Portal for Submission of Applications for the Update of the Manufacturing Flowchart as registered in INFARMED I.P. database

Index

1 General information

Marketing authorisation holders (MAHs) should be aware that the existence of information not up-to-date in Infarmed database regarding the manufacturing flowchart of medicinal products may result in limitations in the submission of online variation applications through the portal SMUH-ALTER, since the online submission of variations impacting the manufacturing flowchart will require applicants to indicate the changes to make in relation to the manufacturing flowchart registered in the database.
The **Portal for Submission of Applications to Update the Manufacturing Flowchart** allows Marketing Authorisation Holders to identify incorrect information regarding the manufacturing flowchart of the medicinal products, as registered in Infarmed's database, and request the respective correction.

External users may access to the portal using the link which is available in Infarmed's website. The portal allows MAH to view the information registered in Infarmed's database regarding the manufacturing flowchart of the medicinal product authorised by national and mutual recognition/decentralised procedures, and if applicable submit an online application to update the information. The relevant supporting documents, namely proof of the correct manufacturing flowchart as authorised by Infarmed, should be submitted with the application. The application and documents will be reviewed and validated by Infarmed before update of the database as requested by applicants.
MAHs may view in the Portal the status of the applications submitted.

2 Using the portal

2.1 FIRST STEPS

The following requirements of use are applicable:

Minimum Hardware

CPU: Intel Pentium 4 (2.8-GHz, 1 MB L2 cache, 800 MHz FSB)
RAM: 1 Gbyte
Hard drive 100 Gbytes
Network card
Keyboard and mouse
Screen and Graphics Card supporting resolution 1024x768

Mandatory Software

Windows XP Professional, Windows Vista or Windows 7
Internet Explorer Version 8 or higher (compatibility mode on)
It is advisable to have an internet connection speed of at least 7.2 Mb/s.

2.1.1 *ENTERING THE PORTAL*

The link available in Infarmed's website opens the login page of the portal, where the appropriate credentials should be inserted by MAHs.

The same Login credentials (user/password) are used for access to the following portals:

- SMUH-AIM for pre-submission of Marketing Authorisation applications, including the portal for information on the status of MA applications (national procedure only).
- SMUH-ALTER for submission of variations to existing Marketing Authorisations.
- Application for confirmation/update of flow chart of a medicinal product.
- Information on the status of reimbursement application.

2.1.2 *CHANGING THE PASSWORD*

To change the password the user should access the portal SMUH-ALTER for submission of variations to existing Marketing Authorisations.

2.1.3 *LOGOUT*

The user may exit the portal, using the logout button on the top right corner of the page, or by closing the page.

2.2 USING THE PORTAL

2.2.1 *LOGIN*

The MAHs should to indicate in this screen the access credentials. If the user/password is valid the MAH will be directed to the screen displaying the terms of use of the portal.

2.2.1.1 LAYOUT

2.2.2 *TERMS OF USE OF THE PORTAL*

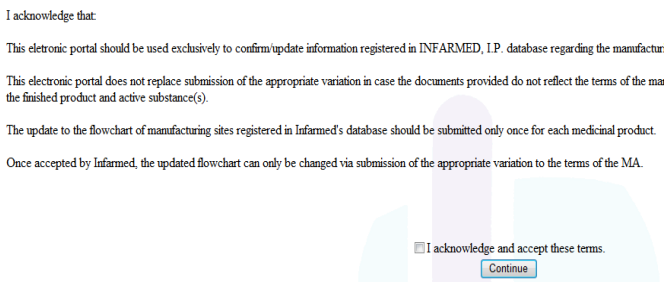
Access to the features of the portal will only be possible further to MAH's acknowledgement and acceptance of the terms of use transcribed below:

"This electronic portal should be used exclusively to confirm/update information registered in INFARMED, I.P. database regarding the manufacturing sites registered for a specific medicinal product.
This electronic portal does not replace submission of the appropriate variation in case the documents provided do not reflect the terms of the marketing authorisation in what concerns the registered manufacturing sites of the finished product and active substance(s).
The update to the flowchart of manufacturing sites registered in Infarmed's database should be submitted only once for each medicinal product.
Once accepted by Infarmed, the updated flowchart can only be changed via submission of the appropriate variation to the terms of the MA."

The portal should only be used for correction of the information registered in Infarmed's database regarding the manufacturing flowchart of the medicinal product.
Using the portal for submission of applications to update (i.e. correct) the information in Infarmed's database does not replace submission of the appropriate variation applications, in case Infarmed considers that the documents presented do not reflect the manufacturing flowchart authorised for the product.

The applicant should confirm acceptance of the terms of use and then select the button "Continue" in order to actually enter the portal.

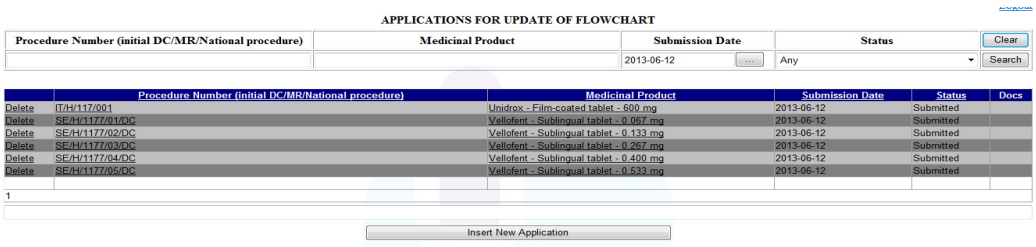
2.2.2.1 LAYOUT



2.2.3 *INITIAL SCREEN*

The initial screen of the ***Portal for submission of applications to update the manufacturing flowchart,*** allows applicants to search submitted applications and create new ones.

