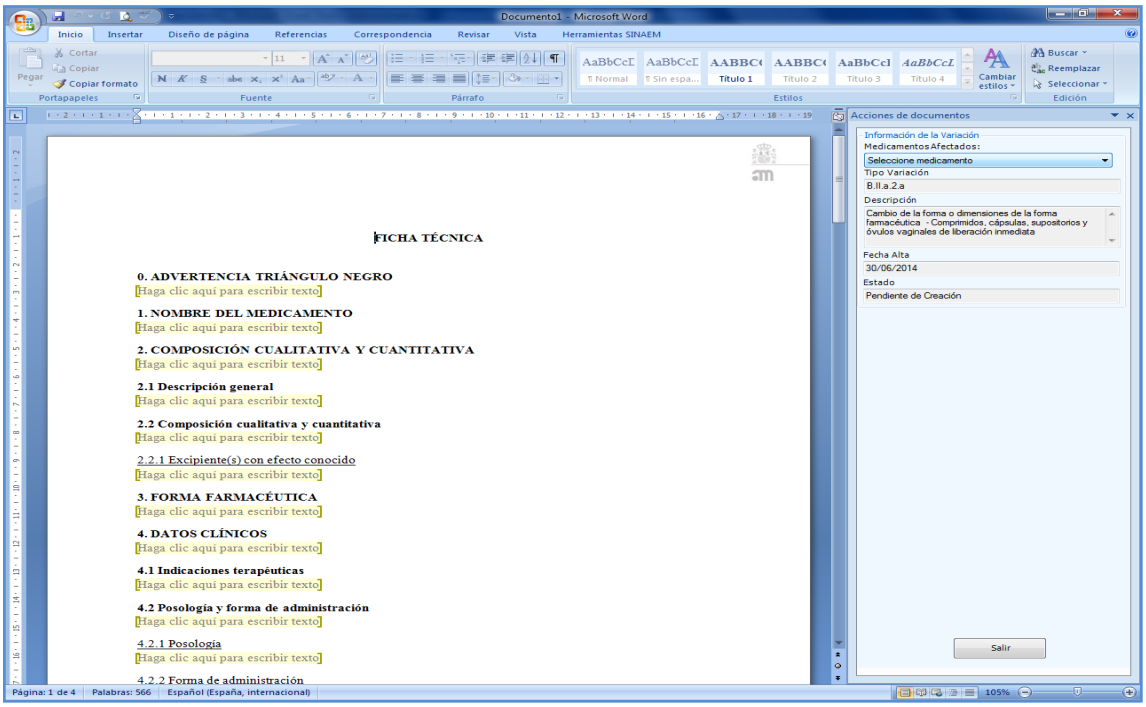
- **Evaluation complete**

  Variation complete, affects a section or not, the variation template can no longer be edited.

