EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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# IRIS guide for applicants

*(How to create and submit scientific applications, for industry and individual applicants)*

Version 2.16




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## Revision History

| Date | Description |
|---|---|
| 27/06/22 | Added Section 9. Registration of an MAH i-SPOC on supply and availability |
| 05/09/22 | Section 7. Inspections updated |
| 10/10/22 | Section 4. Scientific Advice updated |
| 03/05/23 | Section 8. Veterinary Signal Management updated |
| 10/07/23 | Added Section 10. PRIME Eligibility |
| 03/10/23 | Section 10. PRIME Eligibility updated |

## Table of abbreviations

| Abbreviation | Explanation |
|---|---|
| CAP | Centrally Authorised Product |
| CHMP | Committee for Human Medicinal Products |
| COMP | Committee for Orphan Medicinal Products |
| CVMP | Committee for Veterinary Medicinal Products |
| EC | European Commission |
| EMA | European Medicines Agency |
| ESMP | European Shortages Monitoring platform |
| ETF | Emergency Task Force |
| EU | European Union |
| GCP | Good Clinical Practice |
| GMP | Good Manufacturing Practice |
| IAM | Identity & Access Management |
| ITF | Innovation Task Force |
| LoQ | List of Questions |

| Abbreviation | Explanation |
|---|---|
| MS | Member State |
| MSSG | Medicine Shortages Steering Group |
| OD | Orphan Designation |
| OMS | Organisation Management Service (part of SPOR) |
| PD | Parallel Distribution |
| PIP | Paediatric investigation plans |
| PRIME | Priority medicines |
| RPI | Research Product Identifier |
| SA | Scientific Advice |
| SME | Subject Matter Expert |
| SPOR | Management Services for Substances, Products, Organisations and Referential Terms |

# 1. Purpose and context

## *1.1. Purpose of this guide*

This guide has been produced to show applicants how to use the IRIS platform to prepare and submit an application and/or data for a scientific procedure (orphan designation application, scientific advice, ITF briefing meeting requests, marketing status reports, inspections and veterinary signal management) and related activities.

For Parallel Distribution procedures separate user access roles are needed and separate guidance is available on the IRIS home page.

## *1.2. Preliminary requirement*

**EMA Account and appropriate role**: for any type of submission in IRIS, you need an EMA account and an appropriate role in IRIS, to login into IRIS. Registration needs to be done only once and will allow you to submit any type of scientific applications now and in the future. For information on how to request an EMA account and an appropriate IRIS role (these are two separate actions), please consult the separate IRIS guide to registration and the quick interactive guide to IRIS registration process on the IRIS home page. This guide also contains information on how to request or transfer an **RPI (Research Product Identifier)**.

## *1.3. Supported Browsers*

IRIS can be accessed on any modern Web Browser, including but not limited to Google Chrome (latest version), Internet Explorer 11 and above, Edge (including the new, Chromium-based Edge), Safari 12 and above, Firefox (latest version), Vivaldi, etc.

## 2. Common operations for all scientific submission types

### *2.1. Display and sort submissions*

From the IRIS home page, after sign-in, click on any of the options: “**Draft Submissions**”, “**Ongoing Submissions**” or “**Completed Submissions**” present under “**Submissions**” Tab;

If you have an IRIS Industry Manager role, you will see all the submissions that you have created, plus all the submissions in which you have been added as a contributor. If you have a Contributor role, you will see all the Submissions to which you have been added as a Contributor. If you have both roles, you will see all submissions of your own and those for which you have been added as a Contributor. In all cases, you will see submissions for all the Organisations to which you are affiliated (in IAM);

Click on any of the column headings that appear in blue font, and the rows listed in the table will be sorted in ascending order (click again for descending order).

### *2.2. Search for submissions*

You can obtain a restricted subset of your submissions: from the IRIS home page, select first “**Draft Submissions**”, “**Ongoing Submissions**” or “**Completed Submissions**”;

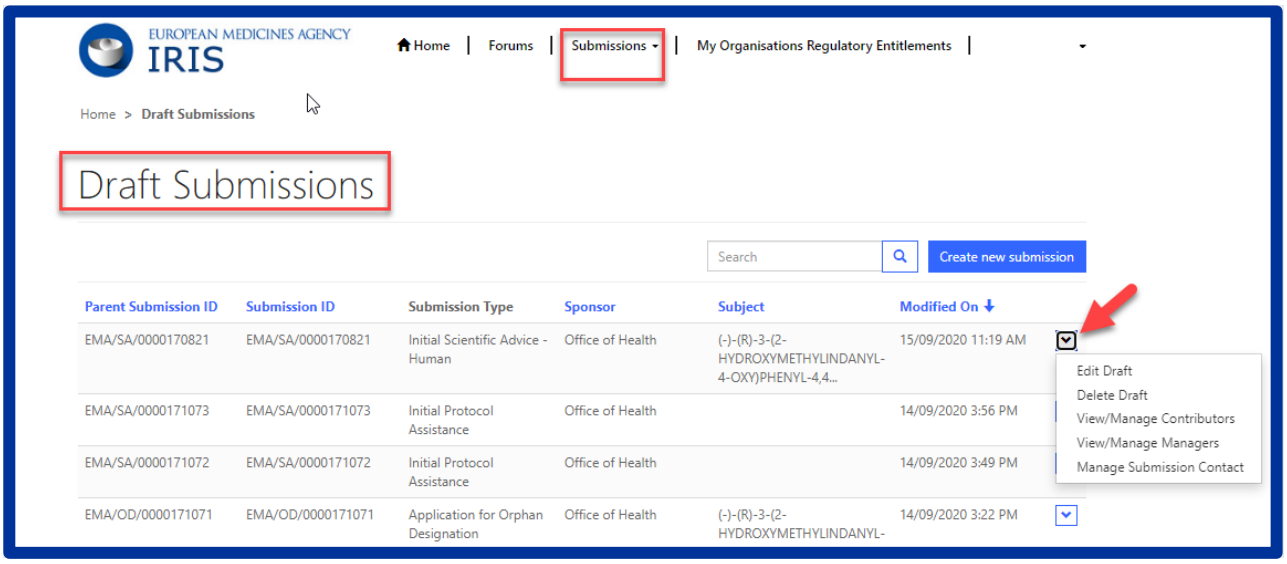
In the search bar, enter any string (combination of letters and/or numbers) that will identify the submission you are looking for and might be contained in the columns that are displayed on screen (e.g. "Submission ID", "Organisation", "Submission Type"); by including an asterisk (*) as first character, the search string will apply to text in any position;

Click on the magnifying glass search symbol or press "**Enter**" on your keyboard to launch the search;

A list of the relevant results that match the search criterion you typed in the search bar will be displayed. The list can be sorted as described in the previous section;

In “**Draft submissions**”, a menu of different actions can be elicited by clicking on the down arrow to the right of the relevant submission. You can edit or delete the submission, manage the contributors and managers, and change the “**submission contact**” (the person who will receive by default all the email communications for the procedure) (see Figure 1).

*Figure 1: Managing draft submissions*




### *2.3. Create a new submission (general procedure for all submission types)*

- From the IRIS home page, click on **"Draft submissions"** sub-tab present under "Submission" tab;
- Click **"Create new submission"** [a screen with the heading "Portal – New Submissions" opens showing 4 stages. The first stage **"1. Choose Applicant Type"** is highlighted in blue];
- From the drop-down arrow on the box below "**Are you applying as an individual or on behalf of an organisation?**" select the appropriate answer and click "**Next**";

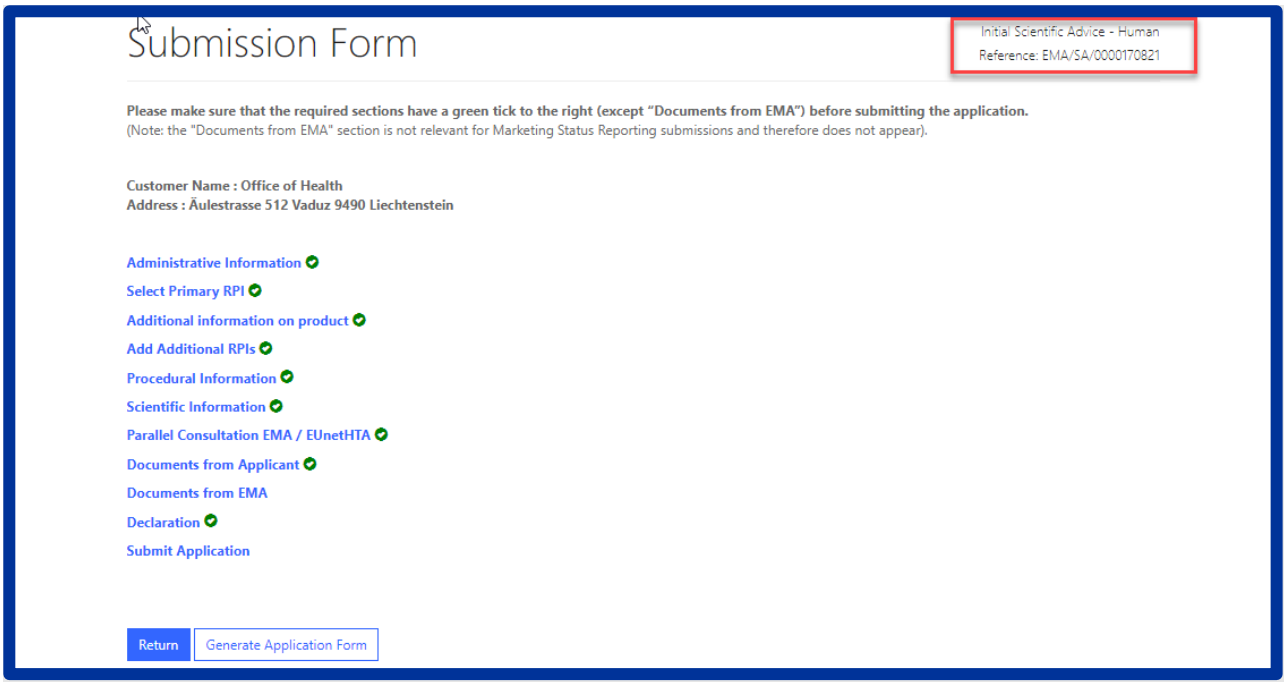
Only if you are applying on behalf of an organisation:

- Use the magnifying glass search symbol to look up the organisations available for you to select (N.B. only the organisation(s) affiliated to the portal user role that you logged into the portal as will be displayed here);
- Pick the right organisation and (there may only be one) and click **"Select"**;
- Use the search symbol to look up the locations available for you to select, pick the right one and click **"Select"**; please note that the Regulatory entitlement (Orphan Designation) will be granted to the address of this location and the relevant organisation;
  **NOTE: it is strongly recommended to use only one location (normally the legal seat of the organisation) for all IRIS submissions, RPIs and regulatory entitlements. This simplifies your management of submissions in IRIS.**
- **"Choose Submission Type"** is now coloured blue and 3 mandatory fields (marked with a red asterisk "*") appear labelled **"Organisation"** **"Location"** and **"Submission Type"** (the first two only if you are applying on behalf of an organisation). Use the search symbol to look up the submission types available, click on the appropriate submission type and then on **"Select"**;
- Add at least one Manager in the specific field (when applying on behalf of an organisation, the pop-up list will only include those people who have been granted an IRIS Industry Manager access role that is affiliated to the specific organisation (Company + Country) you selected in the previous screen. If no-one has done this, the list will be empty). **It is strongly recommended to have at least two**

**Managers (preferably three) for each IRIS submission:** this will allow the applicant continued access to the submission even if one the managers leaves the company or is absent for prolonged periods;

- Click "**Create and Next**". A new screen appears with a reference number (e.g. EMA/XX/0000001234) for your draft submission displayed on the upper right-hand side of the "Portal – New Submission" screen (N.B. It is a good idea to take note of the reference number created). There is also now a list of various tabs (steps) including "**Select RPI**" and ending with "**Declaration**") relating to the submission reference displayed on the left-hand side of your screen (see Figure 2).

*Figure 2: Example of new submission*




- Click on **"Select RPI"** to bring up "Research Product Identifier (RPI)" screen:
- Click the **magnifying glass** search symbol to bring up a list of RPI names;
- In the pop-up window, pick an RPI name from the list and click "**Select**";
- Back in the "Research Product Identifier (RPI)" screen, click "**Save and Return**" and you are returned to the "Submission Form" screen;

If you do not see the RPI for your product in the list:

An RPI tracks the development of a medicinal product. The RPI remains the same when the name of the substance(s) in the product changes, or when development of the product is transferred to a different product. If you have already submitted an application to EMA for your product, it is very likely that an RPI already exists, and that one should be used.

RPIs are assigned to an OMS Location (specific address), not to a parent organisation. Consequently when creating a submission in the name of a specific location, only those RPIs assigned to that location can be chosen. **It is therefore recommended that all RPIs (and regulatory entitlement) for an organisation are assigned to the same location (normally the legal seat of the organisation).**

The RPI may already exist, but "owned" by another sister company in the same or a different country, a different company or a consultant, or it may be assigned to a different location of your organisation. In such cases, it won't appear in the selection list, and you need either to request affiliation to the RPI "owner", or

the "owner" should transfer the RPI to your company, depending on which company should be the sponsor of the orphan designation. To transfer an RPI reference the IRIS guide to registration section 8.3. *"Transfer a Research Product Identifier (RPI)"*.

If you are sure that no RPI exists for the medicinal product yet, please request one via IRIS following IRIS guide to registration section *8.2. "How to request a new RPI"*. This is a separate submission. After receiving communication from EMA that your RPI has been created, you can **go back to your draft submission and** proceed to the steps below.

If your RPI is intended to cover **multiple products** or a **methodology/ technology** or a **method** or **other** (not a single product), please contact ITFSecretariat@ema.europa.eu or ScientificAdvice@ema.europa.eu

- If you plan to submit **SA or Qualification request** you will be requested to complete a specific **Word form** and an **RPI will be crated and provided you**.
- If you apply for **ITF BM** most of the information is already available for ITF Secretariat in the initial request form and an **RPI will be created and provided to you** .
- These '**special' RPIs cannot be requested by you via IRIS**.

Click on "**Additional product information/update**":

- Make sure that the list of innovation/enabling technologies includes at least one term; if not, choose at least one with the **"Add"** button;
- Click **"Save and return"**.

Once the RPI data (and any other mandatory sections) are completed, all the sections (tabs) will turn from grey to blue and will be active (see Figure 2). Fill in each section. Please note that fields with a red asterisk are mandatory. You need to complete each section before you can save it, but it is not mandatory to fill in all the section in one session;

Back in the main "**Submission Form**" Screen, click on "**Documents from Applicant**":

In the next screen that appears, you can directly upload documents to your submission. While there is no maximum number of files or global size, there is a size limit of 50 Mb per file. Please upload individual files for each document, rather than a single Zip file (or similar) for the set of all documents; it is possible to upload multiple files in a single operation. If appropriate, you can merge several PDF files into a single one, using specific software, before uploading. A Zip file is recommended only as the container for the literature references;

- Click **"Save and Return"** when you have finished uploading documents;
- At any stage during the procedure above, clicking "**Return**" on the Submission form page saves the draft submission (which will now appear in your "**Draft Submissions**" list). You can open it again at a later time to edit/add more information;
- Click on **"Generate Application form"** present at bottom of screen next to **"Return"** button to create a word file for the summary of application filled at that point of time by the applicant. Word file will be shown under **"Documents from Applicant";**

When you are ready to submit your final application, click on "**Declaration and re(submission)**":

- **Click on the tick box** to the left of the declaration statement (that begins with the words: "I confirm…") to formally declare that you are authorised to submit the application;
- Click on the "**Declaration and submission**" button;

- If you are unsure or think of any part of the application you want to revise, click “**Review Application**” and this will return you to the draft submission;
- If you are sure you want to submit the application, click” Submit”.

Your application has now been submitted and is locked for edit/upload unless EMA opens it up again for you to add or amend any information or documents.

You are then returned to the portal **“Ongoing Submissions”** tab. You can now look up the submission you have just submitted using the **“Ongoing Submission”.** The latest submission will appear on top once validation is completed in background, as submissions are sorted by date and time of last update.

### *2.4. Communication only to the Submission Contact (Portal contact) for a submission*

The communication model for IRIS is that while there can be any number of Industry managers and Industry contributors associated to a single submission, only one of them is the "submission contact", also called the "portal contact" i.e. the primary contact person to whom all communication is sent (by default) for a given submission. The default "submission contact" is the Industry manager who submits the application.

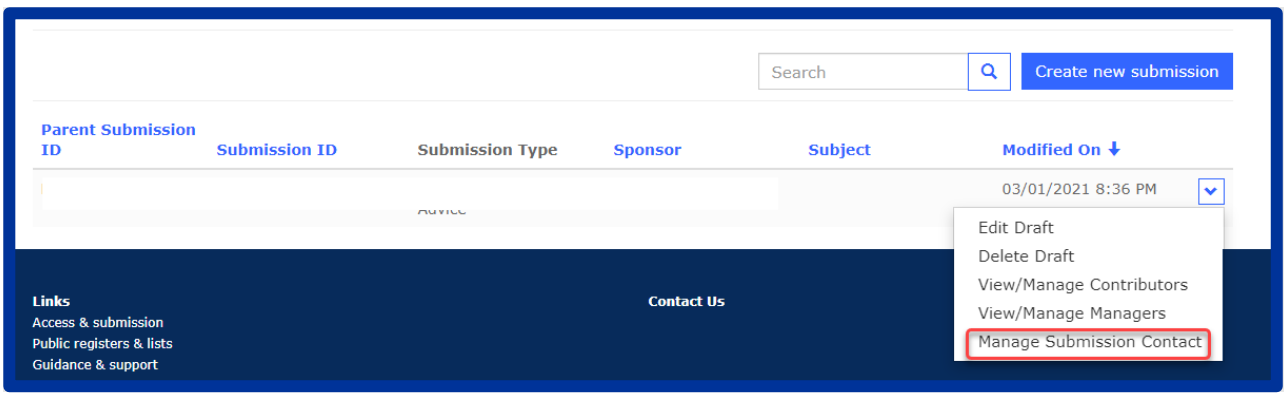
The "**submission contact**" role can be reassigned at any moment, and repeatedly, by any of the Industry managers associated to that submission, but the EMA users of the IRIS system will send **communications** only to the **"submission contact",** by default. This is for efficiency and security reasons.

Applicants can nominate additional Industry managers and reassign the "submission contact" role as required, for example before a period of leave of the "submission contact". This can be done in IRIS, by clicking on the V to the right of the submission and selecting "Manage submission contact", as shown in Figure 3 and below.

In addition, applicants may also wish to set up appropriate auto-forwarding rules in the email system of the "submission contact".

IRIS is being built to allow applicants to self-manage their "submission contact" role for each submission. In future, EMA plans to extend this concept to self-management of the contact person and contact data for interested parties assigned to Regulatory Entitlement, and potentially also for Authorisation Products. Changes will be made by sponsor/marketing authorisation holders directly in the IRIS Industry portal.

*Figure 3: Changing Submission (Portal) Contact*




From the IRIS home page, carry out the following steps (see also Figure 1):

1. Click on "**Draft submissions"/"Ongoing submission"** sub-tab present under **"Submission"** tab;
2. Scroll down and find the application you want from the list of your drafts;
3. On the right hand side, click on the drop-down arrow and select "Manage Submission Contact" (Figure 3);
4. Click "**Change submission contact**", then In the pop-up window, select the name of the person you want to add as portal contact and click on "select" (the list shows all managers associated with that submission).
5. New portal contact will be shown in "Portal contact" field.
6. Click on "Save and Return"

### *2.5. Add managers to a draft/ongoing submission*

You can insert additional managers to a submission also after the creation of submission, but only if the submission is in draft or ongoing status, not if the procedure has been completed. You can only do this for the draft applications for which you have a **"Manager"** role (not if you are a Contributor).

Managers can edit, submit or withdraw the application. From the IRIS home page, carry out the following steps (see also Figure 1):

1. Click on "**Draft submissions"/"Ongoing submission"** sub-tab present under **"Submission"** tab;
2. Scroll down and find the application you want from the list of your drafts;
3. On the right hand side, click on the drop-down arrow and select "View/Manage Managers" as Figure 3;
4. Click "**Add**", then In the pop-up window, click the **magnifying glass search symbol** to bring up a list (and find the name you want to add as a contributor;
5. Click "**Add**" again;

To add more managers to the same application, repeat the steps above.

### *2.6. Add contributors to a draft submission*

You can only do this for the draft applications for which you have a **"Manager"** role (not if you are a Contributor). Contributors can only edit, but not submit or withdraw the application.

From the IRIS home page, carry out the following steps (see also Figure 1):

Click on "**Draft submissions**" sub-tab present under **"Submission"** tab;

1. Scroll down and find the application you want from the list of your drafts;
2. On the right hand side, click on the drop-down arrow and select "View/**Manage Contributors**";
3. Click "**Add**", then In the pop-up window, click the **magnifying glass search symbol** to bring up a list (and find the name you want to add as a contributor;
4. Click "**Continue to submission form**";

To add more contributors to the same application, repeat the steps above.

### *2.7. Delete a draft submission*

You can only do this for the draft applications for which you have a “Manager” role (not if you are a Contributor). Note: you cannot delete a “completed submission”; an “ongoing submission” can be withdrawn, using a similar procedure.