2.2.3.1 LAYOUT



2.2.3.2 AREAS AND FEATURES

Search Area

This area allows MAH to insert serch criteria before executing a search.

The following search criteria area available:

- **Procedure Number (initial DC/MR/National procedure)**
- **Medicinal Product**
- **Submission date**
- **Status**

To search applications using the field "**Procedure Number (initial DC/MR/National procedure)**" proceed as follows:

- Fill 

with the value to search. Its is possible to search using the full procedure number or part of it. The search is not sensitive to the upper or lower case.
- Press 

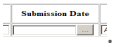
to execute the search.

To search applications using the field "**Medicinal product**" proceed as follows:

- Fill 

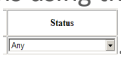
with the value to search. Its is possible to search using the full name of the medicinal product, part of it, or by using the character "%" ras described below:
  X ou X%: will show all results starting by X
  %X: will show all results containing X
  The search is not sensitive to the upper or lower case.
- Press 

to execute the search.

To search applications using the field "**Submission date**" the value date should be selected from the pop-up calendar in the 

. Press 

to execute the search.

To search applications using the field "**Status**" the appropriate status should be selected from the list available in the field 

.
Press 

to execute the search.
The option "**Any"/"Qualquer**" is set by default, and will show all applications regardless of their status.

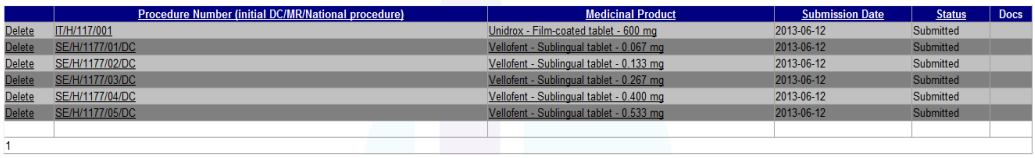
The following statuses are applicable to requests for update the manufacturing flowchart as registered in Infarmed's database:

- **Submitted**: after submission by the applicant

- **Awaits new entity**: after submission by the applicant, when a new entity not listed in Infarmed's database is proposed by the applicant
- **Ongoing**: after assignement of the application to a product manager at Infarmed
- **Concluded**: after closure of the application
- **Refused**: after refusal of the application

Note: The remaining statuses available for selection are not applicable requests for update the manufacturing flowchart as registered in Infarmed's database.

Search Result Area



	Procedure Number (initial DC/MR/National procedure)	Medicinal Product	Submission Date	Status	Docs
Delete	IT/H/117/001	Unidrox - Film-coated tablet - 600 mg	2013-06-12	Submitted	
Delete	SE/H/1177/01/DC	Vellofent - Sublingual tablet - 0.067 mg	2013-06-12	Submitted	
Delete	SE/H/1177/02/DC	Vellofent - Sublingual tablet - 0.133 mg	2013-06-12	Submitted	
Delete	SE/H/1177/03/DC	Vellofent - Sublingual tablet - 0.267 mg	2013-06-12	Submitted	
Delete	SE/H/1177/04/DC	Vellofent - Sublingual tablet - 0.400 mg	2013-06-12	Submitted	
Delete	SE/H/1177/05/DC	Vellofent - Sublingual tablet - 0.533 mg	2013-06-12	Submitted	

1

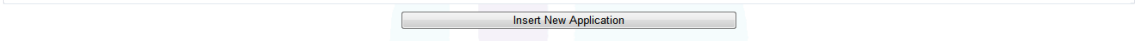
After pressing 

this area will list all the results in accordance with the search criteria inserted.

The following columns are displayed:

- "**Procedure Number (initial DC/MR/National procedure)**": includes a link to acess the screen displaying the application details
- "**Medicinal Product**": lists the name, strenght and pharmaceutical form of the medicinal product and includes a link to acess the screen displaying the application details
- "**Submission date**": indicates the submission date
- "**Status**": indicates the submission date