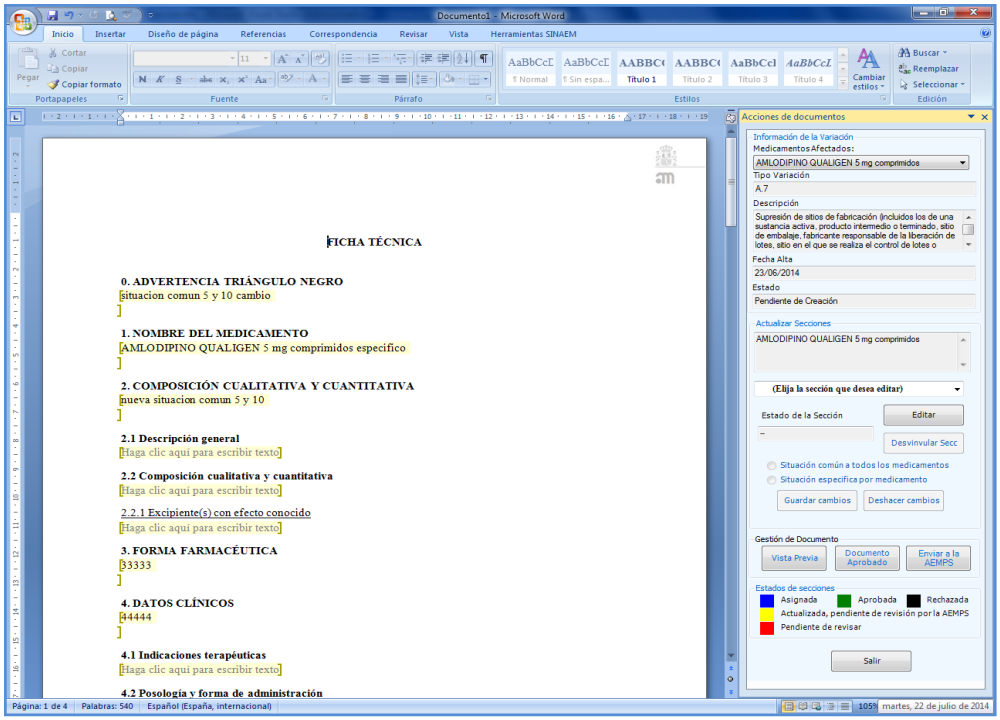
6. USE OF THE WORD APPLICATION TO EDIT DOCUMENTS FOR SECTIONS OF VARIATIONS

The Word add-in panel for variations is very similar to that of medicines, but there are differences, such as the selection of the medicine on which to work from the drop-down list of affected medicines (the listed medicines indicate that they are approved for extraction in Word), as well as the manner to save the situation.

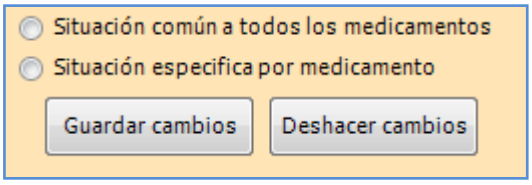
A blank template for the document and depending on the selected medicine it loads all the approved sections for the medicine.



Once the medicine to be worked on has been selected, it loads the template with all the relevant data, and as with medicines, select the section to edit by placing the cursor over the content of said section or by using the drop-down list of sections and clicking the edit button (the panel changes to the colour beige, edit mode) and the content of the section can be edited or new content entered in a section that does not yet exist in the final document of the medicine.



In edit mode, when saving the content of each one of the sections, the software will ask what type of save is required for the edited section:



- **Situation common to all medicines**

  The saving of the content of the section will apply to all medicines affected by the variation (drop-down list of medicines), in such a manner that section X will display the same content in each one of the medicines.

  The evaluation of the section will be common to all medicines, in other words it will be approved or rejected for all.

- **Specific situation for medicines**

  The saving of the content of the section will apply only to the medicine being edited from those selected from the drop-down list of medicines in such a manner that section X will display different content in each one of the medicines.

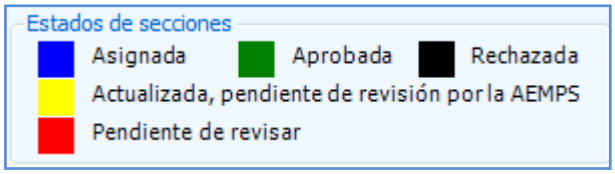
  In other words it will be necessary to select the different medicines and enter the data for the section for each one of them.

  The evaluation of the section will be specific to all the medicines, in other words, the same section may be approved for one medicine but rejected for another.

Note: For the sections that contain part of the editable title, this title must be entered independ-ently for each one of the affected medicines, regardless of the save type selected.

The “Undo changes” button restores the previous content of the section. If the section has just been assigned to the variation and it has not yet been saved, the undo changes action enters the content from the section of the document in the history log, provided that this section is in the approved document.

On the panel itself, there is a key to the possible statuses of each section of the variation:



- **Assigned**

  Section that has already been assigned/edited and will therefore be assessed by AEMPS.

- **Updated, pending review by AEMPS**

  With the document already sent to AEMPS, this indicates that the section has been modified by the laboratory and is pending review by an AEMPS reviewer.

- **Pending review**

  With the document already sent to AEMPS, this indicates that the section has been modified by an AEMPS reviewer and needs to be reviewed by the laboratory.

- **Approved**

  Section approved, this cannot be edited nor deleted, this section will form part of the approved document in the history log if the variation is later authorised.

- **Rejected**

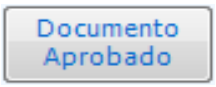
  Section rejected, this cannot be edited nor deleted, this section will NOT form part of the approved document in the history log even if the variation is later authorised.