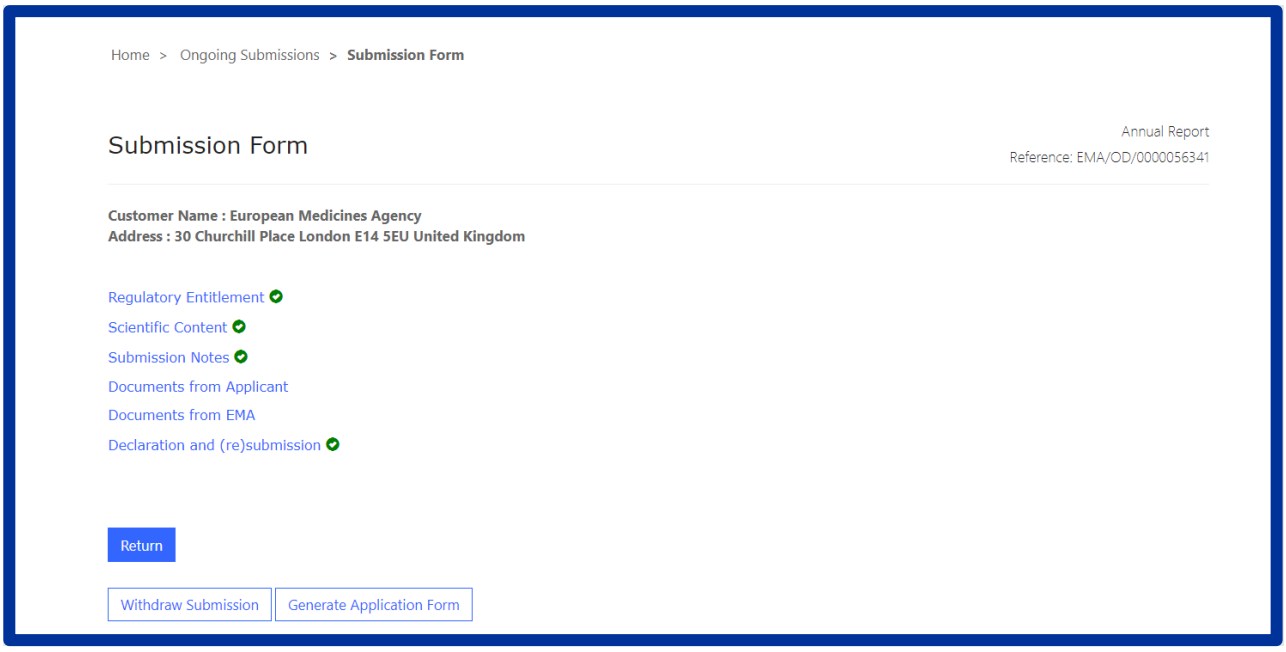
1. Click on "**Draft submissions**" sub-tab present under **“Submission”** tab;
2. Find the application you want from the list of your drafts;
3. On the right hand side, click on the drop-down arrow and select “**Delete Draft**” and a confirmation message will open up in a new window (see Figure 1);
4. Click on the "**Delete**" button to confirm that you want to delete your draft. Note: you cannot undo this afterwards, and the draft submission is permanently deleted from IRIS and cannot be restored.

### *2.8. Withdrawal of a Submission*

You can only do this for the Ongoing applications for which you have a “Manager” role (not if you are a Contributor). Note: you cannot withdraw a “completed submission”;

1. Click on "**Ongoing submissions**" sub-tab present under **“Submission”** tab;
2. Find the application you want from the list of your drafts;
3. On the right hand side, click on the drop-down arrow and select “**Edit/View**”, Submission opens in edit Mode. Click on **‘Withdraw Submission’** Button present at the bottom as shown in Figure 4.A confirmation window will appear, confirm the withdrawal request.
4. Submission status will be in ‘Withdrawal Requested’ as shown in **‘Ongoing Submission’** Tab;
5. Once EMA has processed the request, the submission will move to **‘Completed Submission**’ Tab;

*Figure 4: Withdraw a Submission*




### *2.9. Automatic deletion of draft submissions*

IRIS will scan all the submissions to identify those that have been inactive (no change in data) for more than 7 months, and send an email to the submission contact (a.k.a. portal contact) to inform of the upcoming deletion of the submission unless a change is made to the submission in the following 2 weeks. If no change is made to the submission during that time, it will be deleted and definitively removed from the IRIS system, including any documents uploaded to IRIS. A final email will be sent to the submission contact, to notify the permanent removal of the submission from the system.

### *2.10. Respond to a notification email from EMA requesting changes*

On receipt of a notification email from EMA stating for example that "Validation Supplementary Information (VSI)" relating to one of your Ongoing Submissions is required, or other changes/updates to the submission data, log into the IRIS portal and carry out the following steps:

1. From the IRIS home page, click on "**Ongoing submissions**" sub-tab present under **"Submission"** tab;
2. Locate the submission mentioned in the e-mail by using the sort or search features described in this Guide, or by just scrolling down the list until you find it;
3. At the end of the row in the list where your submission appears, click on the drop-down arrow and select "**View/edit**";
4. In the "**Submission Form**" page that appears click on the sections that you need to update as stated in the notification you received from EMA (e.g.: General Information, Scientific information, etc.);
5. The selected sections will open in edit mode - make the requested modifications and click on "**Save and Return**" - all modifications will have been saved and you will return to the "**Submission Form**" page;
6. If you need to upload updated or new documents, click on "**Documents from Applicant**". Click on **"Save and Return"** when you are done;

7. **Click on the tick box** to the left of the declaration statement (that begins with the words: "I confirm…") to formally declare that you are authorised to submit this request;
8. Click on the "**Declaration and submission**" button;
9. If you are sure you want to submit the application, click" **Submit**", then "**Ok**" and then "**Submit**".

### *2.11. Respond to a List of Questions (LoQ) request*

On receipt of a notification email from EMA regarding a "List of Questions (LoQ)" relating to one of your Ongoing Submissions, after validation and start of procedure, you can upload revised/new documents, but you cannot modify the submission data in the portal. Log into the IRIS portal and carry out the following steps:

1. From the IRIS home page, click on "**Ongoing submissions**" sub-tab present under **"Submission"** tab;
2. Locate the submission mentioned in the e-mail;
3. At the end of the row in the list where your submission appears, click on the drop-down arrow and select "**View/edit**";
4. Click on "**Documents from Applicant**"; click on **"Save and Return"** when you are done;
5. **Click on the tick box** to the left of the declaration statement (that begins with the words: "I confirm…") to formally declare that you are authorised to submit this request;
6. Click on the "**Declaration and submission**" button;
7. If you are sure you want to submit the application, click "**Submit**", then "**OK**" and then "**Submit**".

Your updated application has now been submitted and will appear in your "**Ongoing Submissions**" list and you will receive an e-mail notification to confirm that you have re-submitted the application as requested by EMA.

### *2.12. Check the current status of an ongoing Submission in the IRIS Portal*

The possible status for the Applicant's submission (see Figure 5) are shown in the below table.

*Figure 5: Submission Status*

| Submission Status | Notes |
|---|---|
| Draft | The application is in draft status and can be deleted or submitted (when finalized). Inspection submission cannot be deleted. |
| In Progress | Application submitted; case ongoing at EMA |
| Withdrawal Requested | The applicant has requested a withdrawal, which is being assessed at EMA. |
| Completed-Positive | Case closed, positive outcome |
| Completed-Negative | Case closed, negative outcome |
| Completed-Withdrawn | Case closed as withdrawn, at the applicant's request. |

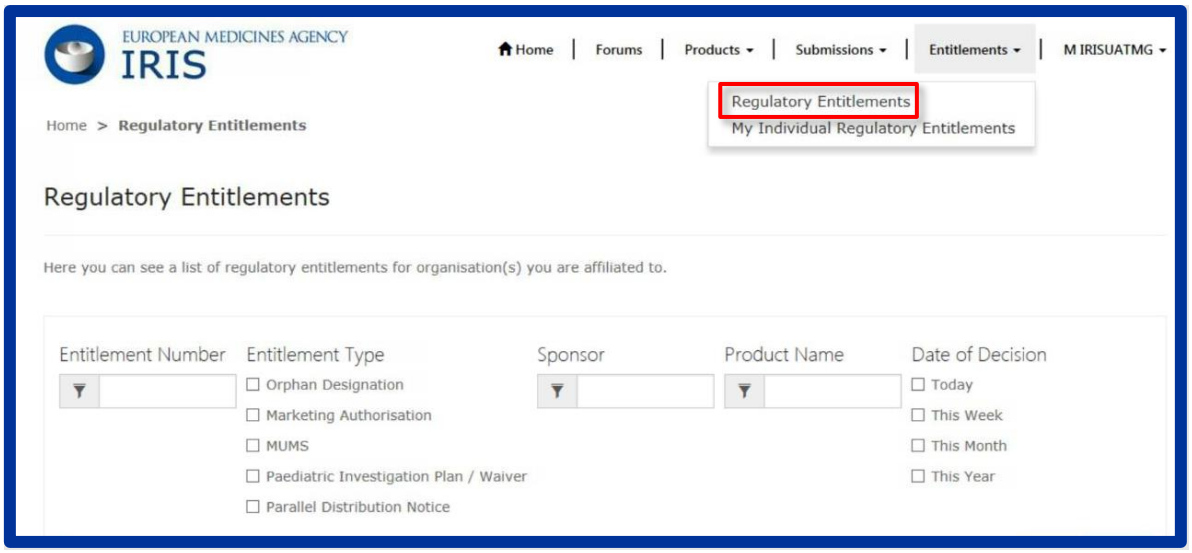
| Submission Status | Notes |
|---|---|
| Completed -Cancelled | Inspection request has been cancelled by CHMP/CVMP |

### *2.13. Regulatory Entitlements Affiliation*

#### 2.13.1. Regulatory Entitlements

This tab enables you to see a list of all regulatory entitlements related to the organisation(s) you are affiliated to. It is possible to filter the regulatory entitlements by entitlement number, entitlement type, sponsor, product name, EU number, and date of decision (see Figure 6

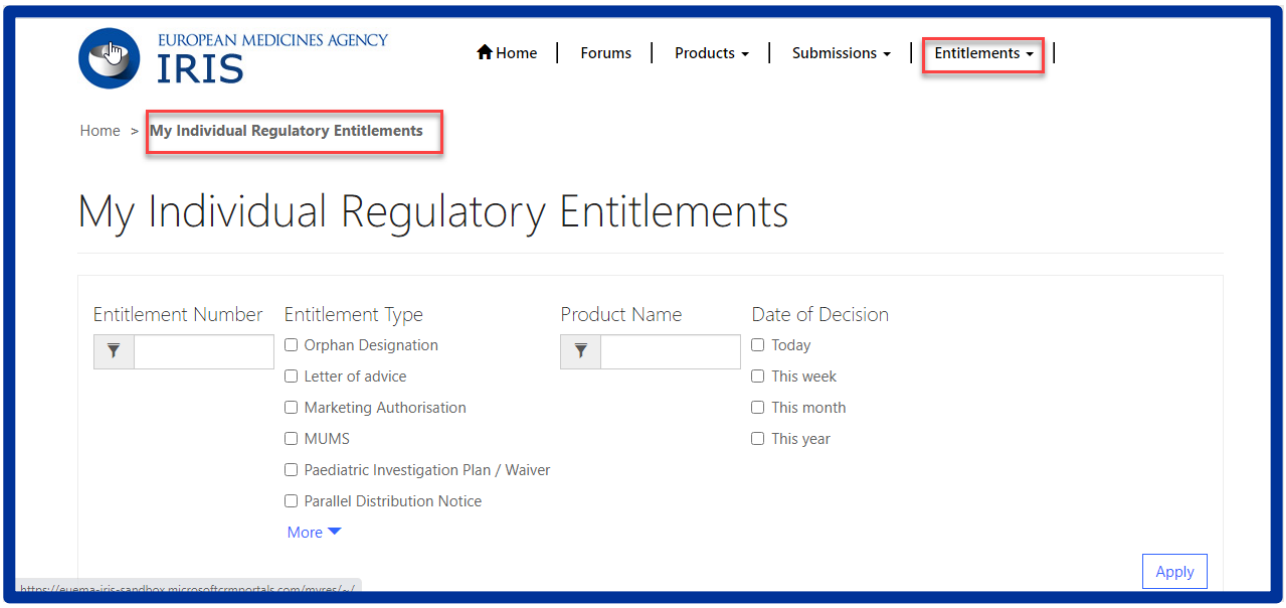
*Figure 6: Regulatory Entitlements*




#### 2.13.2. My Individual Regulatory Entitlements

The tab enables you to see the list of all regulatory entitlements that were granted as an outcome of submissions created by you. It is possible to filter the regulatory entitlements by entitlement number, entitlement type, product name and date of decision.

*Figure 7: My Individual Regulatory Entitlements*



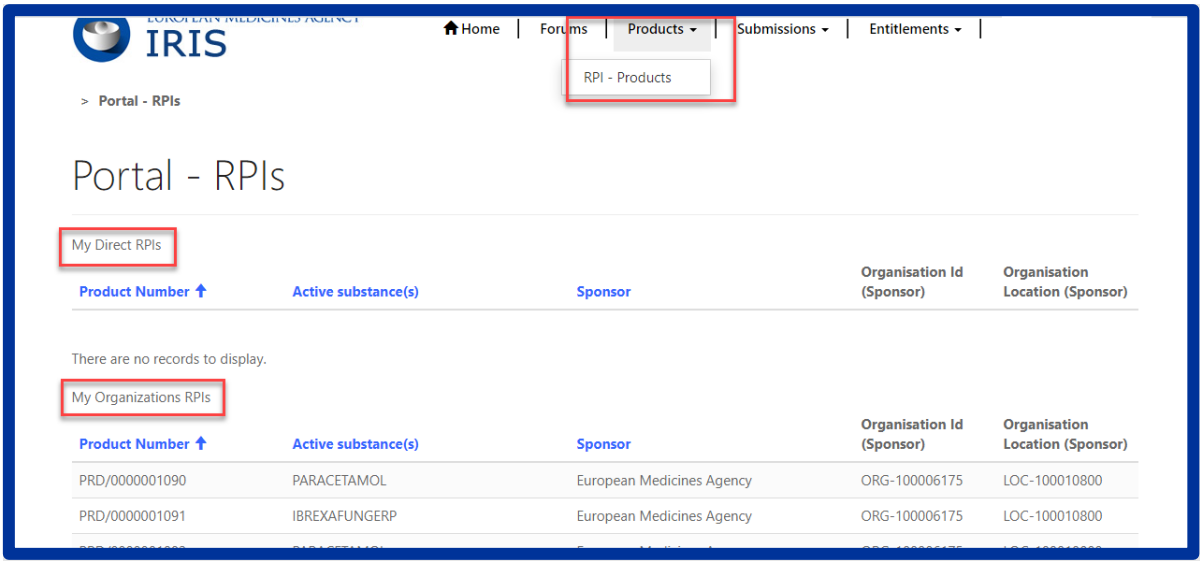

### *2.14. Products - Research Product Identifiers (RPI)*

It is also possible to see all RPIs (Research Product Identifier) for which you are the sponsor, either individually or via an affiliation to one or more companies. Two views are shown (see Figure 8).

"**My Direct RPIs**", which displays all active RPIs for which you are a direct sponsor.

"**My Organizations RPIs**" shows active RPIs for all organization locations you are affiliated to (in any of the locations).

*Figure 8: Product- View of RPI's*



## 3. Orphan submissions

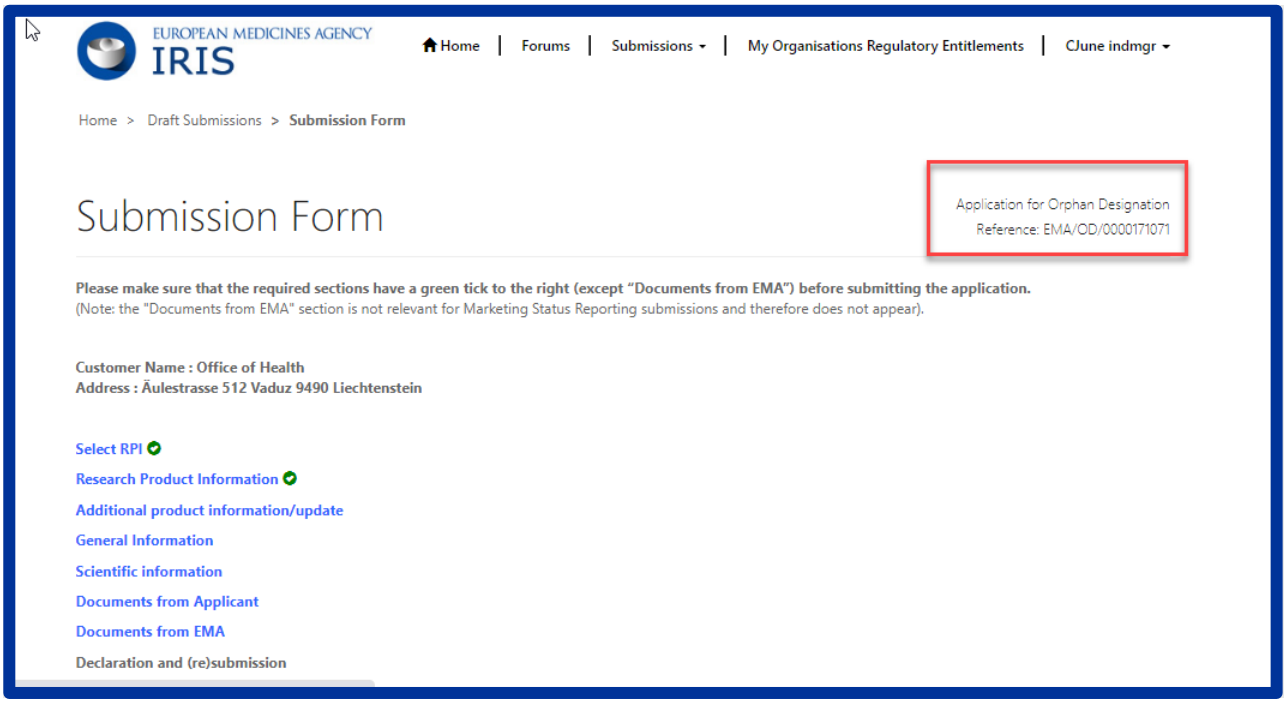
For general information on orphan designation and allied procedures, please consult the Orphan Designation page of the EMA website. For specific information on how to prepare a specific Orphan submission, including how to prepare the Scientific Document, please see the specific sections on the Orphan Designation page.

### *3.1. Create an application for orphan designation*

In addition to the steps in the general procedure described in Section 2.3. "Create a new submission (general procedure for all submission types)", please note the specific issues for Orphan Designation below:

The reference number will have "OD" in it (e.g. EMA/OD/0000001234) for your draft submission displayed on the upper right-hand side of the "Portal – New Submission" screen (see Figure 9).

*Figure 9: Application for orphan designation, main screen*




The sections (tabs) of the submission are: "**General Information**" and "**Scientific Information**". Complete (at least) the mandatory fields marked with a red asterisk "*" and click "**Save and Return**" (N.B. in the prevalence box, enter the prevalence per 10,000 persons in the EU population, as a single number (normally, from 0 to 5.0) and NOT in the form of a ratio). See Figure 9.

### *3.2. Request a Pre-Submission Meeting (for OD)*

**IMPORTANT**: Before creating a request for a **pre-submission meeting**, please create the draft submission for the orphan designations as described above. This must be left as a draft, without submitting it for the moment. Any documents should be uploaded within the draft submission for orphan designations, not in

the pre-submission meeting request. The number of the draft request for orphan designation should be referenced in the pre-submission meeting request;

1. Select "**Request for Pre-Submission Meeting**" as submission type;

2. Click "**Continue to submission form**" and a number (e.g. EMA/OD/0000001234) for your draft submission is displayed on the upper right-hand side of the "Portal – New Submission" screen (N.B. It is a good idea to take note of the reference number created);

3. Back in the Submission Form screen, click on "**Submission Details**", enter the information that you want the EMA Orphan Medicines team to know and click "**Save and Return**";

4. Follow steps 13 and 14 from Section 2.3. "Create a new submission (general procedure for all submission types)"above;

5. Your request for a Pre-Submission Meeting has now been submitted and will appear in your "**Ongoing Submissions**" list.

### *3.3. Request an Appeal (of a COMP Opinion)*

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following:

1. As submission type, click on "**Appeal**" and then click "**Select**";
2. Click "**Create and Next**" – you will see the message "processing…" for a short while;
3. Click "**Continue to submission form**";
4. Click on "**Start Appeal**" and the "View Start Appeal Form" screen appears;
    a. Click on the magnifying glass to select the procedure to be appealed – only cases which have been submitted and are currently in ongoing status are displayed;
    b. Click on one of the procedures listed then click Select" and "Submit";
5. From the "**Submission Form**" screen, click on the "**Ground of appeal**" Section; fill in the relevant information in the mandatory "Applicant's grounds for appeal *" box and click "**Save and Return**";

### *3.4. Submit an Annual Report for an orphan designation*

The process for submitting Annual Reports has now been simplified. Applicants are not requested to compile and submit the previous PDF form, which has been removed from the website. It is now only necessary to complete the information in a few specific data fields in IRIS. Uploading additional supporting documents is still possible but not mandatory.

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

1. As submission type, click on "**Annual Report**" and then click "**Select**";
2. Click "**Create and Next**" and then click "**Continue to submission form**";
3. Click on "**Regulatory Entitlement**" (a generic term for a right granted to a sponsor such as an orphan designation or a transfer of orphan designation);
    a. In the "Regulatory Entitlement" window, **click on the magnifying glass symbol** to search through the existing orphan designations for your organisation;

b. Select the orphan designation for which you are submitting the Annual Report and click "**Save and Return**". If you cannot find your orphan designation, please contact the Orphan medicines office;

4. Click on "**Scientific content**" and complete the information in the data fields, amending the prefilled fields where appropriate. All fields with an asterisk are mandatory. Click on "**Save and Return**";
5. Back in the Submission Form screen, click on "**Submission Notes**", enter any additional free-text information that you want the EMA Orphan Medicines team to know and click "**Save and Return**".

### *3.5. Other post-designation procedures for orphan-designated products*

All other post-designation procedures for existing orphan designations should be submitted via IRIS, choosing the appropriate procedure type. These include:

- Submission of a report for the Maintenance of the Designation Criteria at Marketing authorisation (or extensions);
- Submission of a report for a Review of the Designation criteria after 5 years;
- Request for an Amendment of an existing Orphan designation (to change the condition);
- Request to transfer an Orphan Designation;
- Request of removal of an Orphan designation from the EC Orphan register;
- Change of name and/or address of the Sponsor of an orphan designation.