Area Insert new application



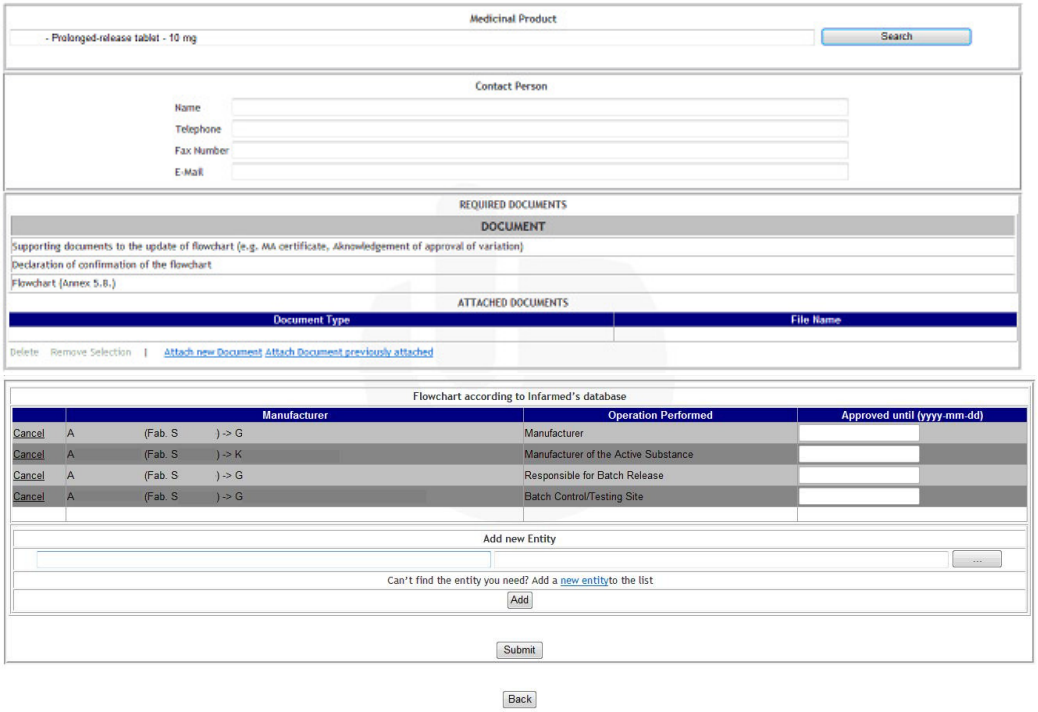
This area/button allows the applicant to access the screen for creation of new applications.

2.2.4 *SCREEN FOR CREATION NEW APPLICATION*

The screen allows MAH to check the manufacturing flowchart for the medicinal products as registered in Infarmed's database, and if applicable, fill na application form for correction of the manufacturing flowchart in the database.

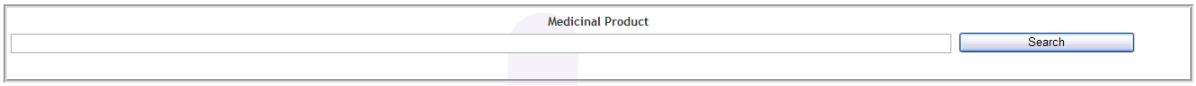
When entering this screen it is only possible to view the area for selection of the medicinal product. The remaining áreas of the application form are only viewed after selecting the medicinal product.

2.2.4.1 LAYOUT



2.2.4.2 AREAS AND FEATURES

Area for selection of medicinal product

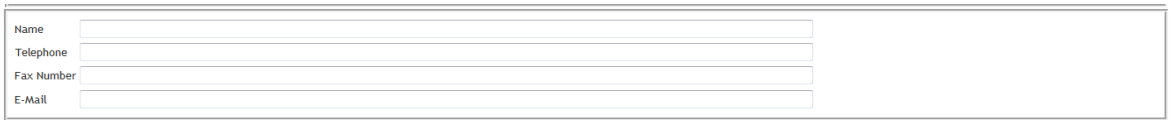


The MAH should use this area to search and select the medicinal product for whihc intends to view the manufacturing flowchart, and if applicable submit the corresponding application for update.

It is possible to search and select:

- Medicinal products authorised by national procedure and for which the MA is Authorised, Suspended or Suspended by Court Decision.
- Medicinal products authorised by mutual recognition/decentralised procedure and for which the MA is Authorised, Suspended or Suspended by Court Decision. Medicinal products for which the national phase of the MRP/DCP is pending will also be available for selection.

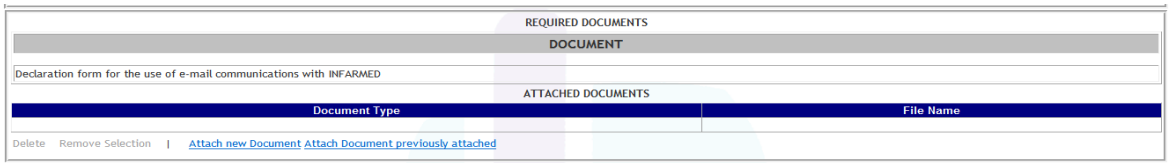
Area for Contact Person Details



The MAH should indicate in this area the details of the contact person to whom any request for supplementary information/clarification regarding the application should be addressed.
The following fields are mandatory:

- "Name"
- "Telephone"
- "Fax Number"
- "E-mail"

Area for Attaching Documents

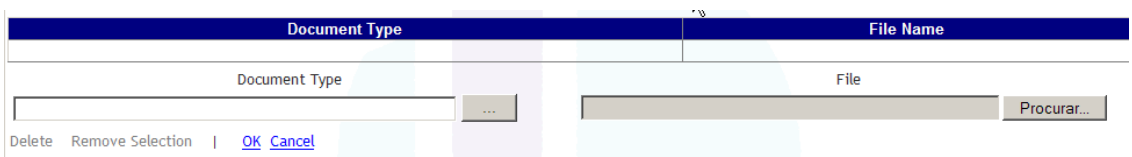


This area allows applicants to attach to the form the documents required for submission of the application to update the manufacturing flowchart.
The following documents are mandatory:

- "**Supporting documents to the update of flowchart (e.g. MA certificate, Aknowledgement of approval of variation)**"
- "**Declaration of confirmation of the flowchart**": applicants should use the Declaration template available in Infarmed's website.
- "**Flowchart (Annex 5.8)**" referring to the manufacturing flowchart authorised for the medicinal product, even if the updated annex 5.8 to the application form has not been included in a variation application.