6.1. Additional word add-in buttons for variations

In addition to the buttons enabled in edit mode (save and undo changes), the following are also available:

This button disassociates the section of the variation from all the content of the section that would have been entered for the section. If the section contains content approved in the history log, it enters the information from this section, otherwise the section will remain blank.

Generate the resulting PDF of the document’s content. This displays the final document with the sections assigned for the variation including the sections that are currently in the history log for the document of the medicine selected from the drop-down list.



View of the document in PDF currently approved in the history log for the medicine selected from the drop-down list.

This sends the document to AEMPS once the sections of the variation have been edited, this applies to both the technical sheet and the patient information leaflet. In other words, the sending of the variation is unique, regardless of whether it is done from the technical sheet parts or the patient information leaflet.

If the variation affects both documents, at least one section must be assigned to each one of them.

The document will only be sent to AEMPS once, after this the extracted section of the variation will change to “In Progress” and the communication period will commence.

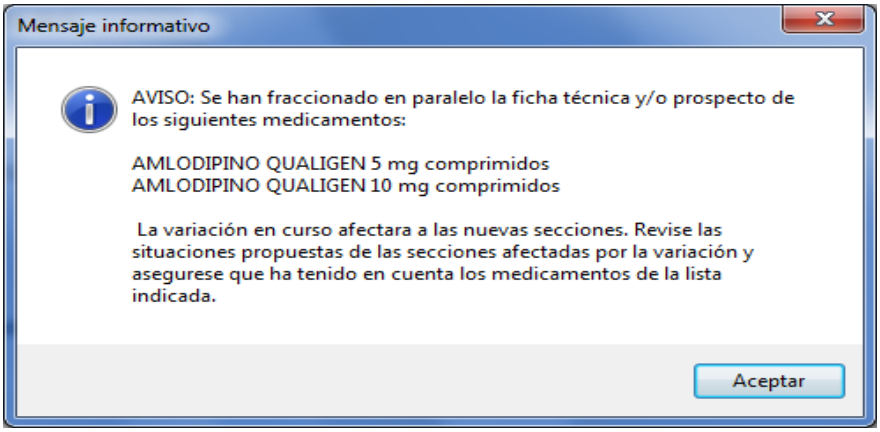
6.2. Situations of importance for variations

- **Extracted medicine that is approved in parallel to the variation**

  Imagine that the variation affects three doses of 10, 20, 40 mg and only the sections for doses of 10 and 20 are approved.

  When applying the variation, it is assigned to section 1, section 4.1 and section 6.5, but only the two approved doses have been taken into consideration, in the case of the dose for 40, as it does not have an approved section there is no access to edit the sections.

  The fraction for the doses of 40 is approved, therefore when entering the variation, a message similar to that below will appear:

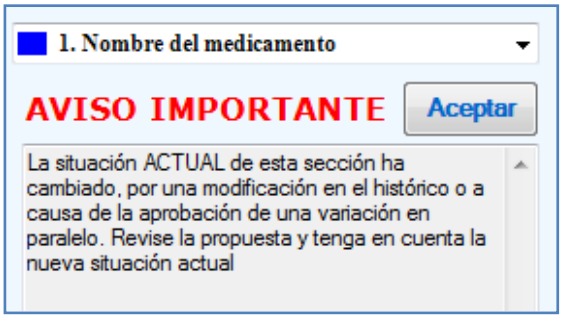


  In other words, it is necessary to also consider the situations for the doses of 40 mg. So that the assigned sections are specific per medicine, it is necessary to enter this situation for the doses of 40 mg, but for the sections in common, if there is already a situation it will be necessary to adapt it to 40 mg as well, because otherwise when it is approved the change will be made to one for 40 mg, without knowing whether the change was that which applied for this dose of 40 mg.