The procedures are very similar to the general procedure as described in Create a new submission (general procedure for all submission types), and are not listed for brevity. For general information on these submission types, see the Activities after orphan designation webpage in the main EMA website.

### *3.6. How to check if an Orphan Drug Sponsor (Location of an organisation) has associated Regulatory entitlements*

Go to https://ec.europa.eu/health/documents/community-register/html/reg_od_act.htm?sort=a and search for EU product e.g. EU/3/19/2181.

Click on the EU number from the search results. For field "Sponsor" -Organisation name and location will be mentioned. This location has Regulatory entitlements and the same can be selected in IRIS while drafting a form.

## 4. Scientific Advice

For general information on Scientific Advice, please consult the Scientific advice and protocol assistance section of the EMA website. For specific information on how to prepare a Scientific Advice submission, including the Scientific Document (Briefing Document), please see the How to submit a scientific advice or protocol assistance request section on the EMA website.

### *4.1. Create an application for an Initial Scientific Advice (Human)*

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", select **"Initial Scientific Advice-Human"** as the submission type. Note the following additional points:

The reference number will contain SA (e.g. EMA/SA/0000001234) for your draft submission displayed on the upper right-hand side of the "Portal – New Submission" screen;

There is a list of eleven steps (tabs) starting with "Administrative Information" and ending with "Declaration" relating to the SA Application displayed on the left-hand side of your screen; the two sections "**Administrative Information**" and "**Select Primary RPI**" must be completed, before the other sections (tabs) become available (they turn from grey to blue);

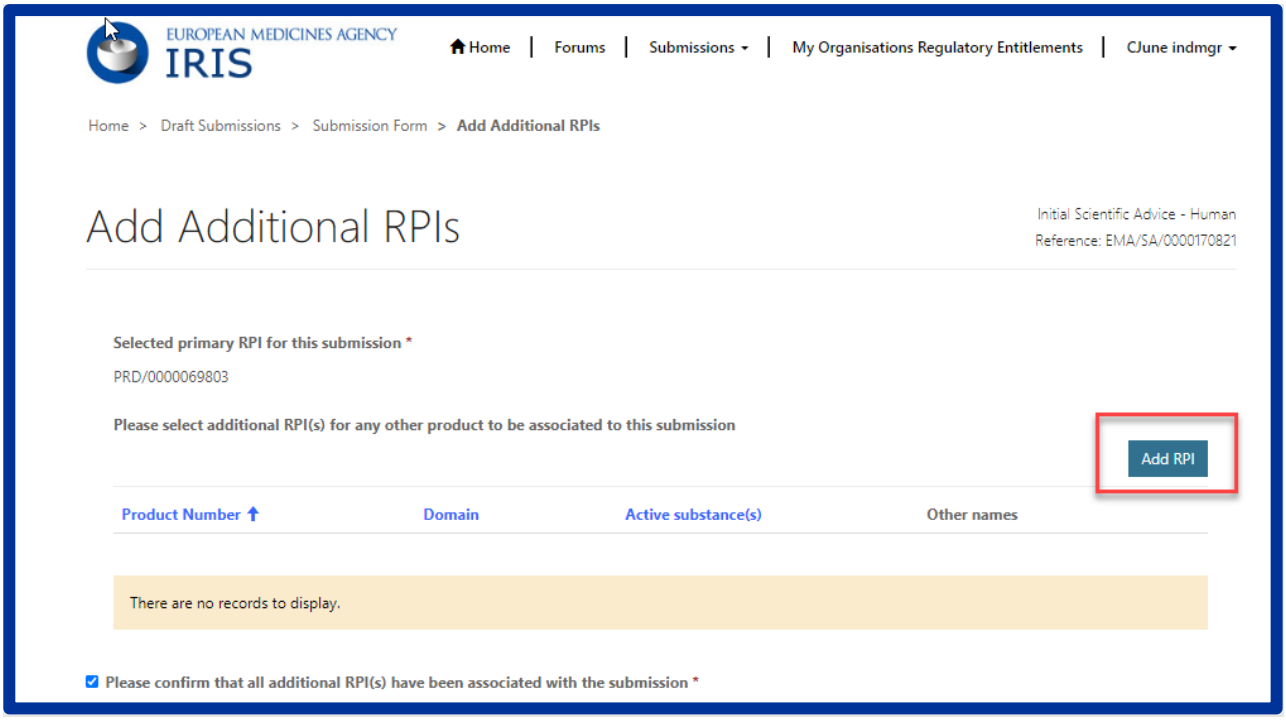
In section "Administrative information" please specify the "Type of Request" to flag if your submission is related to a Standard SA request of if it is a SA request related to a declared or potential public health emergency (see Section 4.2).

You can optionally select additional (secondary) RPIs to link to your procedure by clicking on "**Add Additional RPIs**" (see Figure 10). Note that only RPIs "owned" by the same applicant can be added;

You can also add **"Submission Notes"** with additional information in scientific advice forms. This field can be used to specify why the procedure qualifies for not following standard deadlines (e.g., COVID rapid request).

Some sections/tabs may not be applicable, e.g. "Parallel Consultation EMA/EUnetHTA"; however, at least the mandatory field(s) marked with a red asterisk "*" should be completed.

*Figure 10: How to include additional RPIs*




### *4.2. Create an application for an Initial Scientific Advice (Human) for medicines intended to address a declared public health emergency or a potential future emergency*

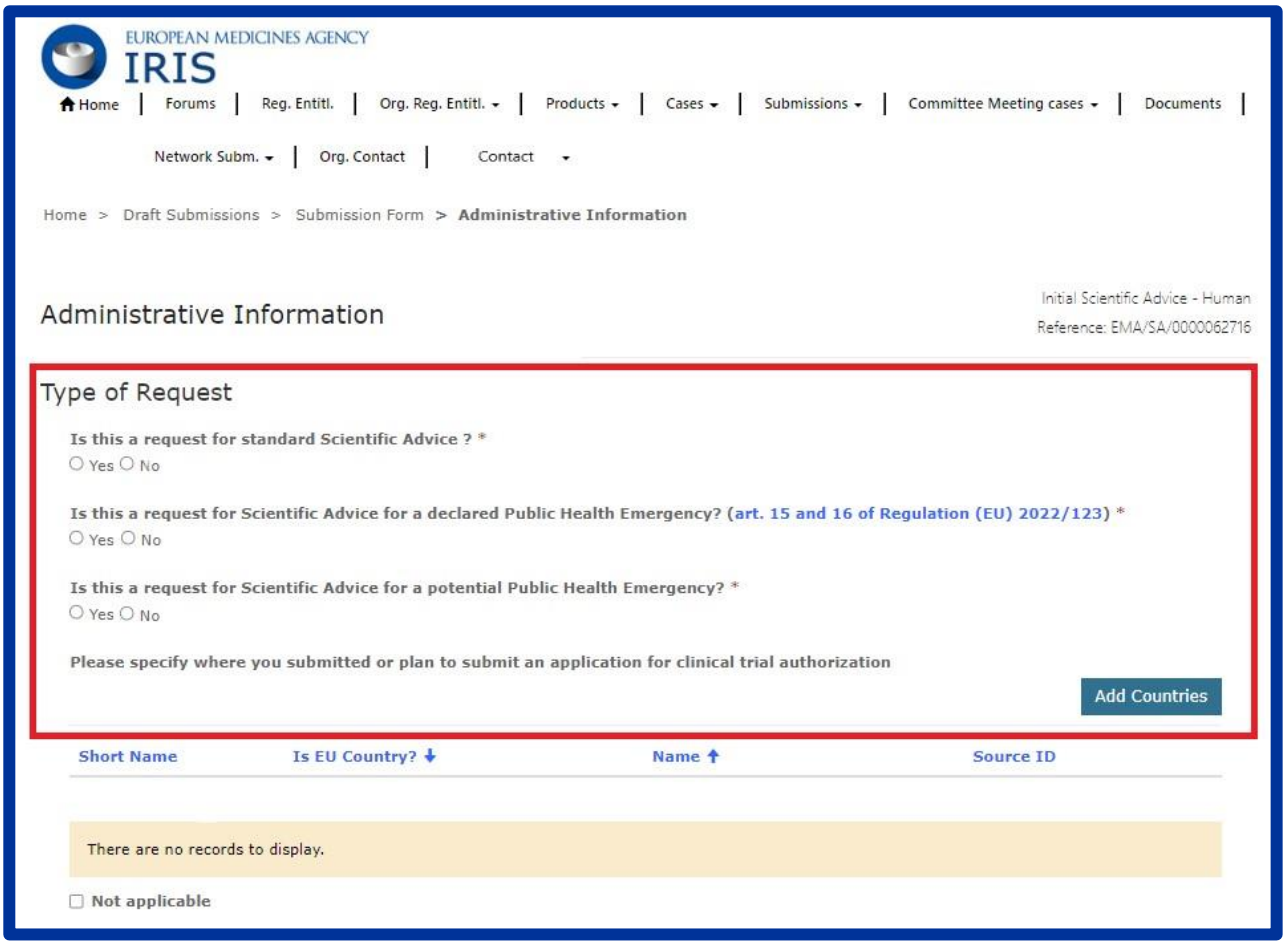
The Emergency Task Force (ETF) is a multidisciplinary expert group established within the EMA by Regulation (EU) No 2022/123, to be convened in preparation for and during a public health emergency (PHE). As such, the ETF is delegated (1) to provide scientific advice on medicinal products targeting the PHE and (2) to provide scientific advice on medicinal products targeting a potential future PHE. A

scientific advice can cover quality, non-clinical and clinical aspects of product development including clinical trial protocols for both types of scenarios mentioned.

For submitting such SAs, follow the steps in the general procedure as described in Section 2.3 “Create a new submission (general procedure for all submission types)”, selecting “Initial Scientific Advice-Human” as submission type.

In the “Administrative information form”, the section “Type of Request” contains questions that help differentiate between standard SAs and SAs on medicinal products addressing a declared or potential PHE (see Figure 11):

*Figure 11: Different types of SA*




If the submission is related to:

- a request for a standard scientific advice, meaning not related to a product or clinical trial targeting a declared or potential PHE, answer with “Yes” to “Is this a request for standard Scientific Advice ?” These applications will be assessed by the SAWP.
- a declared PHE, answer with “Yes” to “Is this a request for Scientific Advice for a declared Public Health Emergency? (art. 15 and 16 of Regulation (EU) 2022/123)”. A public health emergency can be declared by either WHO or the European Commission. Select the specific PHE from the drop-down menu in the subsequent question “Please specify the Public Health Emergency”. These applications will be assessed by the ETF.

- a pathogen which has the potential to cause a PHE, answer with "Yes" to "Is this a request for Scientific Advice for a potential Public Health Emergency?". Specify the pathogen by choosing from the drop-down menu in the subsequent question "Please specify the pathogen or agent" (e.g., Ebola virus, Zika virus, Chikungunya virus). The ETF will provide advice on the pathogens listed in the drop-down menu. However, the list is not exhaustive and for this reason the term "Other pathogens/threats" is included in the drop-down menu. Applicants should select "Other pathogens/threats" when the pathogen they are seeking advice on is not listed in the menu, but it has the potential to cause a future emergency. A free text box will then appear for applicants to list a specific pathogen, either of viral or bacterial origin, which have the potential to cause a future emergency. EMA will consider on a case-by-case basis whether these applications can be assessed by the ETF or by the SAWP.

The question "Please specify where you submitted or plan to submit an application for clinical trial authorization" aims at identifying the member states where the Applicant intends to submit or has submitted a clinical trial application. This will allow the Agency to involve in the scientific advice assessment process the representatives of the clinical trial authority of the MS responsible for the trial authorisation. Click on "Add Countries" and select from the displayed list of countries the country where clinical trials related to the current SA submission have been submitted or are intended to be submitted.

### *4.3. Create an application for other Scientific Advice procedures*

#### 4.3.1. Initial Scientific Advice – Veterinary

Follow the steps in the general procedure as described in Section 2.3 "Create a new submission (general procedure for all submission types)", selecting **"Initial Scientific Advice-Veterinary"** as submission type.

#### 4.3.2. Initial Protocol Assistance

Protocol Assistance is Scientific Advice for designated orphan medicinal products. In addition to questions on quality, safety and clinical aspects, questions on significant benefit may also be discussed.

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

- The applicant must be the same as the Orphan Designation Sponsor;
- While drafting this type of application, applicant cannot proceed further than **"Orphan Designation"** until an existing orphan designation (or at least a positive opinion date), for a product belonging to the same customer, has been selected first and associated to the submission. It is possible to submit the application after a COMP Opinion has been adopted, but before the formal Decision by the European Commission, by choosing the ongoing procedure instead of an Orphan Designation; however, the Decision must be adopted before the start date of the Protocol Assistance procedure;
- Please note that several fields will be prepopulated from the associated orphan case and cannot be changed. These include the RPI and the medical condition (which must be the same as the orphan condition in the designation, by law).

#### 4.3.3. Initial Qualification Procedure

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

Select **"Initial Qualification Procedure"** as submission type.

### 4.3.4. Follow up Scientific Advice – Human

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

Select **"Follow up Scientific Advice-Human"** as submission type;

You will be able to proceed only by selecting a previously completed Scientific Advice procedure (chosen from the popup list, showing procedure number and condition for all scientific advices, from any applicant). This is done in section **"Select Previous Scientific Advice"** for selection;

An RPI is mandatory; if the RPI was present in the previous Scientific Advice, it will be added automatically, otherwise it is necessary to choose an existing RPI (assigned to the same location);

Please note that several fields will be prepopulated from the previously completed initial scientific advice case and cannot be changed. These include the RPI, the medical condition, and the areas of advice. Only previously discussed areas of advice (or a subset) can be included in a follow-up procedure.

### 4.3.5. Follow up Scientific Advice – Human – for medicines intended to address a declared public health emergency or a potential future emergency

Follow the steps described in the previous section "Follow up Scientific Advice – Human".

### 4.3.6. Follow up Scientific Advice – Veterinary

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

- Select **"Follow up Scientific Advice-Veterinary"** as submission type;
- You will be able to proceed only after selecting a previously completed Scientific Advice – Veterinary procedure;
- An RPI is mandatory; if the RPI was present in the previous Scientific Advice, it will be added automatically, otherwise it is necessary to choose an existing RPI (assigned to the same location).

### 4.3.7. Follow up Protocol Assistance

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

Select **"Follow up Protocol Assistance"** as submission type. Please note that it is possible to select this procedure type even if the previous submission was made for Scientific Advice, rather than protocol Assistance;

You will be able to proceed only after selecting a previously completed Scientific Advice or Protocol Assistance procedure. These appear in the section **"Select Previous Scientific Advise"** for selection;

While drafting this type of application, applicant cannot proceed further than **"Orphan Designation"** until an existing orphan designation (or at least a positive opinion date), for a product belonging to the same customer, has been selected first and associated to the submission. It is possible to submit the application after a COMP Opinion has been adopted, but before the formal Decision by the European

Commission, by choosing the ongoing procedure instead of an Orphan Designation; however, the Decision must be adopted before the start date of the Protocol Assistance procedure;

Please note that several fields will be prepopulated from the associated orphan case and cannot be changed. These include the RPI and the medical condition (which must be the same as the orphan condition in the designation, by law).

#### 4.3.8. Follow up Qualification Procedure

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

- Select **"Follow up Qualification Procedure"** as submission type;
- You will be able to proceed only after selecting a previously completed Qualification procedure. These appear in section **"Select Previous Scientific Advice"** for selection.

#### 4.3.9. Transfer a Scientific Advice

Owners of Scientific Advice regulatory entitlements (Letters of Advice) are now able to transfer regulatory entitlements automatically to another owner, similarly to the RPI transfer process. Only scientific advice entitlements can be transferred with this new automated process, which is necessary when the applicant for a follow-up scientific advice or protocol assistance is not the same as the initial advice.

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

Select **"Transfer a scientific Advice"** as submission type.

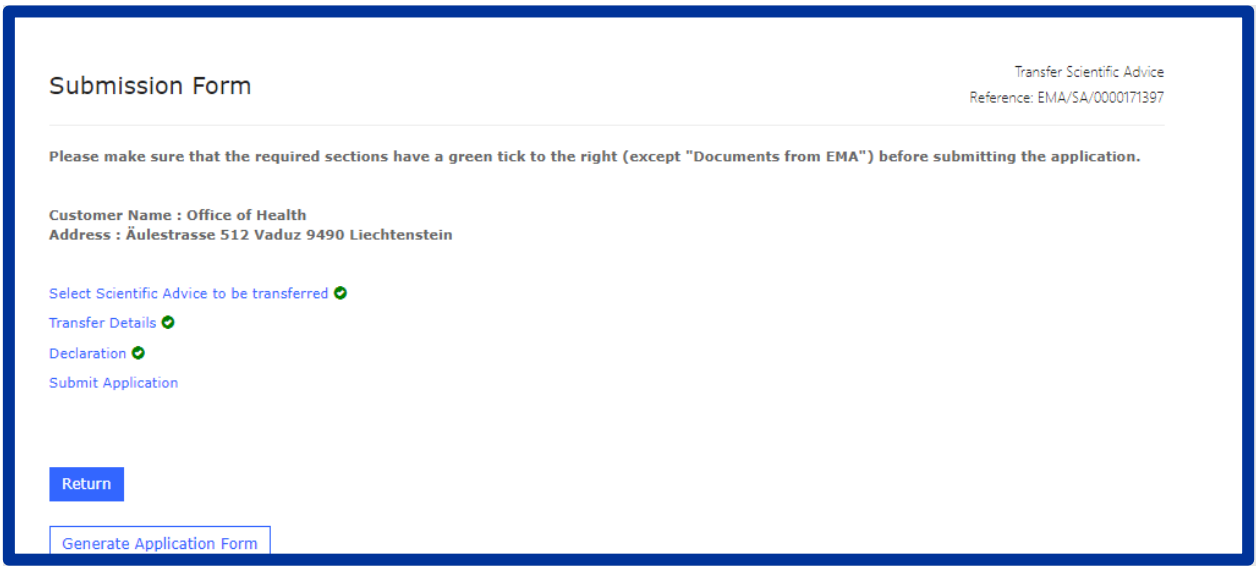
The reference number will contain SA (e.g. EMA/SA/0000001234) for your draft submission displayed on the upper right-hand side of the "Portal – New Submission" screen;

The following four tabs will appear as shown in Figure 12:

1. **Select Scientific Advice to be transferred**: Click on the tab and a new screen will open. Select the desired submission to be transferred, using the search icon option if necessary, and click on "**Save and Return**";
2. **Transfer details:** Click on the tab and a new screen will open. Here the current sponsor details will be shown in "**read-only**" mode and below you can add the **"New Sponsor Type**" as Organisation/Individual, then select the "**New Organisation**" .The organisation address will be shown in read-only mode. Once all details have been added, click on "**Save and Return**".
3. **Declaration**: Click on the tab and a new screen will open. Select the checkbox for the declaration and click on "**Save and Return**";
4. **Submit Application**: Once all the above tabs have been filled and green check marks show, the "**Submit Application**" button becomes enabled. Click on it and a new screen opens, select the checkbox asking for confirmation, and click on "**Submit Button**" box. A pop-up window will appear, giving you a final opportunity to go back and check that all the details have been entered correctly ("Review Application"), or continue and submit.

   Once submitted, the Submission will be shown in "**Outgoing**" tab and the product will be updated with new sponsor type as mentioned while filling the form.

*Figure 12: Transfer Scientific Advice*




### 4.3.10. Clarification on Scientific Advice

Users can request clarification on a closed Scientific Advice case related to an Initial Scientific Advice or Follow Up Scientific Advice by submitting a request "Clarification on scientific advice" in IRIS.

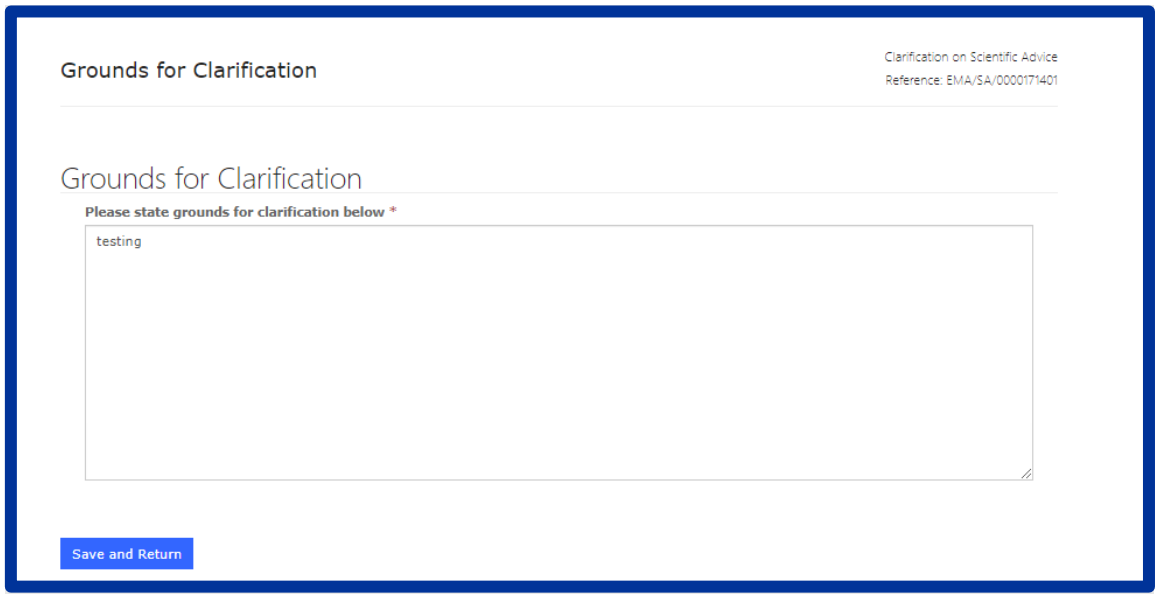
In addition to the steps in the general procedure as described in Section 2.3. “Create a new submission (general procedure for all submission types)”, note the following additional points:

Select **“Clarification on scientific advice”** as submission type. The reference number will contain SA (e.g. EMA/SA/0000001234) for your draft submission displayed on the upper right-hand side of the “Portal – New Submission” screen;

The following six tabs will be shown:

1. **Select previous Advice:** Click on the magnifier of this field, and a new screen will open. Select the desired submission. Click on “**Save and Return”**;
2. **Grounds for Clarification:** Once a previous advice is selected, this tab is enabled for you to add the notes (Figure 13). Once added, click on “**Save and Return”;**

*Figure 13: adding notes for clarification*




3. **Documents from Applicant:** It is possible to add documents under this tab**.** Select that declaration confirming documents have been attached and click on "**Save and Return**";
4. **Documents from EMA:** Can be skipped as part of drafting process;
5. **Declaration**: Click on this tab, and a new screen appears. Select the checkbox for the declaration and click on "**Save and Return**";
6. **Submit Application**: Once all the above tabs have been filled and green check marks show, the "**Submit Application**" button becomes enabled. Click on it and a new screen opens, select the checkbox asking for confirmation, and click on "**Submit Button**" box. A pop-up window will appear, giving you a final opportunity to go back and check that all the details have been entered correctly ("Review Application"), or continue and submit.