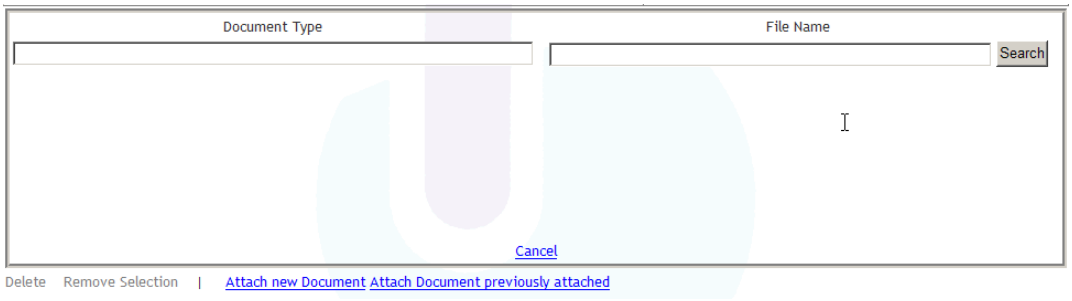
Documents may be attached using the following options:

- Attach new Document : for searching and attaching a document saved in the applicant's computer.



The type of document to attach should be selected from the field "Document type" and the file should be browsed in the field "File". The document is only attached after pressing "OK"
The link "Cancel" closes the area "Attach new Document".

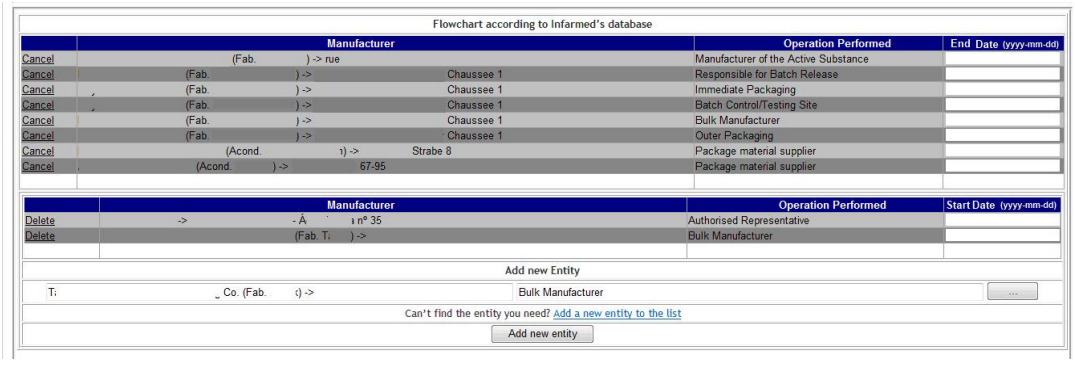
- Attach Document previously attached : for searching and attaching a document saved in the portal, which hás been previously submitted to Infarmed by the same MAH.



The documents previously submitted to Infarmed may be searched by "**Document type**" or "**File Name**". After pressing "**Search**", the document to attach should be selected from the list of results presented.
The link "Cancel" closes the area "**Attach Document previously attached**"

While creating the application it is possible to select a document in the area "**Attached documents**", and subsequently remove it using the button Delete , or unselect the document using the button Remove Selection .

Area to View and Update of manufacturers in the manufacturing flowchart



The area "**Flowchart according to Infarmed's database**" MAHs will view the information registered in Infarmed's database regarding the manufacturing flowchart of the medicinal product selected above. If applicable, MAHs may request the update of the informaion in the database by indicating in this area:

- Manufacturers/Entities (combination of name/address) to be removed from the manufacturing flowchart registered in the database, using the link "**Cancel**".

- Manufacturers/Entities (combination of name/address) to be added to the manufacturing flowchart registered in the database using the field "**Add new entity**".

For **Manufacturers/Entities to be removed**, the date of cancellation of the manufacturer from the dossier should be indicated in the field "**Approved until**" (this date should correspond to the approval date of the regulatory procedure that removed/replaced the manufacturer as registered in Infarmed's database).
For **Manufacturers/Entities to be added**, the date of addition of the manufacturer to the dossier should be indicated in the field "**Approved since**" (this date should correspond to approval date of the regulatory procedure that introduced the manufacturer).

The fields **Approved until**" and "**Approved since**" are mandatory for all manufacturers to be removed or added to the manufacturing flowchart as registered in the database.

The manufacturers responsible for the following operations should always be referred:
- "Manufacturer of the Active Susbtance"
- "Bulk Manufacturer"
- "Immediate packaging"
- "Outer packaging"
- "Responsible for Batch Release"
- "Batch control/Testing site"

It should be noted that a request for update of the manufacturing flowchart of the medicinal product as registered in Infarmed's database should be submitted to split the operation "Manufacturer" in "Bulk Manufacturer" + "Immediate packaging" + "Outer packaging", even if this is the only update to be requested.