- **Section modified by a variation approved in parallel.**

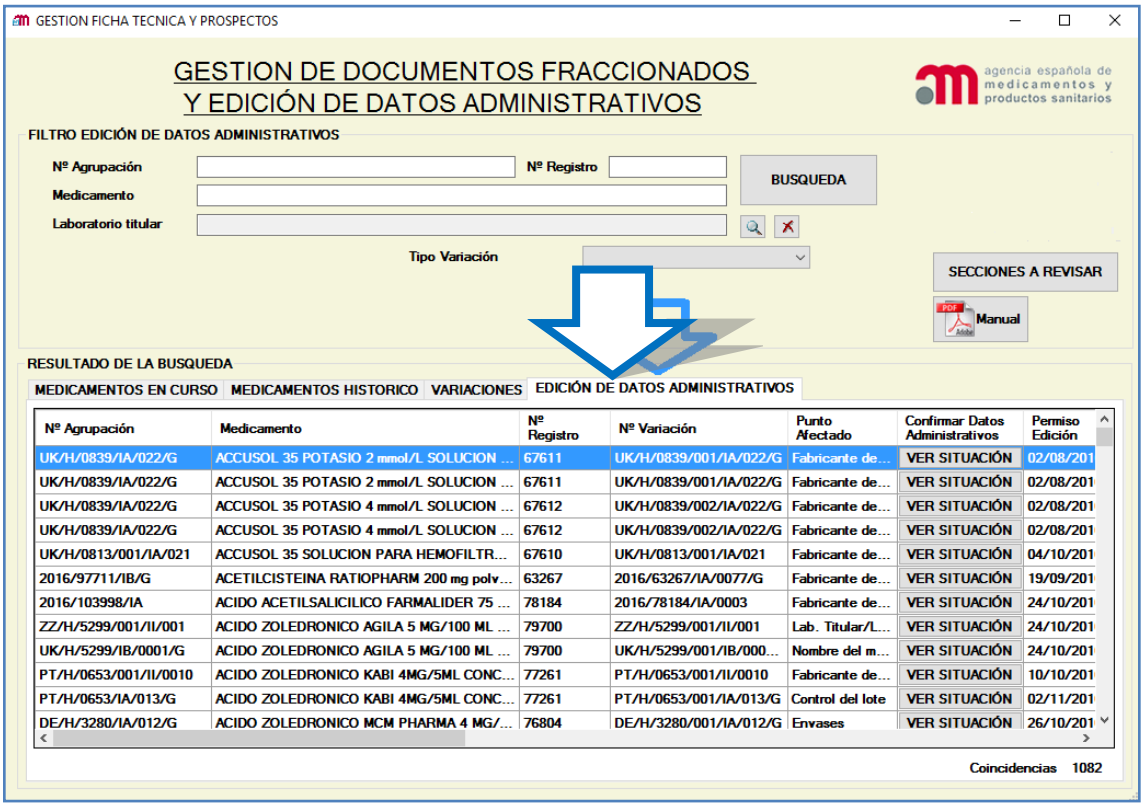
  When a variation is approved, it may be that the section it affects is also contained in a variation in process/pending resolution.

  In this case, for the pending variation, when editing the section the edit and save buttons are dis-abled for that section until we mark that we accept the changes that have been made to the cur-rent section in the history log.



  Once the message is accepted, it will be possible to once again edit the section, adapting the pro-posed situation taking into account the current one for the section, which can be viewed by clicking the “Approved Document” button which indicates the current situation of the history of the medicine.