   Once submitted, the Submission will be shown in "**Outgoing**" tab and the product will be updated with new sponsor type as mentioned while filling the form.

#### 4.3.11. Scientific Advice FAQ

Frequently asked questions related to Scientific Advice can be found in "Forums" tab in **IRIS** website.

## 5. ITF Briefing Meeting Requests

In addition to the steps in the general procedure as described in Section 2.3. "Create a new submission (general procedure for all submission types)", note the following additional points:

- Select "**ITF Briefing Meeting Request**" as submission type;
- The section "**Documents from applicant**" is available to upload any supporting documents;
- The section "Documents from EMA" is where you can find any documents provided by EMA to you, including the minutes from the meeting.

## 6. Marketing Status

Three submission types can be used to address the market changes in IRIS portal. They are listed below

**Marketing Status Notification (Single)-** This function allows to report the same change in marketing status affecting one or more presentations of a CAP (centrally authorised product) in one or more MS (e.g. placing on the market of 3 presentations in 5 Member States on the same day). Please follow the steps mentioned in 6.1.

**Marketing Status Notification (Bulk Upload)-** This function enables to report several different changes in marketing status affecting one or multiple presentations in one or multiple MS, by uploading an excel spreadsheet (e.g. placing on the market of presentation B in CZ, AT and NL + marketing cessation of presentation A in IT on different dates).Please follow the steps mentioned 6.2.

**Marketing Status Withdrawal Notification-** This function allows to report

- A request for **withdrawal of the central marketing authorisation** of your product (This would not replace the formal request to send to the European Commission, see question *How should I request the withdrawal of my central marketing authorisation?)*
- a **decision not to apply for the renewal of the marketing authorisation**
- a **permanent marketing cessation** affecting all presentations of a medicinal product in all MS. Of note, if the marketing authorisation is not withdrawn, it will automatically expire after 3 years of non-marketing under the sunset clause provision (see *Q&A on sunset clause provision*). Please follow the steps mentioned in 0

**Examples on most appropriate paths to report Marketing Status and Withdrawals**

| Example | |
|---|---|
| How to report the market launch of 2 presentations of the medicinal product in ES, FR and IT | Marketing Status Notification (Single)<br><br>Alternatively, you can also use Marketing Status Notification (Bulk) |
| How to report **temporary** marketing cessation of all/some presentations in some EU MS | Marketing Status Notification (Single)<br><br>Alternatively, you can also use Marketing Status Notification (Bulk) |
| After the launch of the tool, how to report the current marketing status of all presentations of medicinal product in all EU/EEA MS. | Marketing Status Notification (Bulk)<br><br>Alternatively, you can also use Marketing Status Notification (Single) |
| How to report the intent to withdraw the marketing authorisation of a medicinal product for commercial reasons | Marketing status Withdrawal notification |

| Example | |
|---|---|
| How to report the **permanent** cessation of all presentations in all EU/EEA MS. (Sunset clause will be triggered) | Marketing status Withdrawal notification |
| How to report the **temporary** cessation of all presentations in all EU/EEA MS. (Sunset clause will be triggered) | Marketing Status Notification (Single)<br><br>Alternatively, you can also use Marketing Status Notification (Bulk) |

### *6.1. Marketing Status Notification (Single)*

In addition to the steps in the general procedure as described in 2.3. Create a new submission (general procedure for all submission types), select **"Marketing Status Notification (Single)"** and note the following additional points:

1. Starting with clicking **"Select Authorised Product"** as the other steps become available after selection of the product (Figure 14);

*Figure 14: Marketing Status Single Notification*

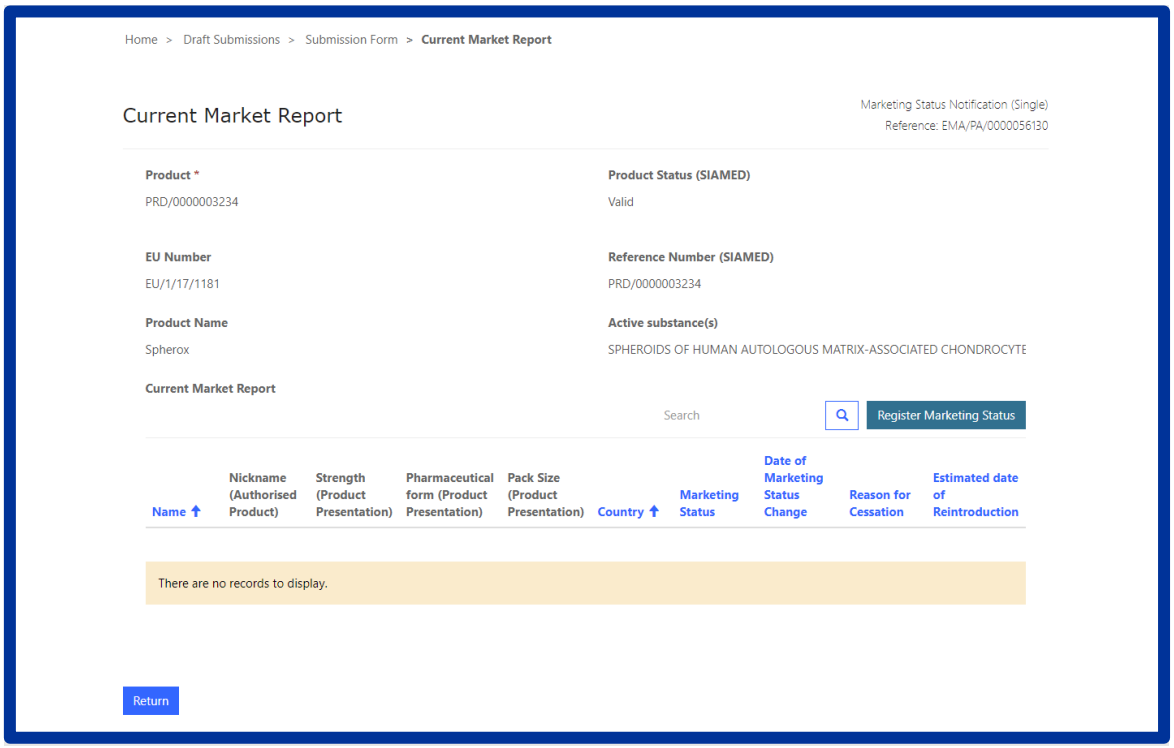

2. Click on the search icon under **"Authorised Product".** A list will appear, which includes all products associated to the selected organisation. Select one, then click on "Save and Return". 2.7. Once the record is saved, the system will auto-populate details like 'Product Status', 'EU number', 'Reference number', 'Active Substance(s)', 'Product Name', when you revisit the **"Select Authorised Product"** tab**.**

   Please note that once you select an authorised product and click on 'Save and Return', you can no longer change the product in this submission. If you need to select a different authorised product,

you can do so by starting a new submission. In this case, you need to delete the submission yourself present under draft submission by following steps mentioned in section 2.7.

3. Click on the section **"Register Marketing Status"-** all product presentations are shown, for the selected 'Authorised Product'. Please note if you are doing this for the selected product the first time, you will not see any presentation listed. You can add the relevant product presentation(s), member state(s) and Marketing availability by clicking on the '**Register Marketing Status'** button, as shown in Figure 15.

*Figure 15: How to add Product Presentations*




All fields marked with red asterisk are mandatory to fill. This page is divided into 3 sections.

**Marketing status** - The fields present under this section are dynamic and will change based on selection of value in the field "Marketing Status":

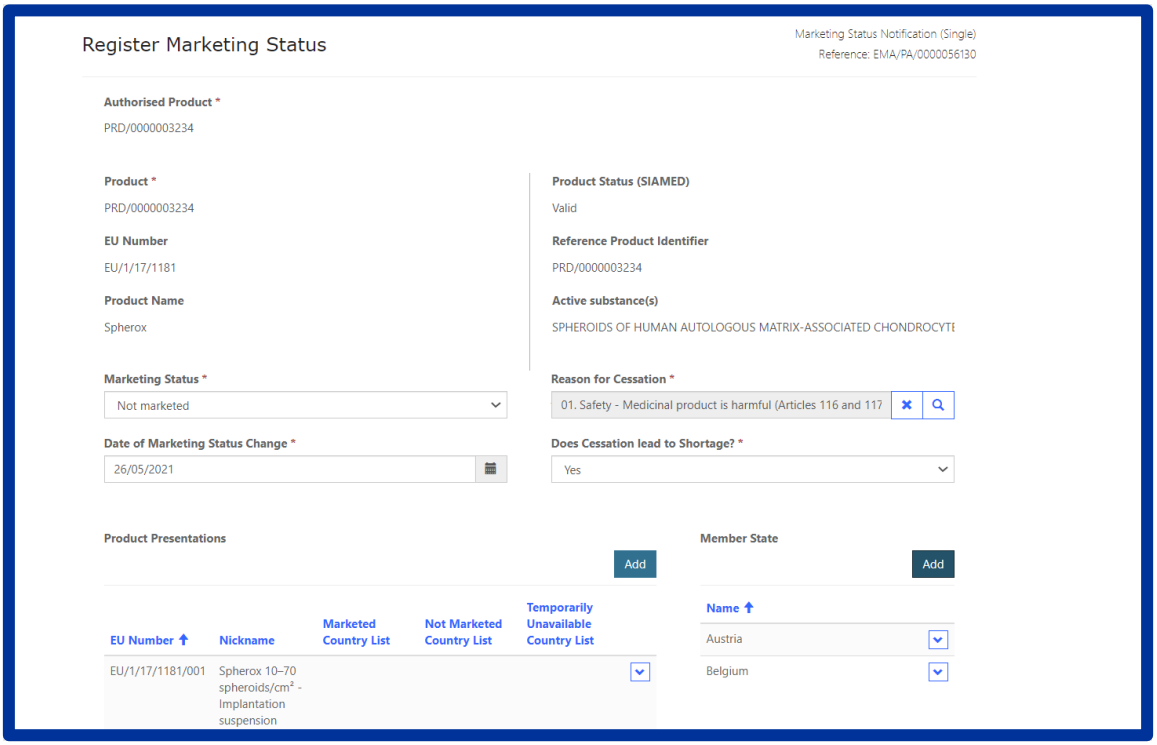
- **Marketing Status = 'Marketed'**: Select this field to report the marketing of one/more presentation(s) of the medicinal product is in one or more Member State(s) of the Union. The user needs to specify the 'Date of Marketing Status Change'.
- **Marketing Status = 'Temporarily Unavailable'**: Select this field to report that one/more presentation(s) becomes temporarily unavailable in one or more Member State(s) then 'Date of Marketing Status Change', 'Reason of cessation', 'Estimated date of Reintroduction', Does cessation lead to Shortage' become **mandatory**.
- **Marketing Status = 'Not Marketed'**: Select this field to report that one/more presentation(s) change the status to permanent cessation/not marketed in one or more Member State(s), then 'Date of Marketing Status Change', 'Reason of cessation', 'Does cessation lead to Shortage' become mandatory and have to be specified by the user to save the details.

- **Marketing Status = 'Never Marketed'**: Select this field to report that one/more presentation(s) of the medicinal product has/have never been marketed in one or more Member State(s) of the Union.

**Please refer to regulatory guidance for [Notifying-change-marketing-status]**

- **Product Presentations** - Single or multiple product presentations can be added by clicking on the 'Add' button present under 'Product Presentations'.
- **Member State** - presentations can be marketed in different countries, single or multiple countries can be selected here.

*Figure 16: Adding product presentation, Marketing Status & Member states*

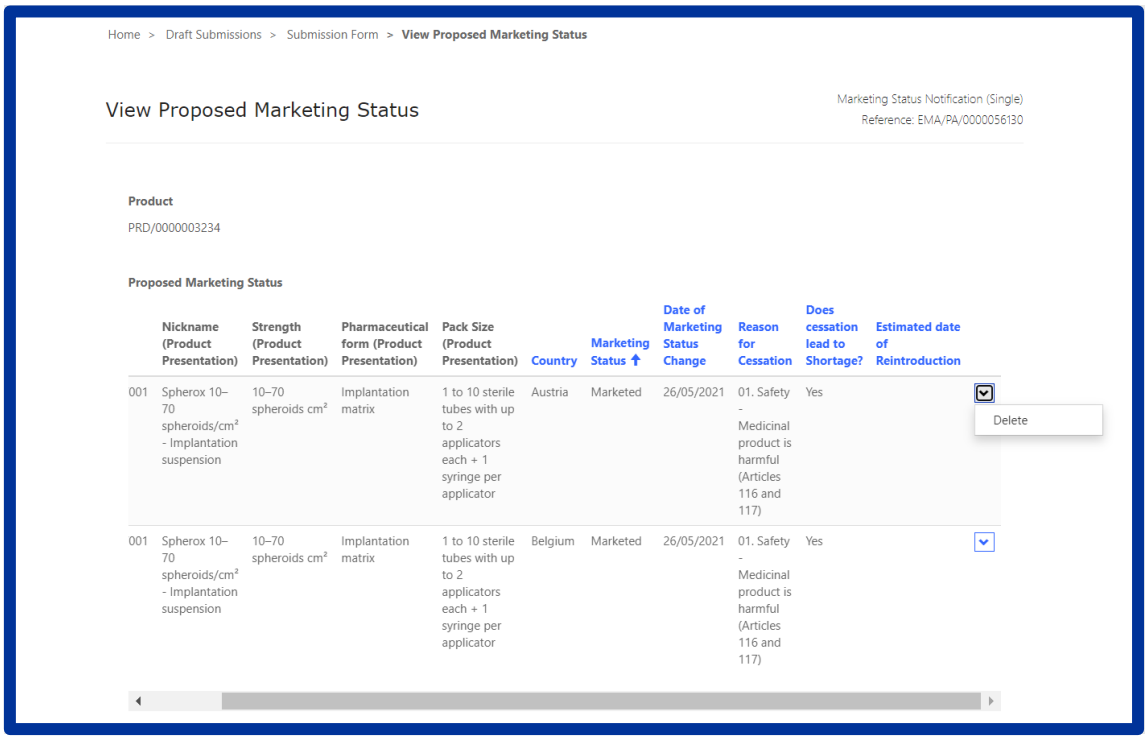



Click **'Have you completed Marketing Status Registration 'Yes/No** at the bottom of the page. It is possible to add a new Marketing Status for different presentations by clicking No and then '**Save and return'**. This will allow you to start again on point 3 and add a new Marketing Status for different presentations/Member states. This can be repeated as many times as needed.

Once you have completed the Marketing Status Registration, click Yes and then click on '**Save and return'** to go back to the previous section. Please note that in 'Current Marketing Status' form, you will not see any of the presentations just added, those will be showing in section **'View Proposed Marketing Status'.**

4. Click on **'View Proposed Marketing Status'** to view the recently added changes in Marketing status pending to be submitted. This section will list all the presentations and their marketing status in the countries selected in Section **'Register Marketing Status'**. You can also delete presentation for a specific member state by clicking on the v-shaped arrow as shown in Figure 17 below. Click on '**Return'** after checking all information;

*Figure 17: Viewing proposed presentations*




5. After completing the steps above, click on '**Declaration'**, confirm the declaration, click Save and Return and submit your application in the '**Submit Application'** section. You will receive a confirmation email on the successful submission.

6. Your submission is shown in the "**Submissions/Ongoing**" sub-tab. After the case (procedure) is automatically processed by the IRIS system, the submission will be moved to the "**Submissions/Completed'** tab. You will receive a confirmation email of the completion of the procedure. Please raise a ticket via the EMA Service Desk by selecting service as '**IRIS'** in case of facing any issues.

### *6.2. Marketing Status Notification (Bulk Upload)*

In addition to the steps in the general procedure as described in **2.3. Create a new submission (general procedure for all submission types)**, select **"Marketing Status Notification (Bulk Upload)"** and note the following additional points:

Select the Authorised product in the section **"Select Authorised Product"**, click **'Save & Return'**.

Click on **"Download Current Marketing Status"** section. All product presentations associated with the product are now displayed in a table; to download the presentations in an Excel file, click on the '**Download'** button. Once the file is downloaded, click on '**Return'** to go back to the main page.

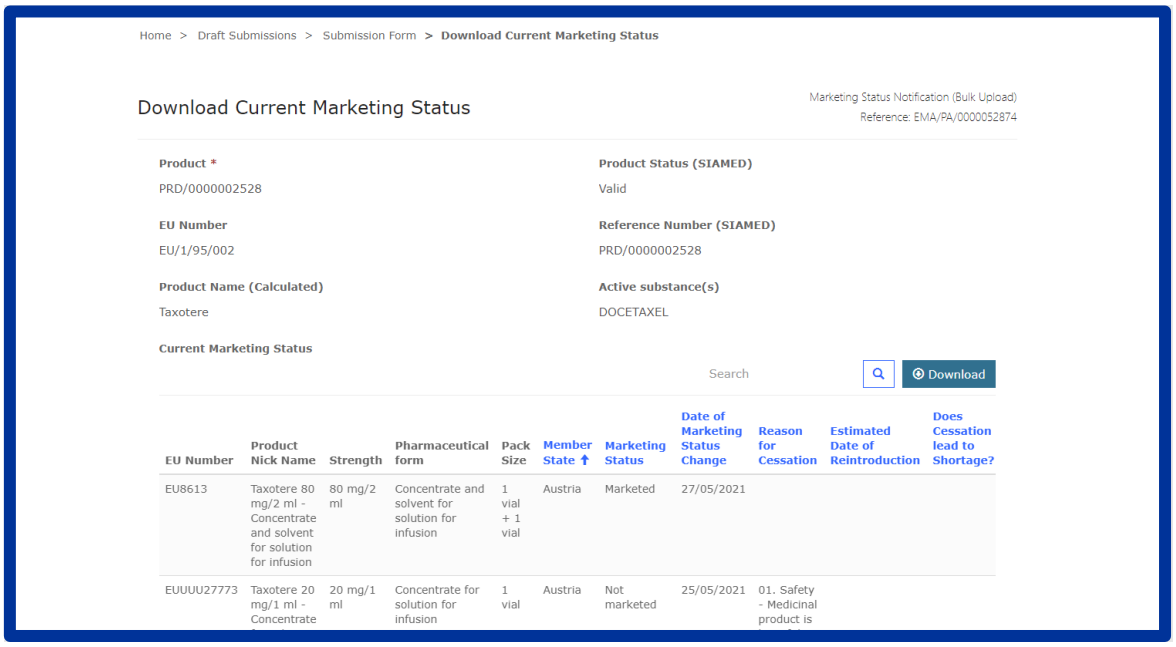
You can then update the data in the file as per your needs. Please make sure that you delete the rows where no changes are required. Also note, all presentations shall belong to same authorised product selected in 0

Please note that the values in each column must be provided in a standardised format; refer to Figure 18 for the correct format and values to avoid validation failures. The order of the columns should also be maintained, and the headers should not be modified.