The following definitions concerning the Type of Entity should be considered:

Type of Entity	Defintion
Manufacturer of the Active Substance	Manufacturer responsible for synthesis/obtention process the active substance (all phases of the process or only final phases, including micronization)
Manufacturer of intermediate compound of active substance	Manufacturer responsible for synthesis/obtention process the intermediate compound of active substance
Batch control/Testing site of active substance	Manufacturer responsible for the quality control/in process control of the active substance
Responsible for	Manufacturer responsible for the batch release of the active substance

batch release of active substance	
Intermediate Stage Manufacturer	Manufacturer responsible for intermediate phases (non-final) of the manufacturing process of the bulk product.
Bulk Manufacturer	Manufacturer responsible for manufacture of the bulk product (all phases or only final phase), excluding primary and secondary packaging.
Manufacturer	Manufacturer responsible for all phases of finished product manufacture (including primary and secondary packaging). → **NOTE**: it is not available for selection in the field "Add new entity"; the options Bulk Manufacturer + Primary packaging + Secondary Packaging should be selected individually
Immediate packaging	Manufacturer responsible primary packaging
Outer packaging	Manufacturer responsible secondary packaging
Batch control/Testing site	Manufacturer responsible for batch control/testing of the finished product in the EEA or in countries for which a MRA exists.
Quality control analysis	Manufacturer responsible for quality control analysis. → **NOTE**: it should not be selected in the field "Add new entity"; the option "**Batch control/Testing site**" should be selected, even if the site performs only one quality control test.
Responsible for Batch Release	Manufacturer responsible for batch release in the EEA.
Medical Devices Supplier	Medical devices supplier/manufacturer.
Package material supplier	Packaging material supplier/manufacturer.
Authorised Representative	Legal representative in the EEA of the manufacturer of medical devices (Note: not applicable in the context of submission of applications for manufacturing flowchart as registered in Infarmed's database)
Local Representative	Local representative of the Marketing authorisation holder (for medicinal products of human use) (Note: not applicable in the context of submission of applications for manufacturing flowchart as registered in Infarmed's database
Distribution	Distributor of the medicinal product
Contract Company used for Bioavailability or Bioequivalence Trials	Company responsible for performing Bioavailability/Bioequivalence Trials (Promotor, Clinical center and/or Analytical center).
Contract Company used for Validation of Blood Product Manufacturing Processes	Not applicable in the context of submission of applications for manufacturing flowchart as registered in Infarmed's database

Contract company used for clinical trials	Not applicable in the context of submission of applications for manufacturing flowchart as registered in Infarmed's database
Contract company used for toxicological trials	Not applicable in the context of submission of applications for manufacturing flowchart as registered in Infarmed's database
Official Medicines Control Laboratory (OMCL)	**Official Medicines Control Laboratory (OMCL)**
Responsible for Pharmacovigilance	Qualified person for pharmacovigilance (corresponding to the european QPPV). (Note: Not applicable in the context of submission of applications for manufacturing flowchart as registered in Infarmed's database)

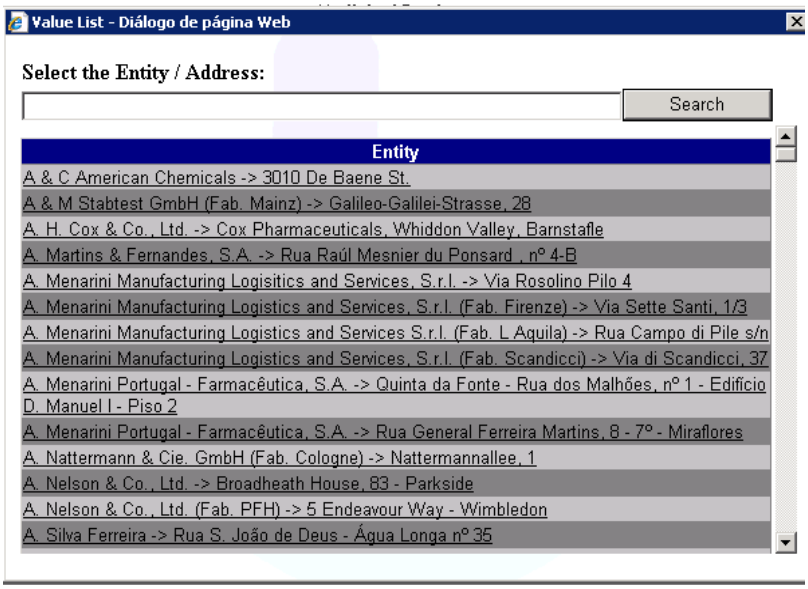
*it should only be added in the field "Add new entity" if referred in the MA dossier

Field "**Add new entity**"

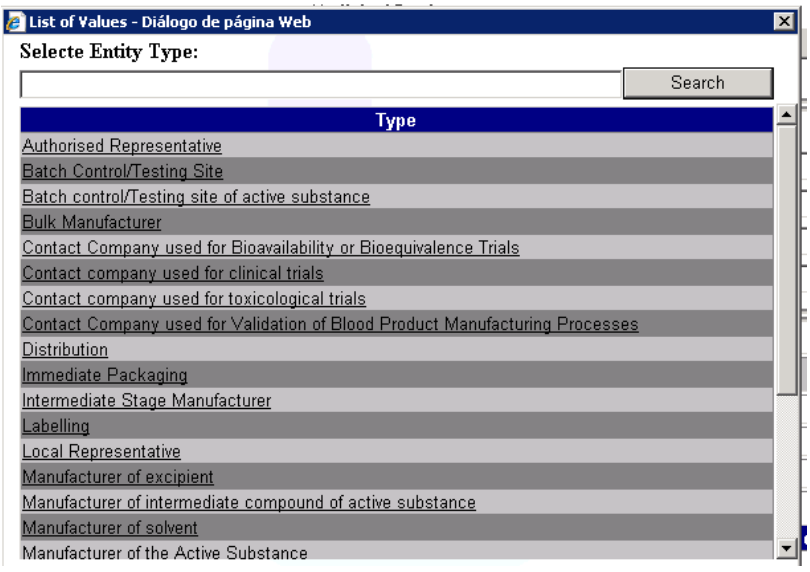
Applicants should use the button  to access the pop-up screens that allows the search and selection of entities registered in Infarmed's database.