6.3. Editing administrative data

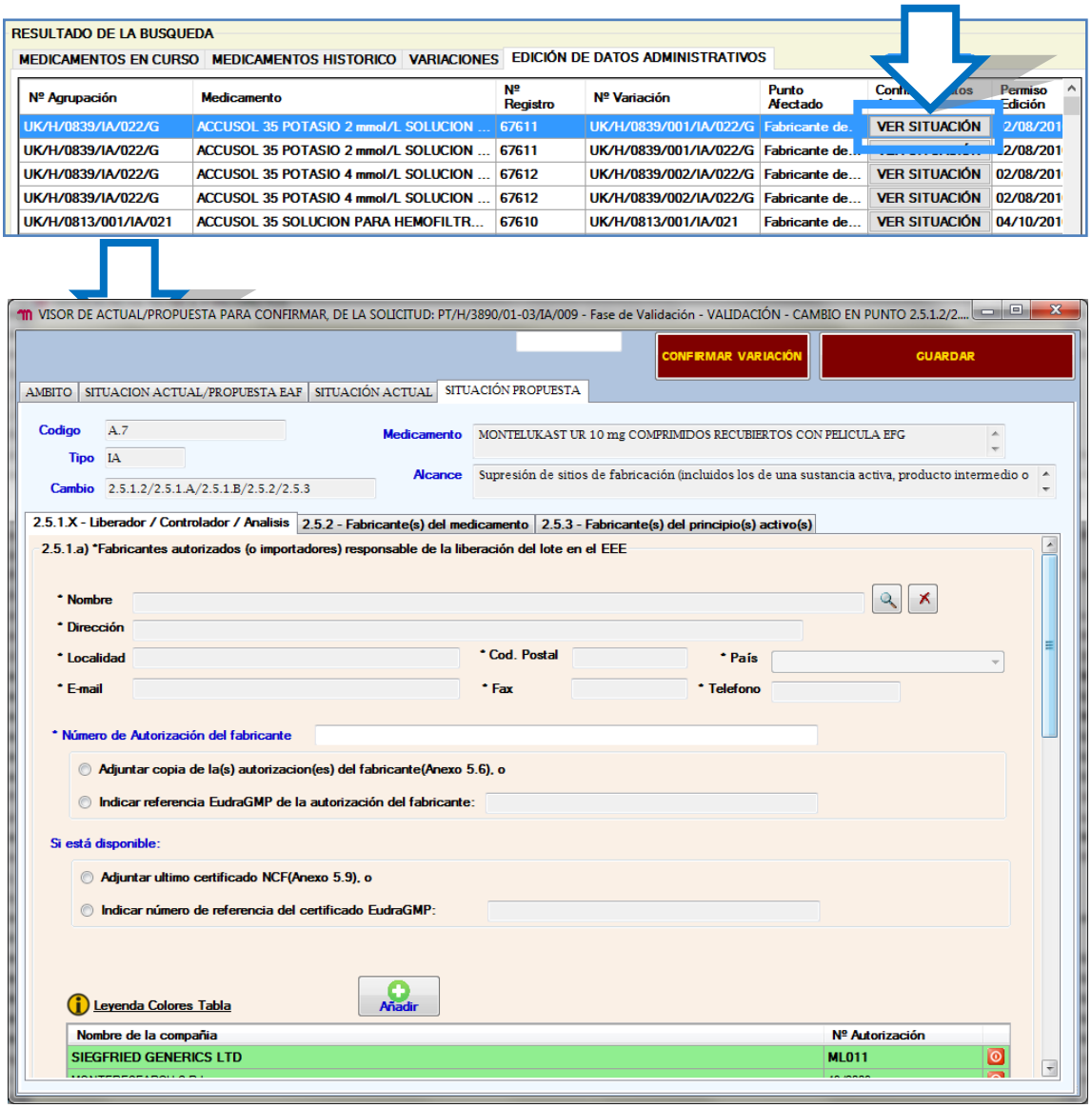


In the case of variations that affect Administrative Data, and once the extracted section is completed and evaluated by AEMPS, the requester will have to log on to confirm the administrative data generated by the variation.

This is accessed from the **EDIT ADMINISTRATIVE DATA** tab. This applies to variations that affect administrative data and which have been validated/authorised and only this edit remains pending (and subsequent review by AEMPS) before finalising/sending the request for signature.

These administrative data must be confirmed in a specific order when they affect the same point and the same medicine, for the correct replication of the data from a later variation. In other words, so that medicine X is affected by two variations relating to a change of manufacturer in the same point, until the first is confirmed by AEMPS, there will be no access to subsequent ones.

In order to access the data, click the **VIEW SITUATION** button.



Here it is possible to view the current/proposed situation of the affected point, the current and proposed complementary situation in two text boxes in the case that it is a eAF request, and the authorisation instructions of the evaluator in the case that it is a variation of a request of a rank higher than IB/II or IA which affects packaging.

Once confirmed, AEMPS shall validate that these data have been entered correctly.

7. PROCESS FOR AUTHORISING VARIATIONS WITH EXTRACTED SECTIONS

Once the evaluation of a variation of the new system for extracting sections is complete, the following process shall include:

- All sections evaluated and APPROVED of the variation shall form part of the final document for both the technical sheet as well as the patient information leaflet for medicines affected by this variation.
- In the case of sections of the variation being evaluated and REJECTED , the section on the final document will not be changed.
- The document for the technical sheet or patient information leaflet with the changes to the sections affected by a variation will be generated in the paths of RAEFAR.

An automatic search shall be carried out of all the variations pending in any of the phases of the medicines affected by the variation, as well as the same approved sections, and a message will be displayed stating that the original situation for the section has been changed for the authorised variation and that it is necessary to adapt the proposal in relation to the new situation (See point 6 .2).