*Figure 18: Format/Values for Fields in csv*

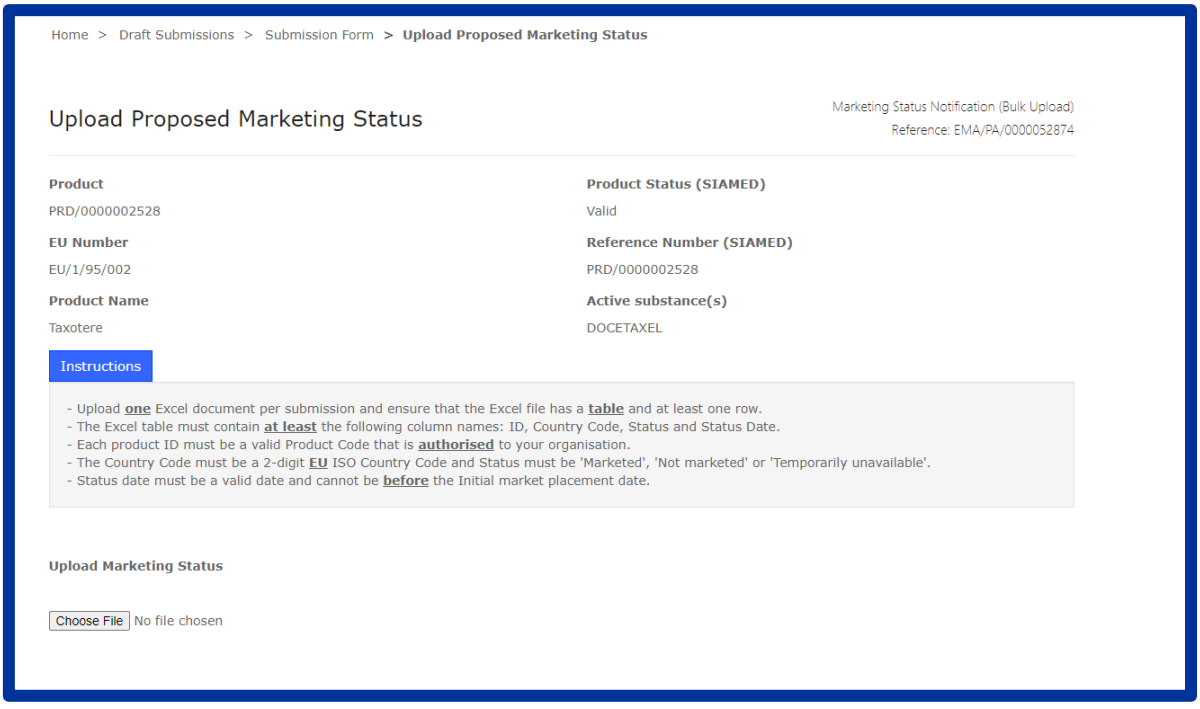
| Data columns | format and allowed values |
|---|---|
| Marketing Status | Marketed<br>Not marketed<br>Temporarily unavailable<br>Never marketed |
| Date of Marketing Status Change (format) | Excel will apply local time and date format to the Excel file with current marketing status. |
| Reason for Cessation | 01. Safety - Medicinal product is harmful (Articles 116 and 117)<br>02. Efficacy - Medicinal product lacks therapeutic efficacy (Articles 116 and 117)<br>03. Benefit/risk - risk-benefit balance is not favourable (Articles 116 and 117)<br>04. Quality - Quantitative and qualitative composition of the medicinal product is not as declared (Articles 116 and 117)<br>05. Quality - Controls of the medicinal product and/or on the ingredients and the controls at an intermediate stage of the manufacturing process have not been carried out or some other requirement or obligation related to the grant of the marketing authorisation have not been fulfilled (Article 117)<br>06. Particulars supporting the application as provided for in Articles 8, 10, 10a, 10b, 10c or 11 are incorrect or have not been amended in accordance with Article 23 (obligation to keep dossier up to date) (Article 116)<br>07. Any conditions referred to in Articles 21a, 22 or 22a have not been fulfilled (PAES, PASS, PV obligations, obligations under exceptional circumstances) (Article 116)<br>08. Commercial reasons (excluding any ground of art 116 or 117) |
| Does Cessation lead to Shortage | Yes<br>No |
| Country | ISO code (2 digit)<br>AT,BE,BG,HR,CY,CZ,DK,EE,EL,FI,FR,DE,,HU,IS,IE,IT,LV,LI,LT,LU,MT,NL,NO,PL,PT,RO,SK,SI,ES,SE,XI |

*Figure 19: Download Excel*




The **'Upload Proposed Marketing Status'** section is now enabled to upload the Excel file. Please do not use the excel downloaded from the Marketing Status Report since it has a different format, use only the excel downloaded as explained in this section (above points). Click on the '**Notification'** button to read the instructions on uploading the file. Upload the file by clicking on the '**Choose file'** (Figure 20) button**.** Once the file is uploaded, click on **'Save and Return'.**

*Figure 20: Upload CSV file*



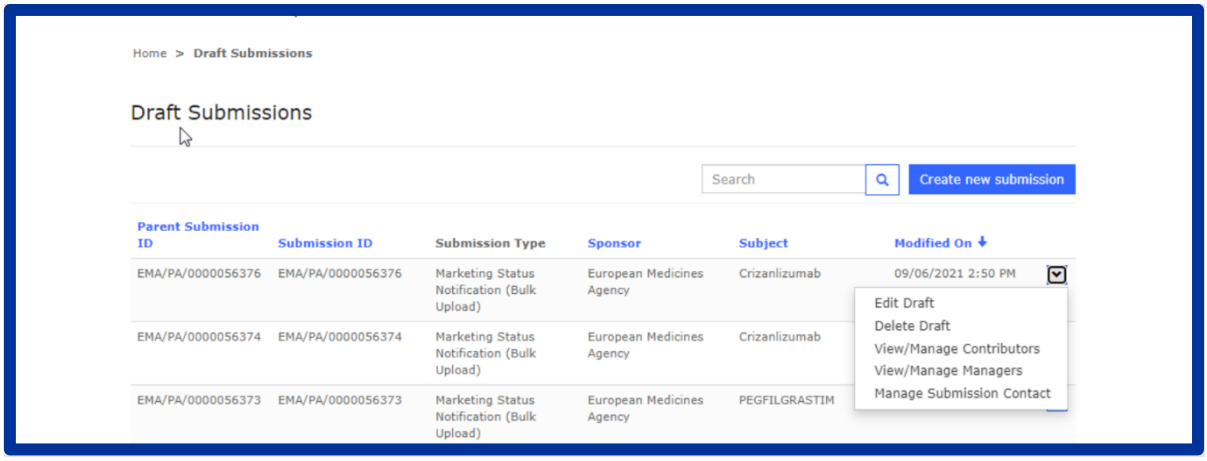

The **"View Proposed Marketing Status"** section will be blank at the time of submission. Data is added to the view once EMA has processed the case.

After completing the steps above, confirm the declaration and submit your application in the '**Submit Application'** section. You will receive a confirmation email on the successful submission.

Your submission is shown in the "**Submissions/Ongoing** "sub-tab.

You will receive an email if the system finds errors in the uploaded file. The submission will move back to the **"Draft Submissions"** section if errors are found. Please login to the IRIS portal, open the same submission by clicking on **'V'** shaped button in the right end corner of the record and selecting "edit draft".

*Figure 21: Opening the submission in edit mode*




Click on the **'Upload Proposed Marketing Status'** section. Errors will be shown under section **'Input File Validation'** as shown in Figure 23

*Figure 22: Excel Validation Errors*

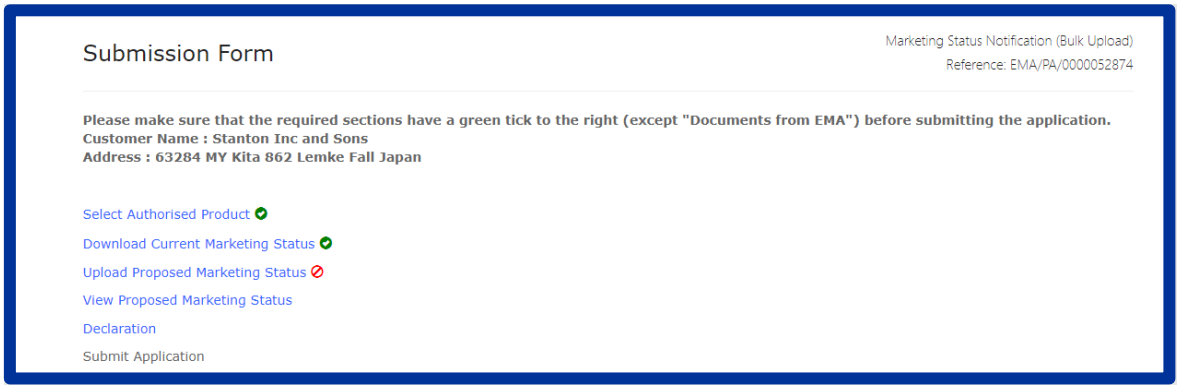
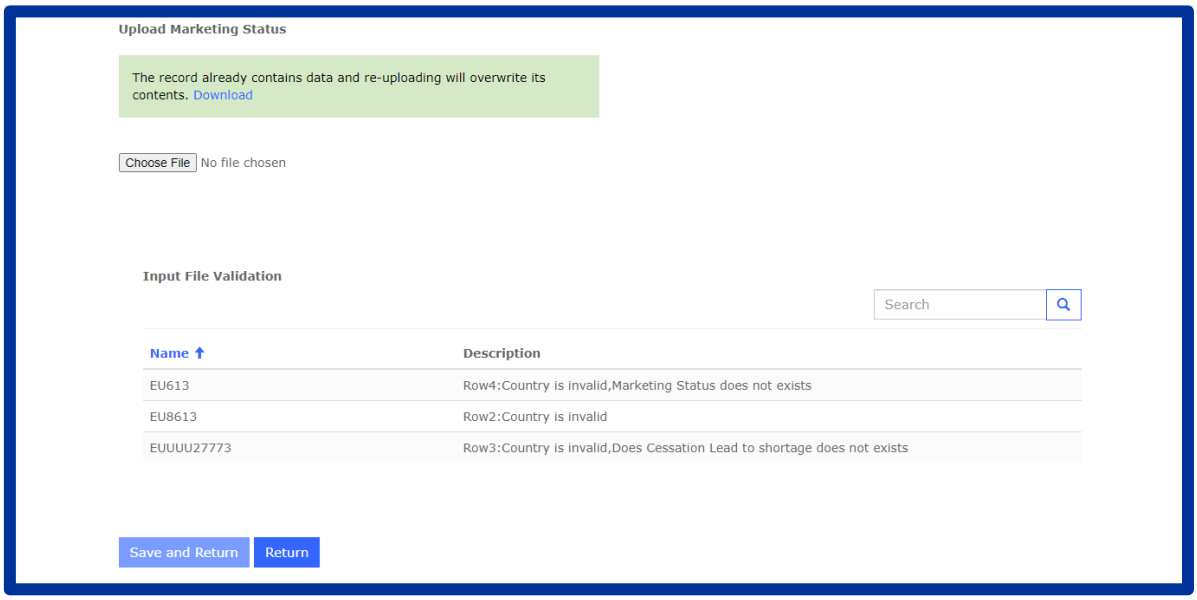


*Figure 23: Showing Validation errors and required corrections*




Download the file again by clicking on 'Download', correct the data and make a new submission.

### *6.3. Marketing Status Withdrawal Notification*

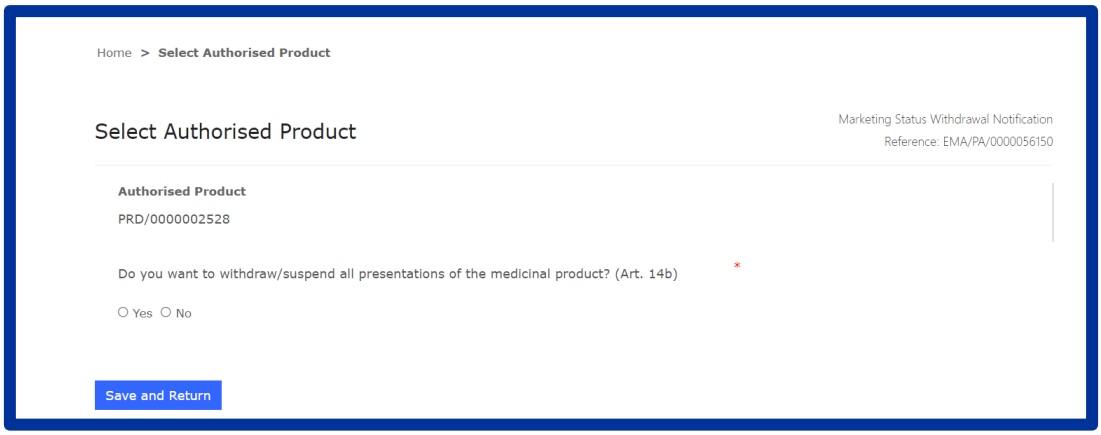
In addition to the steps in the general procedure as described in 2.3. Create a new submission (general procedure for all submission types), select **"Marketing Status Withdrawal"** and note the following additional points:

1. Select the Authorised product in section **"Select Authorised Product"**, click 'Next', and select one of the options to proceed further. Please note if you select **'No'** as option, then the system will provide a relevant message on proceeding further (Figure 24).You have to delete this draft submission yourself (2.7. Delete a draft submission);

*Figure 24: Withdrawal of one or more presentations*

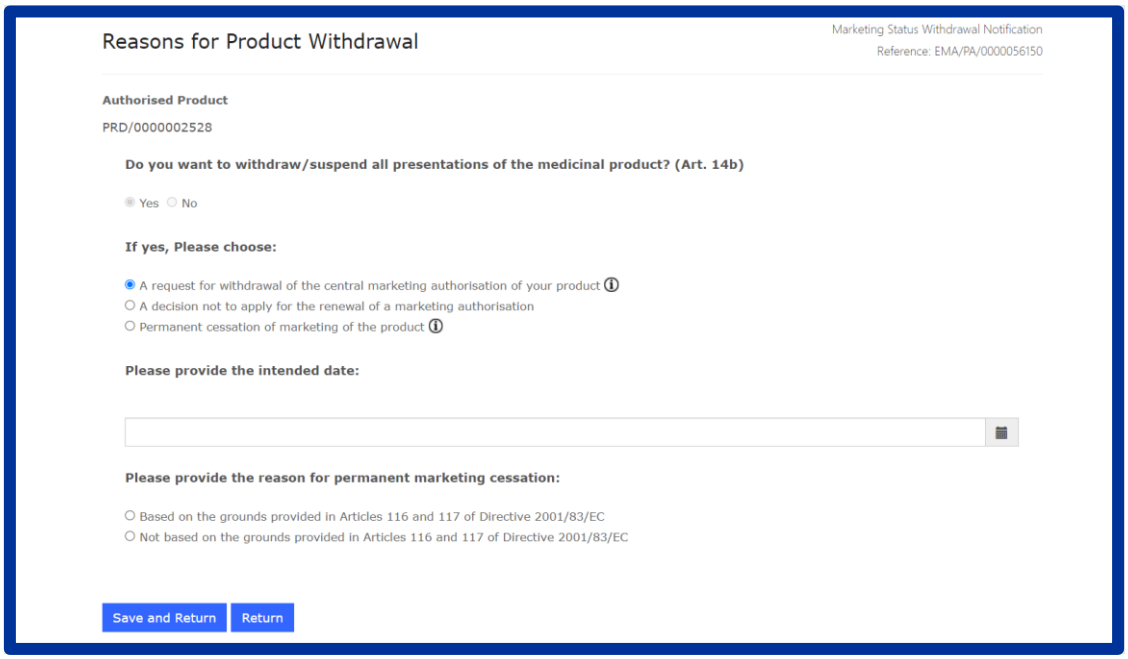

If you have selected '**Yes'**, the system will proceed to next step after clicking on 'Save and Return' button

*Figure 25: Withdrawal of all presentations*




Click on the section **"Reasons for Product Withdrawal"** and choose one of the options as shown in Figure 26 and enter the details as requested based on the selection of data. Once you have entered the data in all the fields, click on 'Save and Return'.

*Figure 26: Adding Reason for withdrawal*




2. After completing the steps above, confirm the declaration and submit your application in the '**Submit Application'** section. You will receive a confirmation email on the successful submission.
3. Your submission is shown in the "**Submissions/Ongoing** "sub-tab. After the case (procedure) is completed by EMA, the submission will be moved to the "**Submissions/Completed'** tab. You will receive a confirmation email of the completion of the procedure.

### *6.4. Marketing Status Report*

The Marketing Status Report can be accessed in IRIS Portal under the "**Products**" Tab; Marketing Status Report. This report allows users[1] to see only the products they are entitled to visualise, i.e. those associated with an organisation to which they are affiliated to (for Industry users). Users will be able to filter and search the registry based on the data columns shown in Figure 27. Searches can be made using a wildcard search (*/1/00/129/*) or selecting a value from the dropdown.

Once the search criteria have been selected, click on the '**Apply**' Button. The report is generated with all presentations as per the selected criteria.

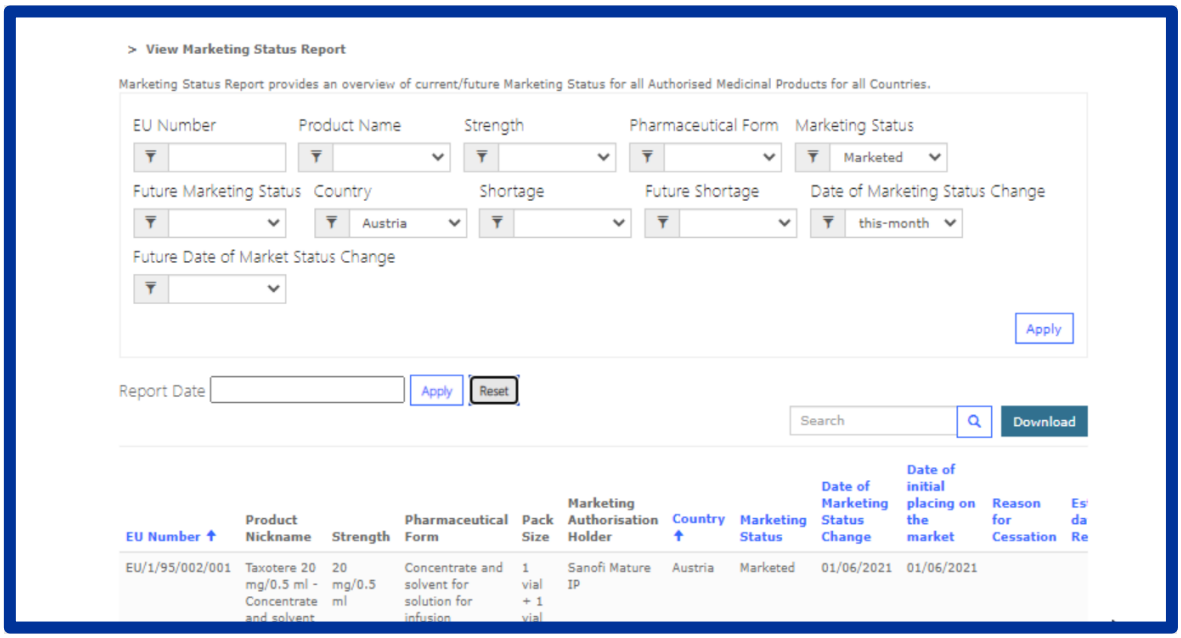
Users can download the data shown in the table in an Excel file by clicking on the '**Download'** button. To reset and make new selections click on the '**Reset'** Button.

Select the **'Report Date' in the future** to see the forecasted Marketing Status for all Authorised Products, all Presentations for all Countries on that selected date in the Marketing Status Report page. Please note that the ''**Download'** button will be disabled when this feature is on.

System allows to reset the report date to see Marketing Status for all Authorised Products, all Presentations for all Countries on current date.

[1] Industry Portal users

*Figure 27: Marketing Status Report*



# 7. Inspections

## *7.1. GMP inspections*

These inspections are requested by the Committee for Medicinal Products for Human Use and/or the Committee for Medicinal Products for Veterinary Use to verify compliance with Good Manufacturing Practice (GMP) of sites responsible for the manufacture of centrally authorised products.

The details of each of the inspections adopted by the Committee(s), including the contact details of the persons in the inspection services who will be involved can be found in the IRIS Industry portal: a new "submission" record is created for every organisation involved in an Inspection. Of note, this is different from the normal IRIS behaviour, where an application is created by an applicant, and the EMA procedure is created only at the time of submission.

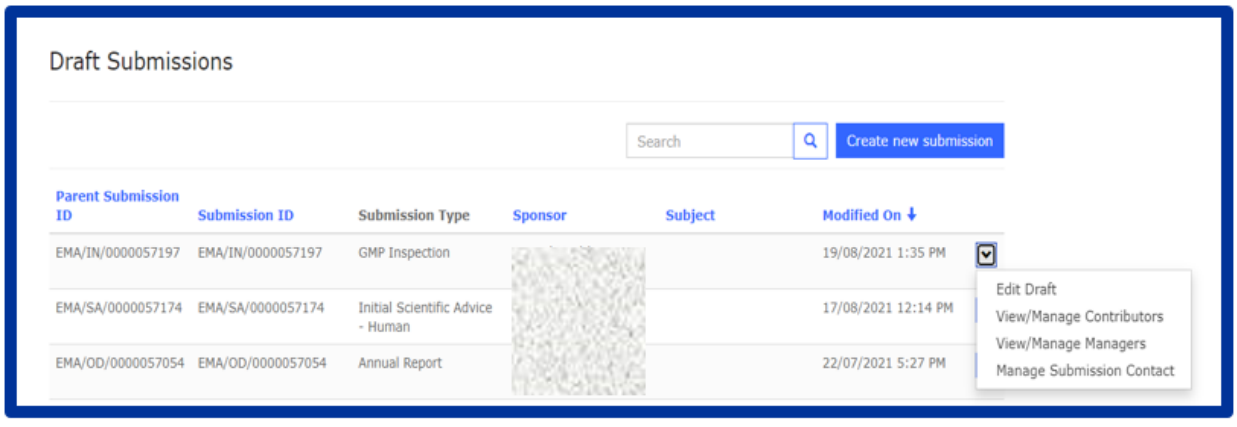
Please let EMA know immediately, by replying to the email e-mail address from which the notification of the inspection request has been received, if any of the information given has changed or is incorrect. The inspectors will contact you to finalise the dates and detailed arrangements.

Upon adoption of a GMP inspection request by the CHMP or CVMP, the user[2] will receive a notification from EMA indicating that an inspection request has been adopted by the relevant committee (CHMP or CVMP) for one of their products. It is recommended that the e-mail address linked to the user is a personal e-mail address instead of a general e-mail address (e.g. john.doe@pharma.com instead of pharma.product@company.com).

At that point, you must update the submission with the necessary information (e.g. Purchase Order number) and submit it via the IRIS Portal, within 10 working days of the inspection announcement. Please follow the steps below to submit the required information.