Applicants should consider the rules below before using the pop-up "**Select Entity /Address**":

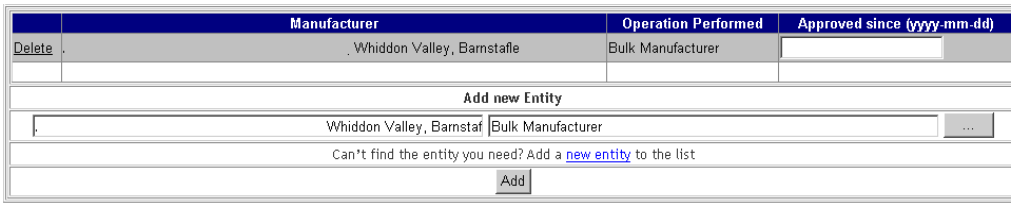
- Entities that do not contain the expression **(Fab. ...)** are referrent to administrative site addresses and are used to identify Marketing authorisation Holders or Representatives, therefore in the context of submission of applications to update manufacturing flowchart, only entities that do have the expression **(Fab. ...)** referred in the address registered in the database, should be chosen since these are referent to manufacturing site addresses.
- Applicants should carefully check if the name/address of the entity chosen selected is correct, since there are several entities with similar names and addresses.
- Somes entities in the list will be started by [3 spaces], which means that the entity's name or address as listed is not the current name/address of that entity.



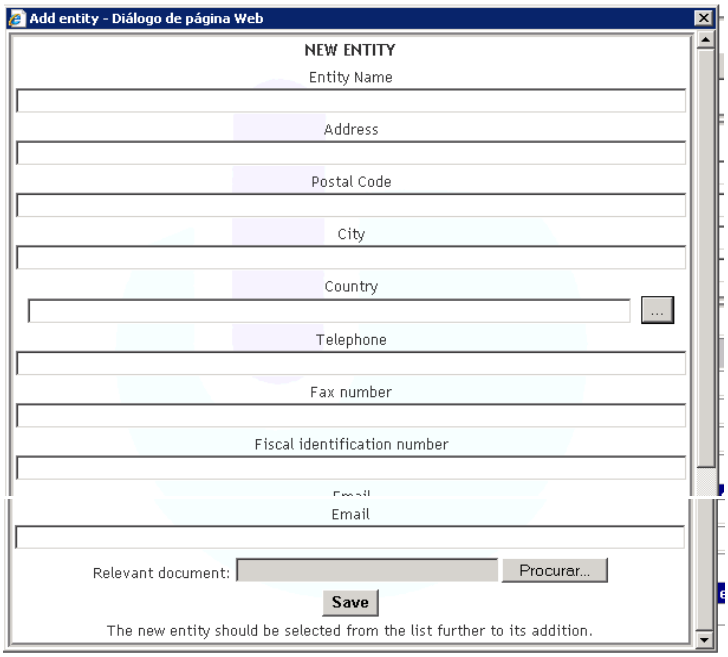
Further to selecting the Entity/Address, the type of manufacturing operation performed should be selected from the pop-up "**Select Entity type**".



Further to selecting the Entity and the corresponding type of operation, the button "**Add**" should be pressed in order to formally add the manufacturer to the list of manufacturers/entities to be added to the manufacturing flowchart as registered in the database. Entities can be removed from this list of entities using the link "Delete"



Whenever a manufacturer/entity is not available in the pop-up **Select Entity /Address**", or is listed with an outdated name/address, applicants should request creation of a new entity using the link "**Can't find the entity you need? Add a new entity to the list**"



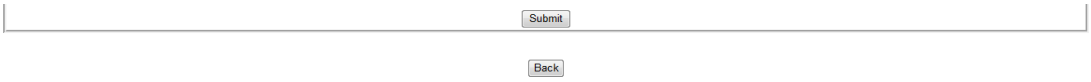
The following information will be required to be filled in order to request creation of a new entity:

- "**Entity Name**" – it is mandatory to indicate the full name of the entity, including abbreviations if applicable (Ex.: Ltd.; Lda.; S.A.; Co.; GmbH; etc).
- **Address**" – it is mandatory to indicate the full manufacturing site/plant address; please avoid using abbreviation (Ex.: Av. instead of Avenue)
- "**Postal code**"
- **"City**" – it is mandatory to indicate the city
- **"Country**" – it is mandatory to select the countr from the list
- "**Telephone**" – do not use spaces between the numbers, except to separate the international or area codes
- "**Fax number**" - do not use spaces between the numbers, except to separate the international or area codes
- "**Fiscal Identification number**" – number for fiscal purposes used in the entity's country
- "**Email**"

- "**Relevant Document**" – it is mandatory to add at least one relevant document of proof: GMP certificate, Manufacturing Authorisation or CEP, in case the entity to create is a manufacturer; or proof of establishment/national registration of the entity, in case the enity to create is a MAH.