1. Login into IRIS Portal with EMA credentials and access '**My Draft Submissions'** present under '**Submissions'** tab;
2. You should have a Submission starting with **'EMA/IN/00000XXXXX'** and a submission type as '**GMP Inspection'.** Open the submission in edit mode by clicking on the 'V' icon present on the right-hand side of the screen as shown below (Figure 28);

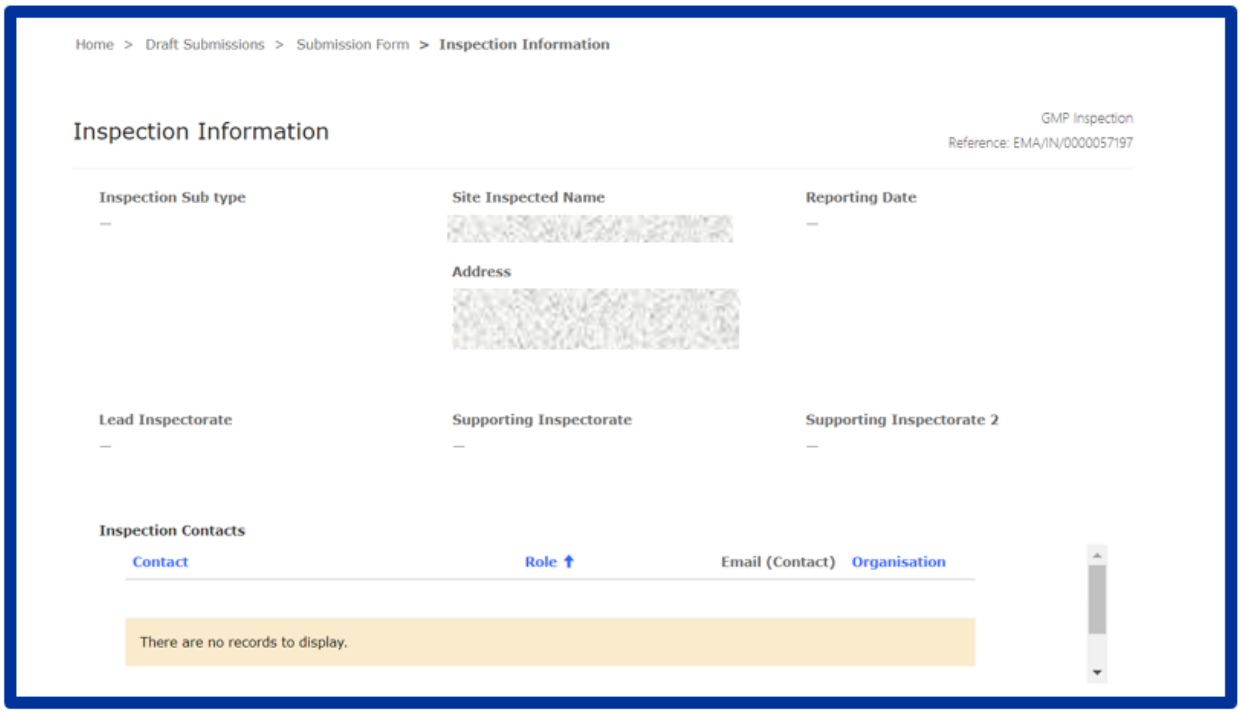
*Figure 28: Edit Mode*




[2] The notified user is the existing Product Contact as already notified to EMA (integrated from SIAMED2); this user becomes the Portal Contact (a.k.a. Submission Contact) for the ongoing submission. To change the product contact, use the existing procedure.

3. Click on the **'Inspection Overview'** section as shown in Figure 29. Inspection related information will be shown: 'Inspection Sub Type', Site Name & address, Reporting date, Lead Inspectorate, Supporting Inspectorate and Contacts. click on '**Return'** to go back to the main menu;

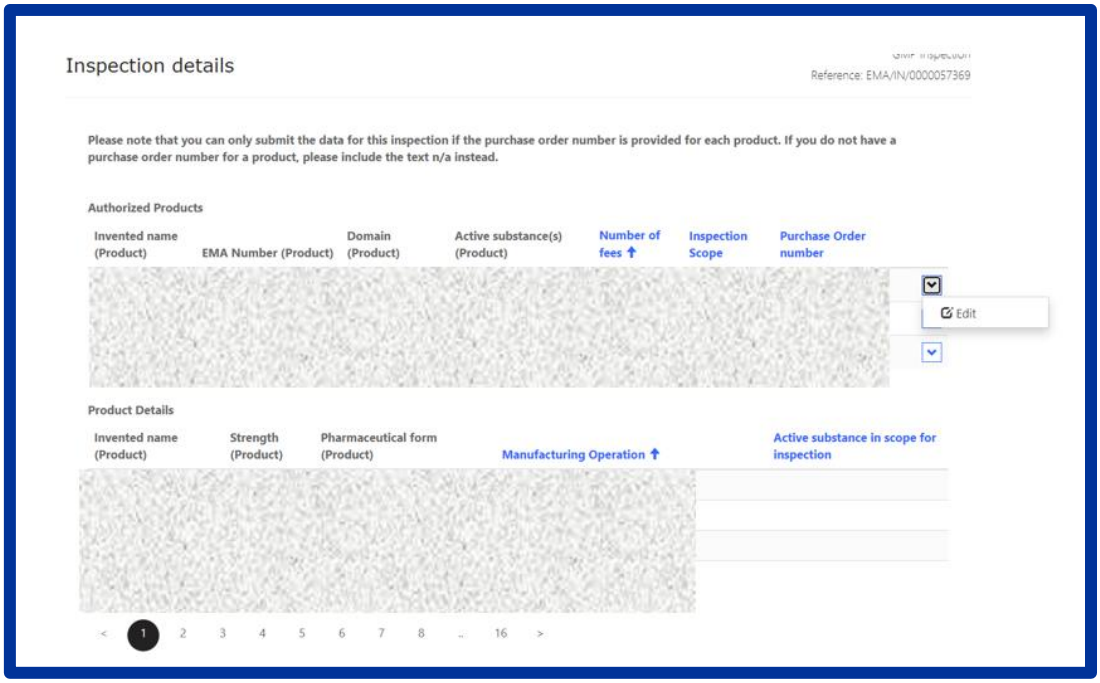
*Figure 29*




4. Click on the **'Inspection Details'** section to view the information on Authorised Products.

   Under the '**Authorised Products**' section, all authorised products are listed. You must add the Purchase Order Number for one of the products to submit the submission.

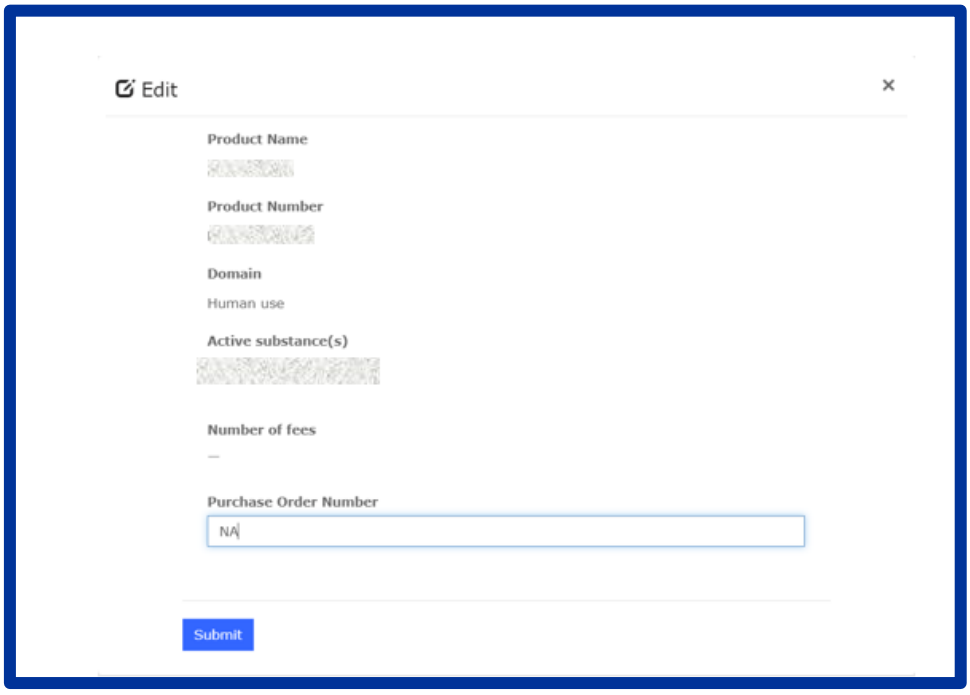
*Figure 30: To Edit Purchase Order and fees*



Click on edit as shown in Figure 30: To Edit Purchase Order and fees, enter the PO number. If you do not have a PO number, please add the text '**N/A'**, since this field is mandatory to proceed with the submission. Purchase order information will be quoted on the invoice issued for the inspection carried out. Please note that the EMA will not accept delays on payments based on missing purchase order (PO) reference number information. Once updated, click on the '**Submit**' Button and you will be taken back to the Inspection details screen. You can also add remarks under the section **'General Comments'**. If you have any questions related to the inspection case, please do not enter them in the general comments field but address them to the relevant EMA inspection co-ordinator by replying to the IRIS notification you received at the start of the process. When replying, please do not change the subject of the message to ensure the e-mail is correctly routed.

Click on '**Save and Return'** to save the details;

*Figure 31: Adding Purchase Order Number*




5. **Documents from Applicant**: It is possible to add documents under this tab. Select the declaration confirming that documents have been attached and click on "Save and Return";
6. **Documents from EMA**: Can be skipped as part of the drafting process (this tab is used to check if any documents have been made available by EMA);
7. **Declare and Submit changes**: Once all the above tabs have been filled and the green check marks show, the "**Declare and Submit changes**" button becomes enabled. Click on it and a new screen will open, select the checkbox asking for confirmation and click on the "**Submit Application"** button box. A pop-up window will appear, giving you a final opportunity to go back and check that all the details have been entered correctly ("**Review Application**"), or continue and submit. Once submitted, the submission will be shown in the "**Ongoing Submissions**" tab.

### *7.2. GCP Inspections*

Good clinical practice (GCP) is an international ethical and scientific quality standard for designing, recording and reporting trials that involve the participation of human subjects. Compliance with this

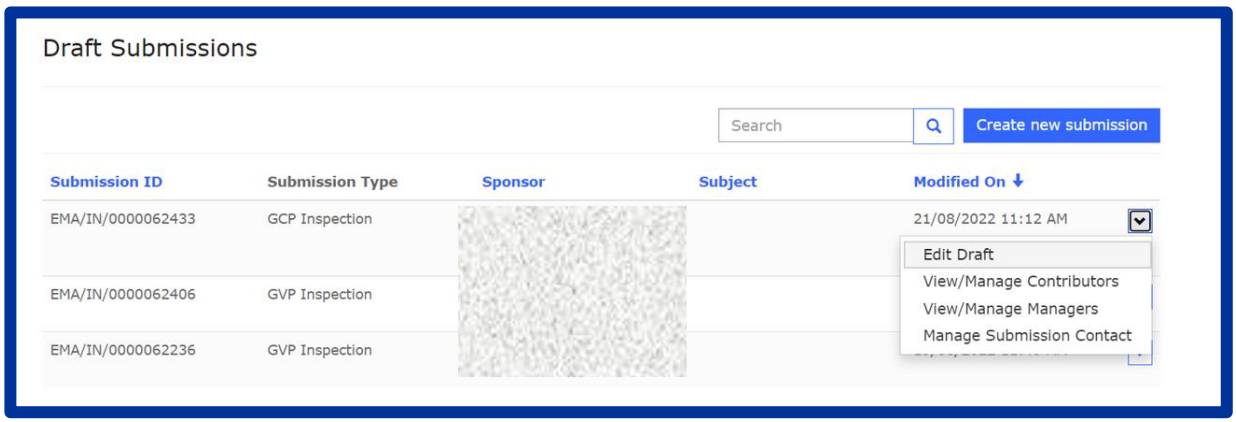
standard provides public assurance that the rights, safety, and wellbeing of trial subjects are protected, and that clinical-trial data are credible.

GCP inspections are adopted by the CHMP or CVMP and may be routine or may be triggered by issues arising during the assessment of the dossier. They are usually requested during the initial review of a marketing authorisation application, but could also be requested post-authorisation following a regulatory submission.

Upon adoption of a GCP inspection, the user will receive an e-mail notification from EMA indicating that an inspection request has been adopted by the relevant committee (CHMP or CVMP) for one of their products. At that point, you must update the submission with the necessary information (i.e. Purchase Order number and requested documents) within 10 working days of the inspection announcement or otherwise agreed with the Reporting Inspector and submit it via the IRIS Portal. Please follow the steps below to submit the required information.

1. Login into IRIS Portal with EMA credentials and access '**My Draft Submissions'** present under '**Submissions'** tab.
2. You should have a Submission starting with **'EMA/IN/00000XXXXX'** and a submission type as '**GCP Inspection'.** Open the submission in edit mode by clicking on the 'V' icon present on the right-hand side of the screen (Figure 32).

*Figure 32*



A submission form will open with the following sections: 'Inspection Overview', 'Inspection Details', 'Documents from Applicant', 'Documents from EMA' and 'Declare and Submit the changes' (Figure 33).

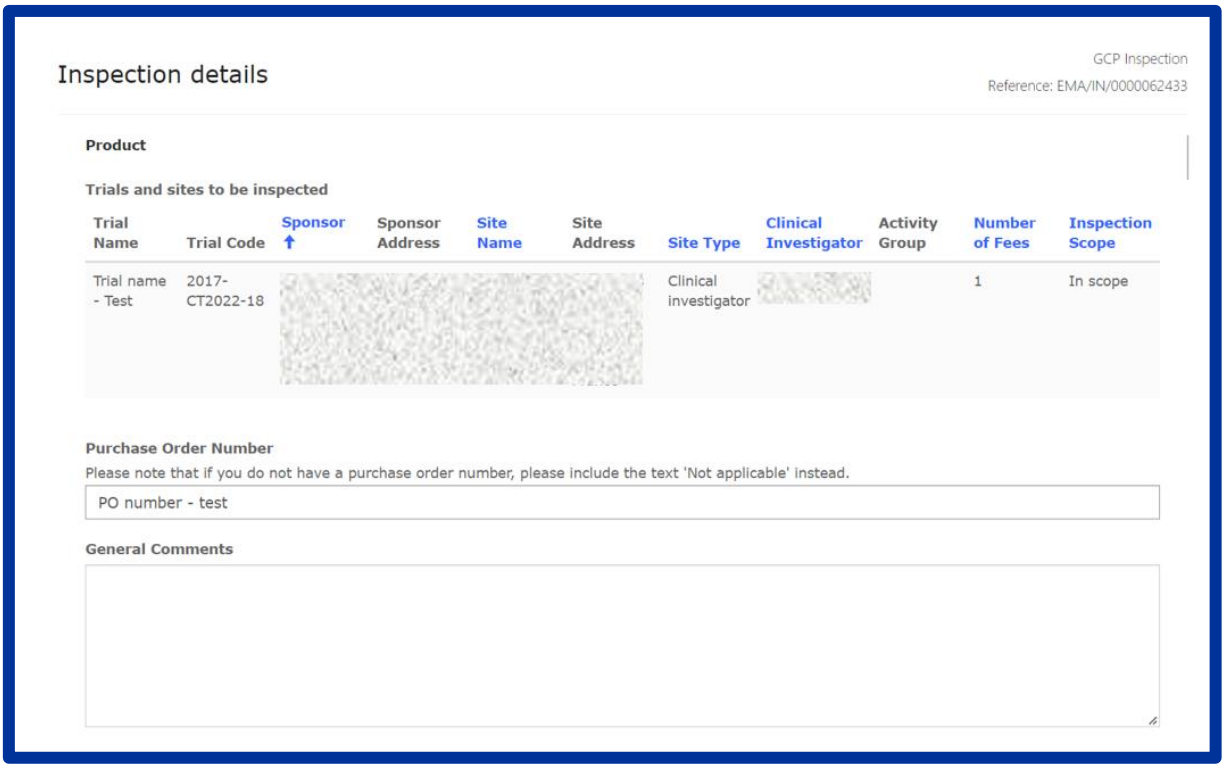
*Figure 33*


3. Click on the **'Inspection Overview'** section. Inspection related information will be shown: Product Name, Inspection Sub Type, Reporting deadline, Reporting Inspectorate, Supporting Inspectorates and Contacts. Click on '**Return'** to go back to the main menu.

4. Click on the **'Inspection Details'** section to view the information on trials and sites to be inspected. At the end of the page, you must add the Purchase Order Number in order to submit (Figure 34).

   If you do not have a PO number, please add the text '**N/A'**, since this field is mandatory to proceed with the submission. Purchase order information will be quoted on the invoice issued for the inspection carried out. Please note that the EMA will not accept delays on payments based on missing purchase order (PO) reference number information. You can also add remarks under the section **'General Comments'**. If you have any questions related to the inspection case, please enter them in the general comments field or address them to the relevant EMA inspection co-ordinator by replying to the IRIS notification you received at the start of the process. When replying, please do not change the subject of the message to ensure the e-mail is correctly routed. Once updated, click on the 'Save and return' Button and you will be taken back to the Inspection details screen.

*Figure 34*




5. **Documents from Applicant**: It is possible to add documents under this tab. Select the declaration confirming that documents have been attached and click on "Save and Return".
6. **Documents from EMA**: This tab is used to check if any documents have been made available by EMA (e.g. the Integrated Inspection Report at the end of the process (if applicable)).
7. **Declare and Submit changes**: Once all the above tabs have been filled and the green check marks show, the "**Declare and Submit changes**" button becomes enabled. Click on it and a new screen will open, select the checkbox asking for confirmation that you have read this guidance and the 'Guidance for applicants/MAHs involved in GMP and GCP inspections co-ordinated by EMA' and click on the "**Submit Application"** button box. A pop-up window will appear, giving you a final opportunity to go back and check that all the details have been entered correctly ("**Review Application**"), or continue and submit. Once submitted, the submission will be shown in the "**Ongoing Submissions**" tab.

### *7.3. GVP Inspections*

GVP inspections are conducted to ensure that requirements for monitoring the safety of medicines are met. The responsibility for carrying out the inspections rests with the national competent authorities. EMA is co-ordinating GVP inspections requested by the Committee for Medicinal Products for Human Use and the Committee for Medicinal Products for Veterinary Use.

Upon adoption of a GVP inspection, the QPPV for the pharmacovigilance system subject to the inspection will receive an e-mail notification from EMA indicating that an inspection request has been adopted by the relevant committee (CHMP or CVMP). Details of an inspection can be viewed by logging into the IRIS

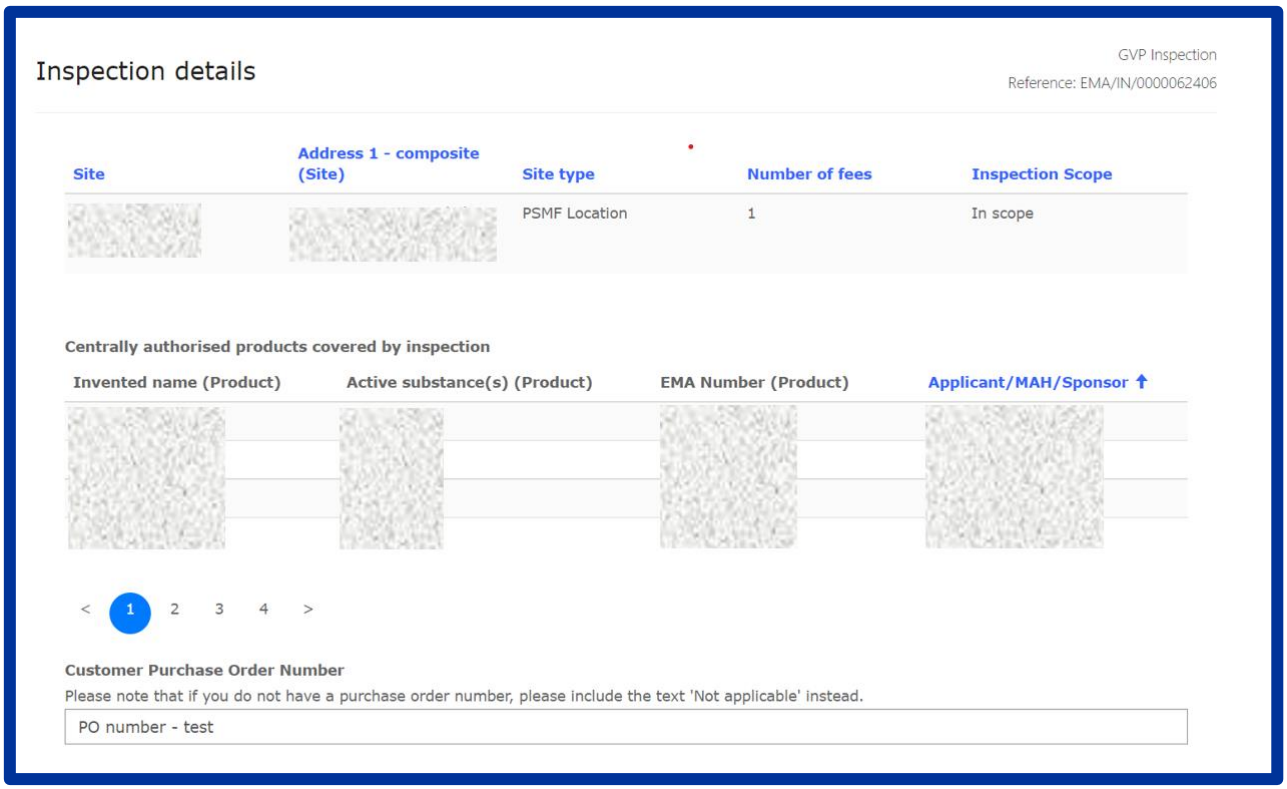
portal. At that point, you must update the submission with the necessary information (i.e. Purchase Order number and requested documents) within 10 working days of the inspection announcement or otherwise agreed with the Reporting Inspector and submit it via the IRIS Portal.

Please follow the steps below to submit the required information:

1. Login into IRIS Portal with EMA credentials and access '**My Draft Submissions'** present under **'Submissions'** tab.
2. You should have a Submission starting with **'EMA/IN/00000XXXXX'** and a submission type as '**GVP Inspection'.** Open the submission in edit mode by clicking on the 'V' icon present on the right-hand side of the screen (Figure 30).
3. Click on the **'Inspection Overview'** section. Inspection related information will be shown: PSMF Code, Inspection Sub Type, Reporting deadline, Reporting Inspectorate, Supporting Inspectorates and Contacts. Click on '**Return'** to go back to the main menu.
4. Click on the **'Inspection Details'** (Figure 35) section to view the information on the sites to be inspected and products covered by the inspections. At the end of the page, you must add the Purchase Order Number in order to submit.

If you do not have a PO number, please add the text '**N/A'**, since this field is mandatory to proceed with the submission. Purchase order information will be quoted on the invoice issued for the inspection carried out. Please note that the EMA will not accept delays on payments based on missing purchase order (PO) reference number information. Once updated, click on the 'Save and return' Button and you will be taken back to the Inspection details screen.

*Figure 35*



5. **Documents from Applicant**: It is possible to add documents under this tab. Select the declaration confirming that documents have been attached and click on "Save and Return".

6. **Documents from EMA**: This tab is used to check if any documents have been made available by EMA (e.g. the Integrated Inspection Report at the end of the process (if applicable).

7. **Declare and Submit changes**: Once all the above tabs have been filled and the green check marks show, the "**Declare and Submit changes**" button becomes enabled. Click on it and a new screen will open, select the checkbox asking for confirmation that you have read this guidance and the 'Guidance for applicants/MAHs involved in GMP, GCP and GVP inspections co-ordinated by EMA' and click on the "**Submit Application"** button box. A pop-up window will appear, giving you a final opportunity to go back and check that all the details have been entered correctly ("**Review Application**"), or continue and submit. Once submitted, the submission will be shown in the "**Ongoing Submissions**" tab.

## 8. Veterinary Signal Management

For specific information on veterinary signal management please consult the document "Guideline on veterinary good pharmacovigilance practices VGVP) Module: Signal Management" on the Pharmacovigilance (veterinary medicines) page of the EMA website and the tutorial documents on the "Union Pharmacovigilance Database: webinar on signal detection and analysis" page of the EMA website.

### *8.1. Annual statements submission*

In addition to the steps in the general procedure as described in Section 2.3. "**Create a new submission (general procedure for all submission types)**", select **"Annual statements submission"** as the submission type. Note the following additional points as shown below (Figure 36: Submission Form):

*Figure 36: Submission Form*


1. The reference number will contain VS (e.g. EMA/VS/0000001234) for the draft submission.

2. Click on "**Select Authorised Products**" and then click on "**Add Products**", select the relevant product(s) (grouping of products will be allowed on the basis of same or similar products), click on "**Add**" and once the product(s) is(are) added, click on "**Save and Return**";

3. Click on "**Submission Details**", select the "**Period of analysis**" (i.e. "Date From" and "Date To") and select the relevant statement on the tab "**Benefit-risk balance**" (i.e. "I confirm that the benefit-risk

balance remains unchanged" or "A procedure is ongoing concerning a new risk identified or a change to the benefit-risk profile"). The "Submission Details" step is completed once you click on the tick box next to the statement (that begins with the words: "I confirm...") and then click on "**Save and Return**";

4. Click on "**Documents from Applicant**" and add all corresponding documents (if applicable) by clicking on "**Add files**". For each uploaded document select the appropriate Document type (i.e. "Literature data" or "Other relevant risks identified" or "Other information"). Click on "**Save and Return**";
5. "**Documents from EMA**": This tab can be skipped initially, as part of the creation of a new submission process, as no documents are required from the applicant. It is used to check if any documents have been made available to you by EMA at a later stage;
6. Click on "**Declaration and Submission**", click on the tick box to the left of the declaration statement (that begins with the words: "I confirm…") to formally declare that you are authorised to submit the application and then click on "**Submit Application**" to complete the submission of the annual statement.

### *8.2. Signal management submission*

In addition to the steps in the general procedure as described in Section 2.3. "**Create a new submission (general procedure for all submissions type)**", select "**Signal management submission**" as the submission type and note the following additional points:

1. Click on "**Select authorised products**" and then click on "**Add products**". Select the relevant product(s), click on "**Add**" and then click on "**Save and return**";
2. Click on "**Submission details**";
    a. Fill in the **signal title** according to the following format:

    "*Active substance – PRODUCT NAME = VeDDRA term (PT level) in species affected"*
    Please ensure the signal title is specific and does not concern general issues such as potential drug interactions or medication errors. In these cases, the consequences of the potential drug interaction or medication errors should be specified (e.g. "serious adverse drug reactions including bleeding events following potential drug interaction between X and Y").

    b. Under "**Type of signal**", select if it concerns a Signal or an Emerging safety issue (for which a 3-day notification requirement applies).

    c. Under "**Date of Analysis**", select the date when the assessment was performed.

    d. Click on "**Add Species**" and select the concerned animal species, then click "**Add**".

    e. Click on "**Add VeDDRA**", select the concerned VeDDRA PT term(s) and then click on "**Add**".

    f. Under "**Previous signal submission**" you may link the current signal submission to any previous signal submissions in IRIS. E.g., if you previously submitted a signal concerning the same with the proposal to refute the signal, but with the current submission, the conclusion is to propose further regulatory actions such as an SPC update.

    g. Under proposal for action, select the appropriate regulatory action(s).

    h. Under "**Proposal for action description**", please describe the specific proposals for regulatory action(s) indicated above in detail.

        For example: in case of amendment of the product information, you should provide here the specific wording to be amended or added to the SPC and the corresponding

section(s) to be updated. In case of the signal being proposed to be refuted or for close monitoring, you should provide a brief summary of the review of the cases, including the total number of cases, and the justification for the conclusion of the assessment.

i. Click on "**Save and return**".

3. Click on "**Documents from applicant**". Then click on "**Add files**" and add the corresponding additional documents from the signal assessment. In case a thorough assessment is required, such as for signals with proposals for further regulatory action (30-day notification), please add here the filled template used for the signal assessment. Then click on "**Save and return**";
4. Click on "**Declaration and submission**", click on the tick box to the left of the declaration statement (that begins with the words: "I confirm…") to formally declare that you are authorised to submit the application and then click on "**Submit application**" to complete the signal management submission.

## 9. Registration of an MAH i-SPOC on supply and availability

### *9.1 Purpose of this section*

This section has been developed to show Marketing Authorisation Holders (MAHs) how to use the IRIS platform to establish and maintain an Industry Single Point of Contact (i-SPOC) on supply and availability issues for their portfolio of medicinal products (for human use) authorised in the Union.

The registration of an MAH i-SPOC takes place in a 2-step approach, as follows:

- **Step 1** - Set up of an EMA account and role. This prerequisite needs to be met to allow a successful registration in the IRIS portal. Further instructions are available within **Section 9.2** and **9.3**.
- **Step 2** – Create or maintain an MAH i-SPOC in the IRIS portal. Information on a successful creation or maintenance of an MAH i-SPOC is further detailed in **Section 9.5, 9.6, 9.7**.

### *9.2 Preliminary requirement as defined in step 1*

EMA Account and appropriate role: for any type of submission in IRIS,

- You need an EMA account and,
- an appropriate role in IRIS, to login into IRIS.

IAM registration needs to be done only once; and this will allow you to register an MAH i-SPOC on supply and availability issues as defined in step 2.

For information on how to request an EMA account and an appropriate IRIS role (these are two separate actions), please consult the separate IRIS guide to registration and the quick interactive guide to IRIS registration process on the IRIS home page.

Please be aware of the following timelines when registering an EMA account and role:

- User access request to IRIS with a "IRIS Industry User Admin" role can take up to 2 working days;

- Registration of a new organisation[3] takes up from 5 to 10 working days.

### *9.3 Supported Browsers*

IRIS can be accessed on any modern Web Browser, including but not limited to Google Chrome (latest version), Internet Explorer 11 and above, Edge (including the new, Chromium-based Edge), Safari 12 and above, Firefox, Vivaldi.

### *9.4 Background*

Regulation (EU) 2022/123 provides the European Medicines Agency (EMA) with a framework to monitor and mitigate potential and actual shortages of centrally and nationally authorised medicinal products for human use considered critical to address a given 'public health emergency'[4] or 'major event'[5].

Regulation (EU) 2022/123 article 9 requires that the Agency establish and maintain a list of Industry Single Points of Contact (i-SPOC) of MAHs for all medicinal products authorised in the Union. In the event that an authorised product is included in a list of critical medicines identified for a specific public health emergency or major event, this list of contacts will be used to enable rapid, two-way communication between EMA and the MAHs of those identified critical medicines to detect, report, and prevent or manage supply and availability issues.

Therefore, all MAHs in the Union are required to register an i-SPOC on supply and availability so that EMA can quickly engage with them if their medicines are included in the lists of critical medicines. The Agency's IRIS platform will be used to collect details of i-SPOCs for all MAHs and to facilitate future communication with those MAHs of identified critical medicines during public health emergencies or major events. The i-SPOCs should oversee the product supply chain, manufacturing capacity management and shortages. According to the legislation, MAHs are required to submit the information (i.e. i-SPOC details) to the Agency by **2 September 2022.**

MAHs may wish to set their i-SPOC at company Headquarter level, instead of company affiliate level. In this respect, during the registration process the system will allow MAH users to create or maintain a single i-SPOC person for **multiple local affiliates (or organisations)**. For additional instructions on how to select multiple local affiliates and assign a single i-SPOC person to all relevant organisations, please refer to **Section 2.4.**

---

[3] Data relating to an organisation such as MAH, sponsors, regulatory authority, manufacturers. Includes organisation level data (e.g., organisation name) and location level data (e.g., location address). Each organisation can have one or many locations. An active organisation must have at least one active location linked to it.

[4] 'public health emergency' means a public health emergency recognised by the European Commission in accordance with Decision No 1082/2013/EU.

[5] 'major event' means an event which is likely to pose a serious risk to public health in relation to medicinal products in more than one Member State. Such an event concerns a deadly threat or otherwise serious threat to health of biological, chemical, environmental or other origin or incident that can affect the supply, demand or quality, safety, and efficacy of medicinal products. Such an event may lead to shortages of medicinal products in more than one Member State and necessitates urgent coordination at Union level in order to ensure a high level of human health protection according to Article 2(b) of Regulation 2022/123.

### *9.5 Registering an MAH i-SPOC as defined in step 2*

Who can register an i-SPOC?

In order to register the i-SPOC, user should have already a “MANAGER” role in IRIS. Please be informed that only the user with a “MANAGER” role in IAM/IRIS can successfully register an MAH i-SPOC within the IRIS portal.

Who can be an i-SPOC?

MAH staff registered as an i-SPOC must also be affiliated to the organisation in IAM/IRIS.

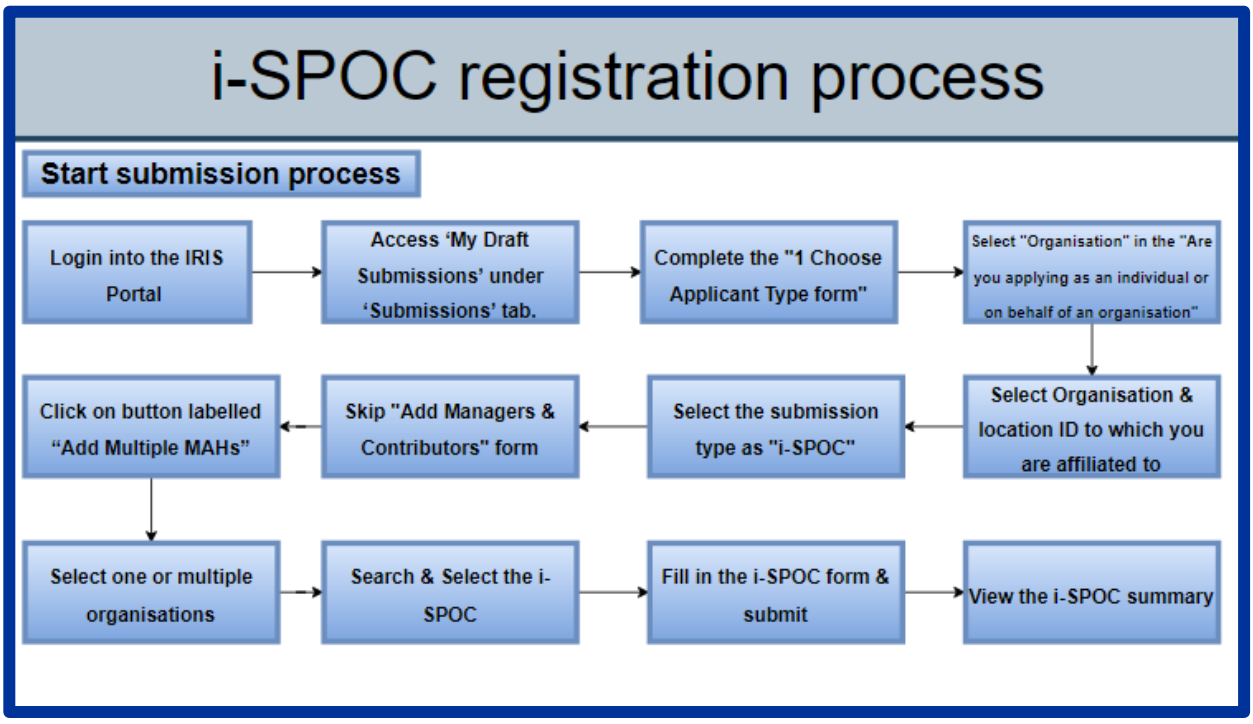
The nominated i-SPOC person can, nonetheless, be any MAH user with a “MANAGER” or a “CONTRIBUTOR” role in IAM/IRIS.

Registration process in IRIS portal - workflow

The workflow below illustrates the various steps which need to be followed in order to complete a successful registration/maintenance of an MAH i-SPOC within IRIS portal end-to-end.

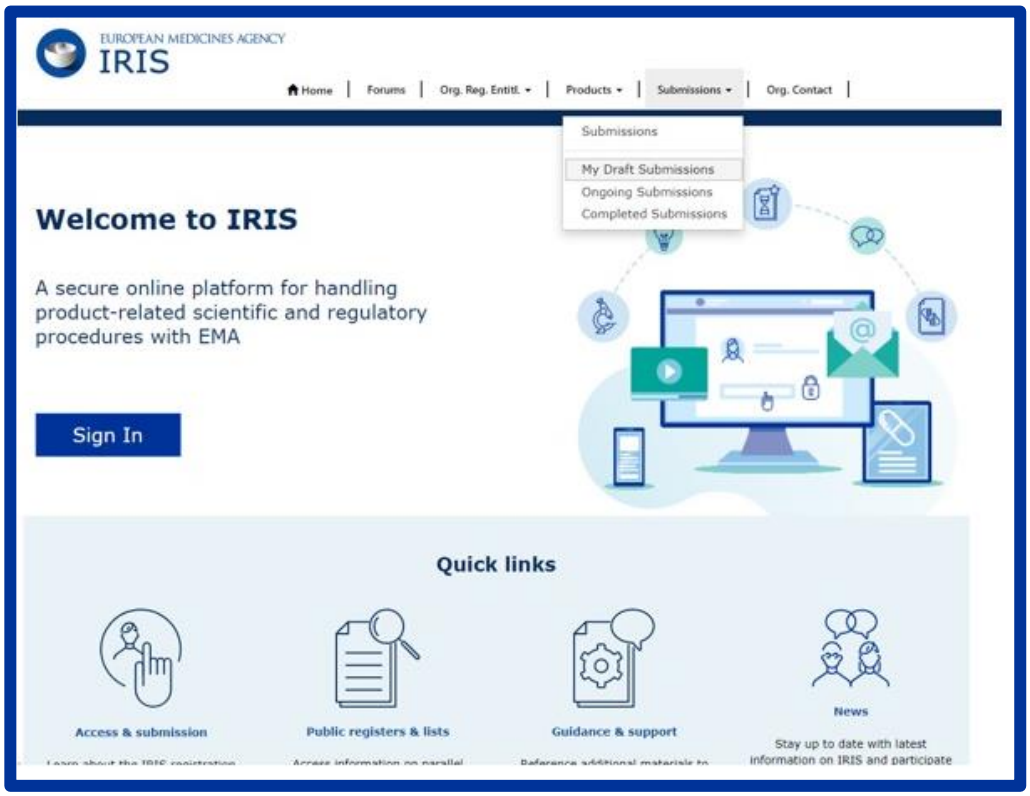
A detailed description of the various individual steps is further available below.

*Figure 37*



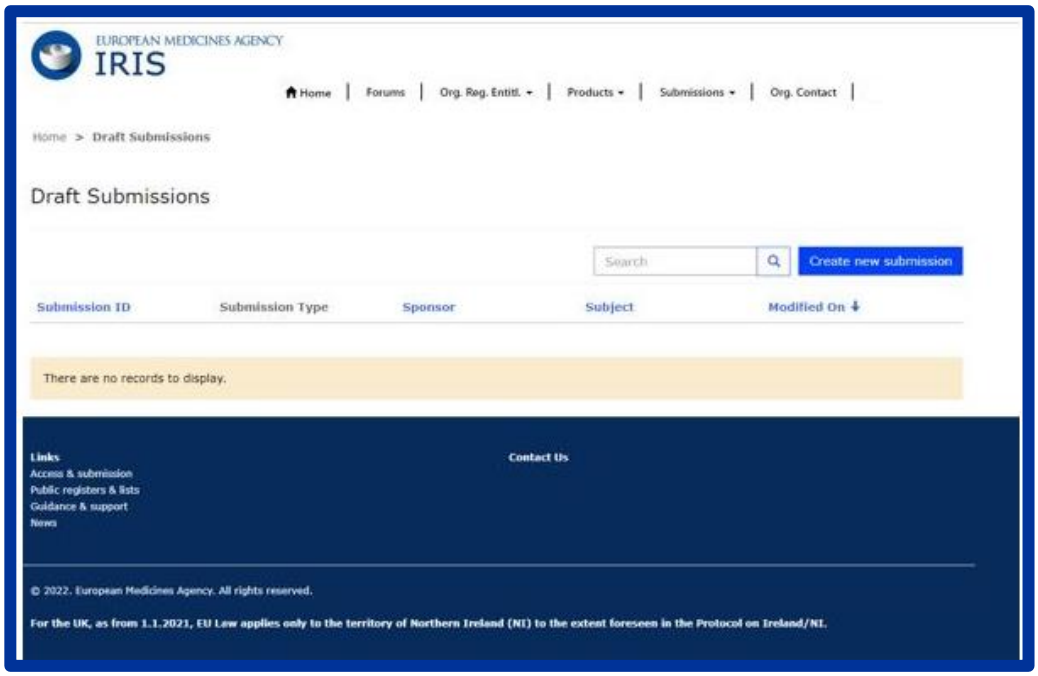

1. Login into the IRIS Portal with your account credentials and access ‘My Draft Submissions’ present under ‘Submissions’ tab.

*Figure 38*




2. For the registration of an i-SPOC, a new submission should be created

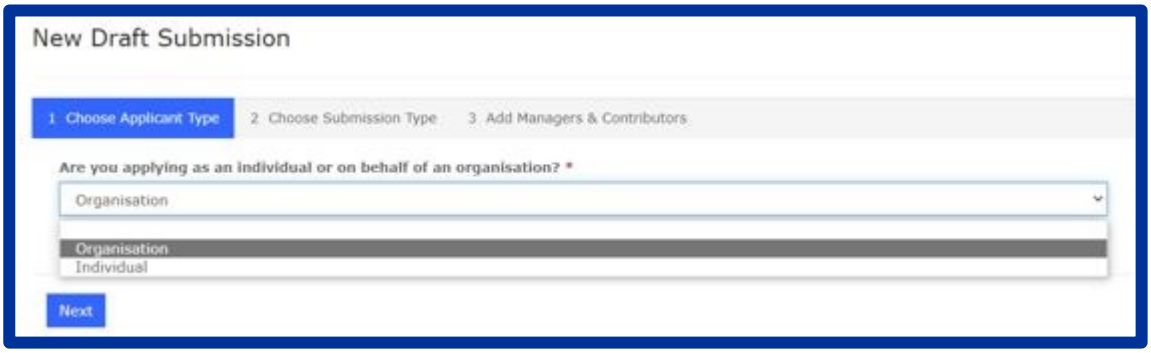
*Figure 39*



3. Following the standard submission procedure, complete the "1 Choose Applicant Type form" by filling in the mentioned fields:

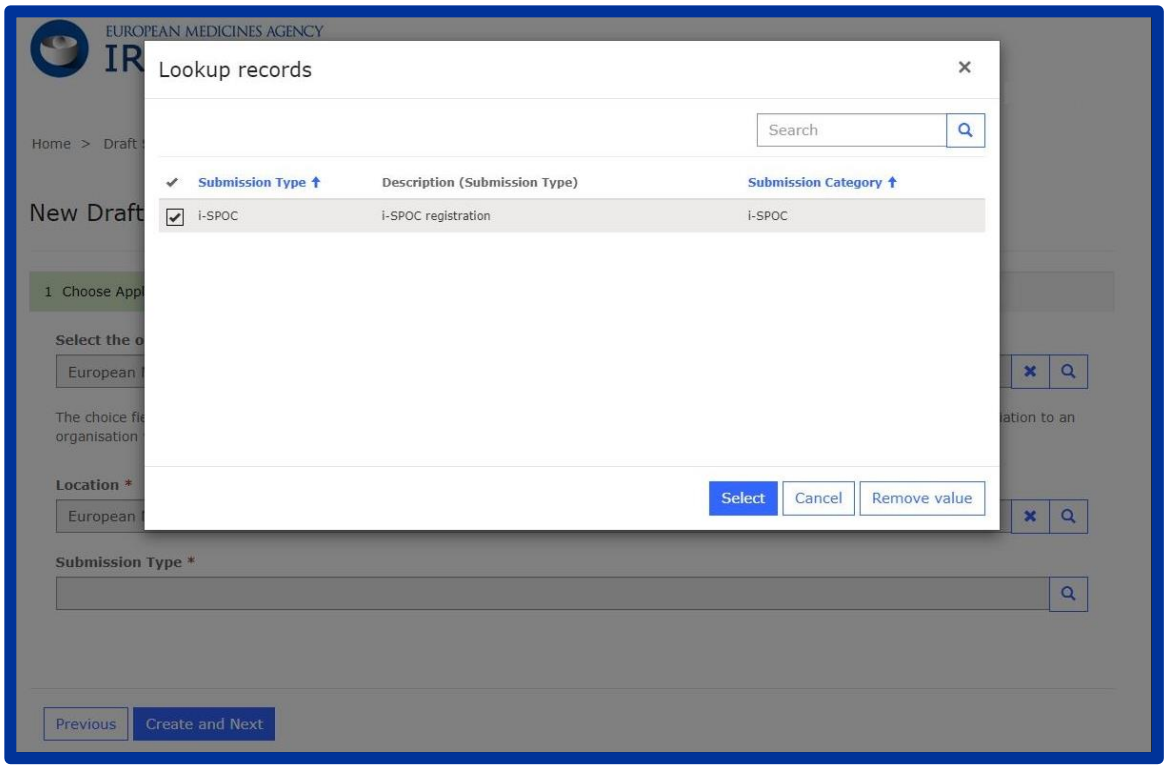
    a. Select **"Organisation"** in the "Are you applying as an individual or on behalf of an organisation" & click on "Next" button