The button "SAVE" should be used to proceed and close the pop-up. The new entity created should be selected from the pop-up "**Select Entity /Address**", in order that it can be considered as entity to be added to the manufacturing flowchart of the medicinal product.

Area for Action



In this area applicants may proceed with submission of the application using the button "**Submit**", or cancel it by pressing the button "**Back**".

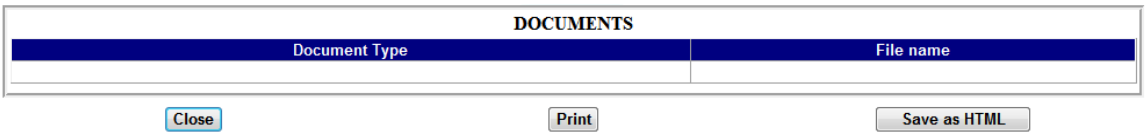
Submission of the application is only possible if at least one manufacturer/entity is cancelled or added to the manufacturing flowchart of the medicinal product as registered in Infarmed's database. It is not possible to save information the online form, so if the screen is closed by using the button "Back" all the information filled will be lost.

2.2.5 *SCREEN – VIEW OF DETAILS OF THE APPLICATION*

This screen allows MAHs to view the details of previously submitted applications for update of the manufacturing flowchart.

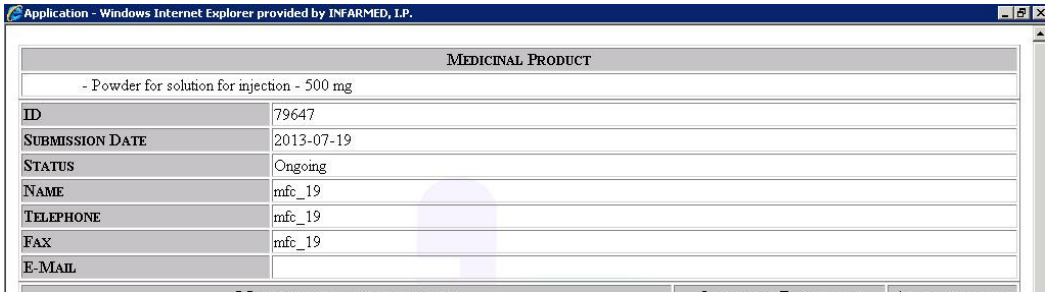
2.2.5.1 LAYOUT

MEDICINAL PRODUCT			
- Effervescent tablet - 2081.8 mg			
ID	68899		
SUBMISSION DATE	2013-04-29		
STATUS	Submitted		
NAME	asfd		
TELEPHONE	asf		
FAX	asf		
E-MAIL	asf@asd.pt		
MANUFACTURER TO BE REMOVED		OPERATION PERFORMED	End Date
- O Chaussee 1		Immediate Packaging	
- O Chaussee 1		Responsible for Batch Release	
- rue		Manufacturer of the Active Substance	
MANUFACTURER TO BE ADDED (EXISTING ENTITY)	MANUFACTURER TO BE ADDED INSERTEDENTITY (NEW ENTITY)	OPERATION PERFORMED	Start Date
- Rua Ponsard, 4 B		Batch control/Testing site of active substance	
Completed Flowchart			
MANUFACTURER	MANUFACTURER (NEW ENTITY)	OPERATION PERFORMED	
-> Rua 4 B		Batch control/Testing site of active substance	
-> 67-95		Package material supplier	
(Fab.) -> S. Chaussee 1		Batch Control/Testing Site	
(Fab.) -> S Chaussee 1		Bulk Manufacturer	
(Fab.) -> S Chaussee 1		Outer Packaging	
-> n° 9 Carcavelos		Responsible for Pharmacovigilance	
-> Strabe 8		Package material supplier	



2.2.5.2 AREAS AND FEATURES

Area for Information of the procedure



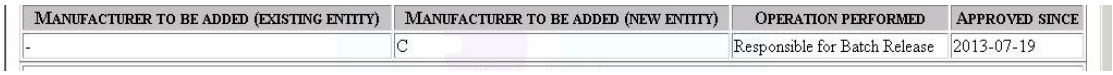
This area contains information on the application procedure.

Area for Information on the Entities to be Cancelled or Added to the manufacturing flowchart

Entities to be Cancelled

MANUFACTURER TO BE REMOVED	OPERATION PERFORMED	APPROVED UNTIL
- ., S.A. -	Responsible for Batch Release	2013-07-17
›, S.A. La_	Manufacturer	2013-07-18

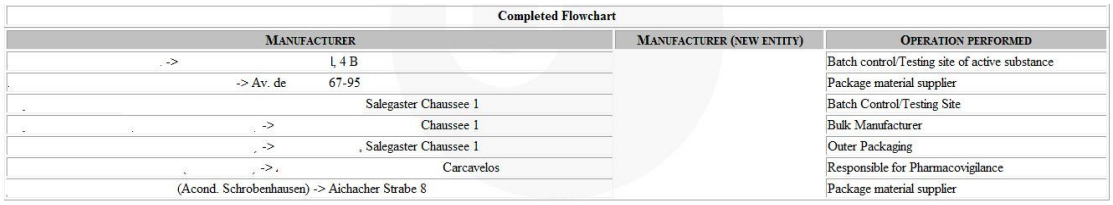
Entities to be Added



MANUFACTURER TO BE ADDED (EXISTING ENTITY)	MANUFACTURER TO BE ADDED (NEW ENTITY)	OPERATION PERFORMED	APPROVED SINCE
-	C	Responsible for Batch Release	2013-07-19

This area allows MAHs to view the entities to be cancelled or added to the manufacturing flowchart, and corresponding "**Approved until**" and "**Approved since**" dates, as requested in the online application form.

Area for Information on the Completed Flowchart

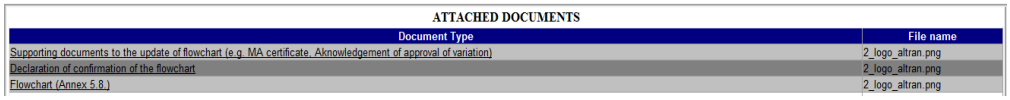


Completed Flowchart

MANUFACTURER	MANUFACTURER (NEW ENTITY)	OPERATION PERFORMED
. -> l, 4 B		Batch control/Testing site of active substance
-> Av. de 67-95		Package material supplier
Salegaster Chaussee 1		Batch Control/Testing Site
-> Chaussee 1		Bulk Manufacturer
, -> , Salegaster Chaussee 1		Outer Packaging
, -> , Carcavelos		Responsible for Pharmacovigilance
(Acond. Schrobenhausen) -> Aichacher Strabe 8		Package material supplier

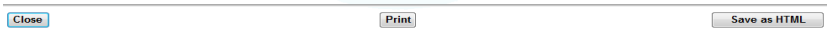
This area allows MAHs to view the completed flowhart of the medicinal product after the requested updated.

Area of Attached Documents



This area allows MAHs to view and open documents attached to the online application form.

Area for Action

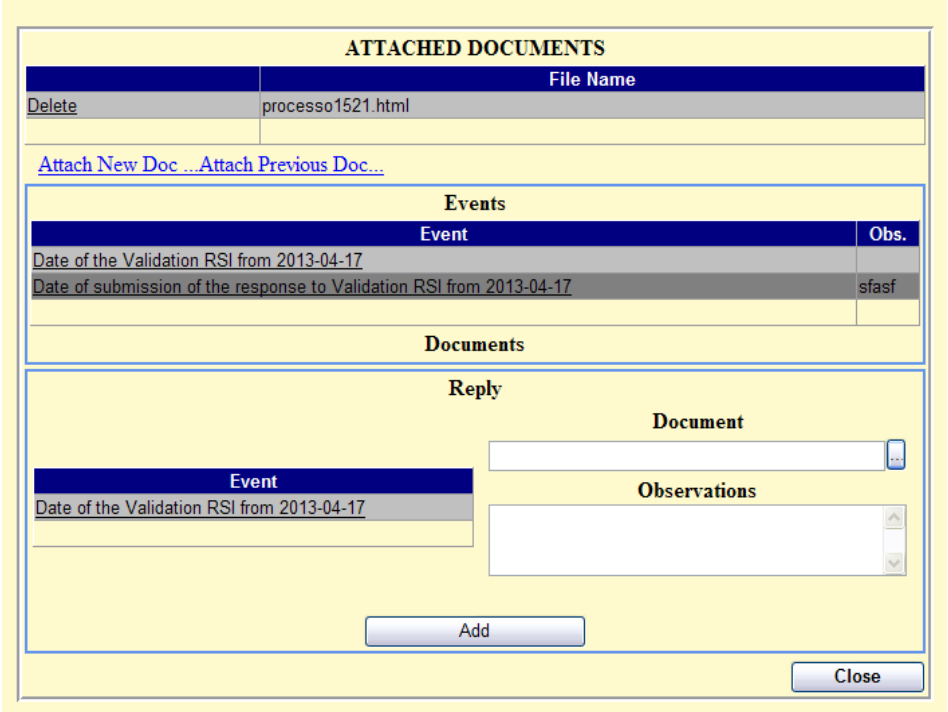


This area allows MAHs to close the screen using the button “Close”, print the screen using the button “Print” and save the information in the screen in HTML format, using the button “Save as HTML”.

2.2.6 *SCREEN FOR SUBMISSION OF RESPONSE TO REQUEST FOR SUPPLEMENTARY INFORMATION*

This screen is accessible via the link “**Attach New Doc**” available in the column “**Docs**” in the Area of Search results listed in the Initial screen of the portal.
It allows applicants to add new documents to the application, in response to Infarmed’s request for supplementary information/clarification. The link is only available if the product manager at Infarmed responsible for the procedure allows applicants to add new documents to the applicantion.

2.2.6.1 LAYOUT



2.2.6.2 AREAS AND FEATURES

Applicants should add the response document in the area "**Attached documents**", using the links Attach New Doc .. or ...Attach Previous Doc... , as decribed in section 3.4.2.2.

The response document is only formally submitted to Infarmed after association of the document to the event "Date of the Validation RSI from dd-mm-aaaa" indicated in the filed "Event" available in the Area "Reply", and further to pressing the button "Add".
Applicants should confirm creation of the event "Date of submission of response to Validation RSI from dd-mm-aaaa" in the Area "Events".

2.2.7 *DELETION OF APPLICATIONS*

MAHs may delete applications for update of manufacturing flowchart as registered in Infarmed's database using the link "**Delete**" available in the first column of the Area of Search Results listed in the initial screen of the portal.
It is only possible to delete applications that are in the status "Submitted".