*Figure 40*




4. In the submission type form, select organisation & location ID to which you are affiliated to
5. In the field "Submission Type", click on the search button, select the submission type as **"i-SPOC"** & click on "Select" button

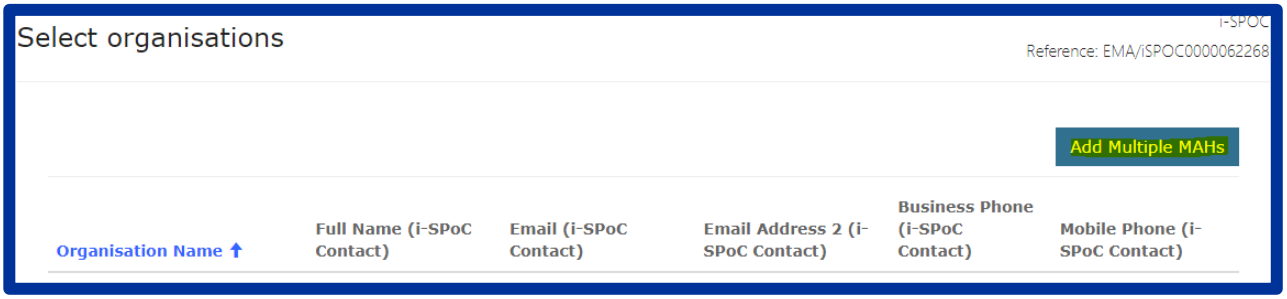
*Figure 41*




6. System will navigate the user to the next form named "Add Managers & Contributors". For i-SPOC registration, **no user action is required on this form** hence click on NEXT button & proceed to the next screen/form

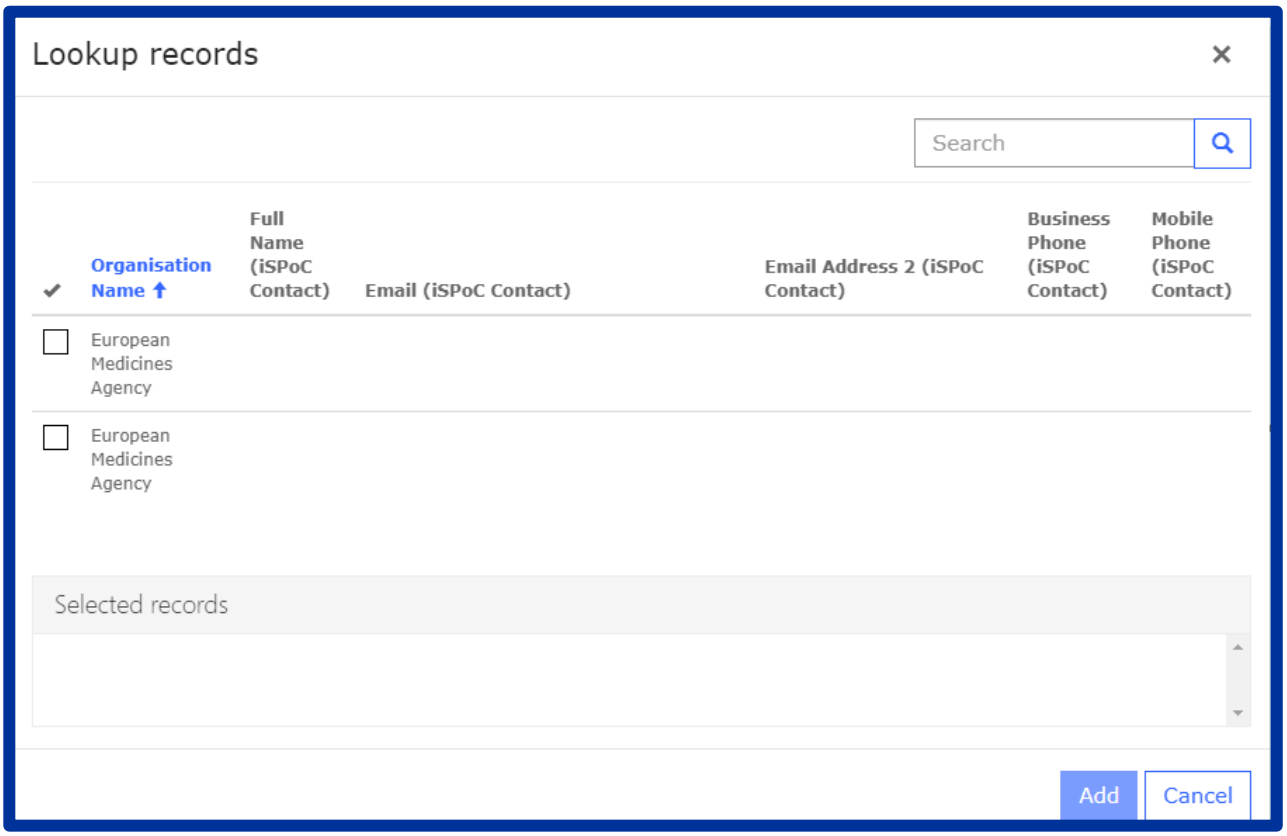
7. In the next screen, click on button labelled “Add Multiple MAHs”. System will display the list of your affiliated organisations

*Figure 42*




8. Select your organisation for which you want to register an i-SPOC. Post selection, click on "Add" button.

*Figure 43*

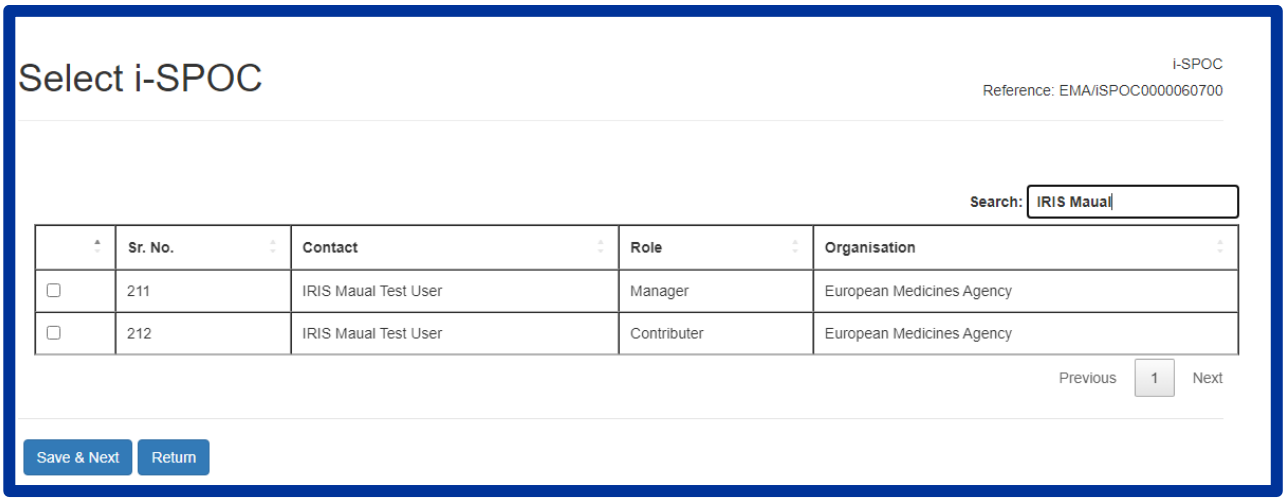



NOTE: Listing of organisations in this screen is **dependent on your affiliations in IAM**. The system will list all the organisations to which you are affiliated with a manager role.

9. After the selection of the organisation, system will prompt you to select the i-SPOC. All the affiliated users with MANAGER or CONTRIBUTOR role can be selected as an i-SPOC. A list is

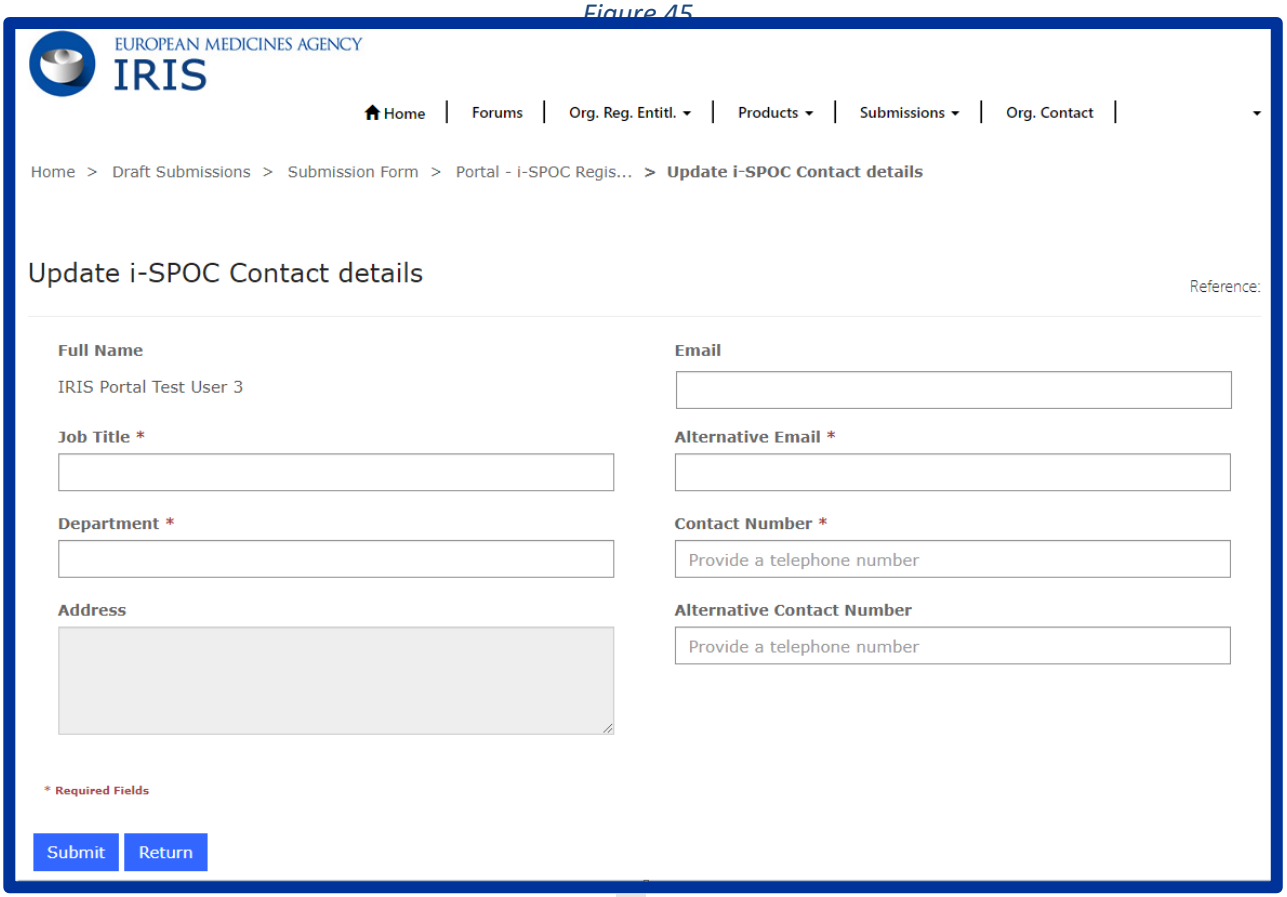
presented/displayed with all affiliated users for selection. You can filter/search for i-SPOC user & select an individual record. Click on Save & Next button

*Figure 44*




10. User is prompted to fill in the additional information about the contact details of the MAH i-SPOC. Fields "Job Title", "Department", "Alternative Email" are mandatory in nature. Simultaneously, ensure that “Alternative email” address is different than the i-SPOC email address. Either “contact number” or “Alternative contact number” information should be provided. System will prompt an error message if the mandatory information is not populated. Mandatory information is marked with an asterisk (*). Click on the Submit button

*Figure 45*

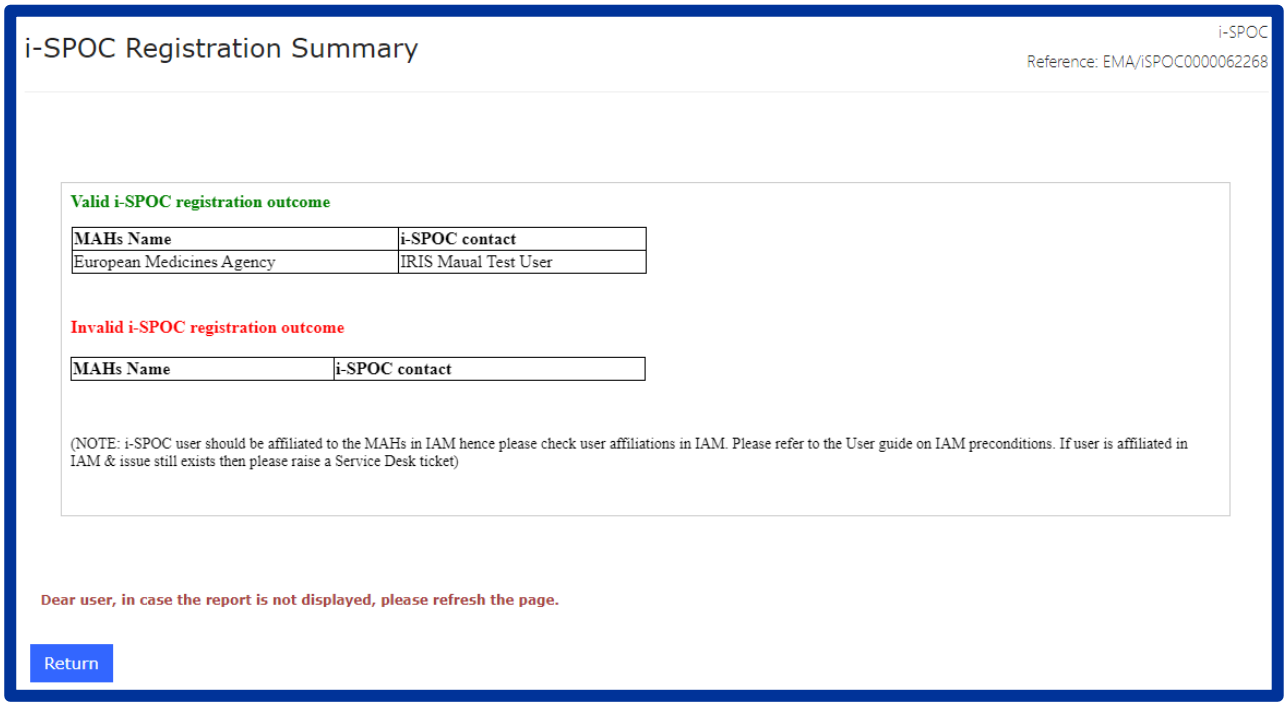


11. System will notify you of the registration outcome (i.e., successful/unsuccessful) by displaying an outcome summary screen message.

    a. **Valid** registration outcome - i-SPOC user should be affiliated in IAM/IRIS with the organisation. During the registration process, if the user selects the i-SPOC who is affiliated to the selected organisation; then the registration will be successful & information will be displayed in the section under the green font header.

    b. **Invalid** registration outcome – When the user registers an i-SPOC for multiple organisations at once, then it my happen that selected i-SPOC is not affiliated to all the selected organisations. In such case, system will not register the i-SPOC & list the same in the section under the red font header.

*Figure 46*




12. Click on "Org. Contact" menu option to view the registered i-SPOC contact(s)

*Figure 47*

### *9.6 Update an MAH i-SPOC*

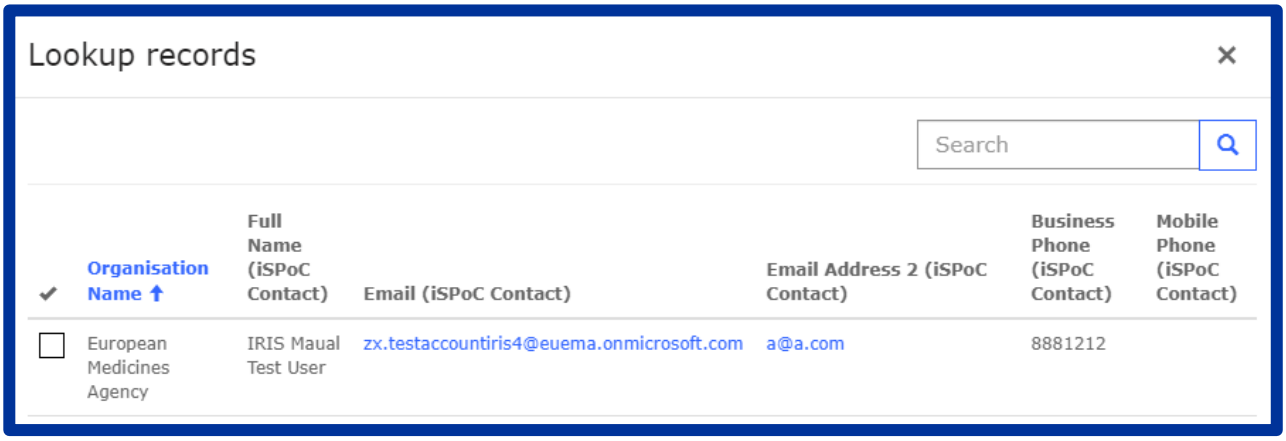
For modification of an MAH i-SPOC, user will have to create a new submission & follow the same steps to create an i-SPOC as further defined in section 2.2.

**Who can update an i-SPOC?**

In order to update/change the i-SPOC, user updating the i-SPOC record, should have a “MANAGER” role in IAM/IRIS. Only the user with a “MANAGER” role in IAM/IRIS can register or update an i-SPOC.

1. Login into the IRIS Portal with EMA account credentials and access ‘My Draft Submissions’ present under ‘Submissions’ tab.
2. For the modification of an i-SPOC, a new submission should be created
3. Following the standard submission procedure, complete the "1 Choose Applicant Type form" by filling in the mentioned fields:
4. Select "Organisation" in the "Are you applying as an individual or on behalf of an organisation" & click on "Next" button
    a. In the submission type form, select organisation & location ID to which you are affiliated to
    b. In the field "Submission Type", click on the search button, select the submission type as "i-SPOC" & click on "Select" button
5. System will navigate the user to the next form named "Add Managers & Contributors". For i-SPOC registration, no user action is required on this form hence click on NEXT button & proceed to the next screen/form
6. In the next screen, click on button labelled “Add Multiple MAHs”. Select your organisation for which you want to register an i-SPOC. Post selection, click on "Add" button.

*Figure 48*




7. Current i-SPOC details will be displayed on the screen

*Figure 49*


8. After the selection of the organisation(s), system will prompt you to select the i-SPOC. All the affiliated users with “MANAGER” or “CONTRIBUTOR” role can be selected as an i-SPOC. List displays all the affiliated users for selection. You can filter/search for i-SPOC user & select an individual record. Click on Save & Next button
9. User is prompted to fill in the additional information about the MAH i-SPOC contact details. Fields "Job Title", "Department", "Alternative Email" are mandatory in nature. Simultaneously, ensure that “Alternative email” address is different than the i-SPOC email address. Either “contact number” or “Alternative contact number” information should be provided. System will prompt an error message if the mandatory information is not populated. Mandatory information is marked with an asterisk (*). Click on the Submit button
10. System will notify you of the registration outcome (i.e., successful/unsuccessful) by displaying an outcome summary screen. Previous record is overridden with the new i-SPOC contact details.
11. Click on "Org. Contact" menu option to view the registered i-SPOC contact(s)

### 9.7 Maintain the same i-SPOC for multiple local affiliates

MAHs may wish to maintain their i-SPOC at company Headquarter level, instead of an i-SPOC at each individual company affiliate level. Hence, during the registration process the system will allow MAH users to create or maintain a single i-SPOC person for multiple, local affiliates (or organisations).

Please be aware that in order to have a MAH centralised at Headquarter level the MAH user must be affiliated in IAM/IRIS to multiple local organisations.

Please follow the standard steps of the i-SPOC registration described in section 2.2.

1. In the “Select organisations” screen, click on button labelled “Add Multiple MAHs”. System will allow the user to select one or multiple organisations

*Figure 50*

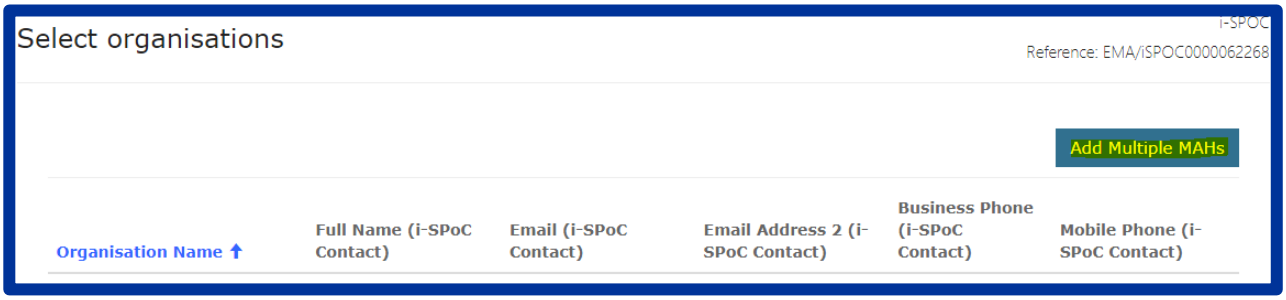
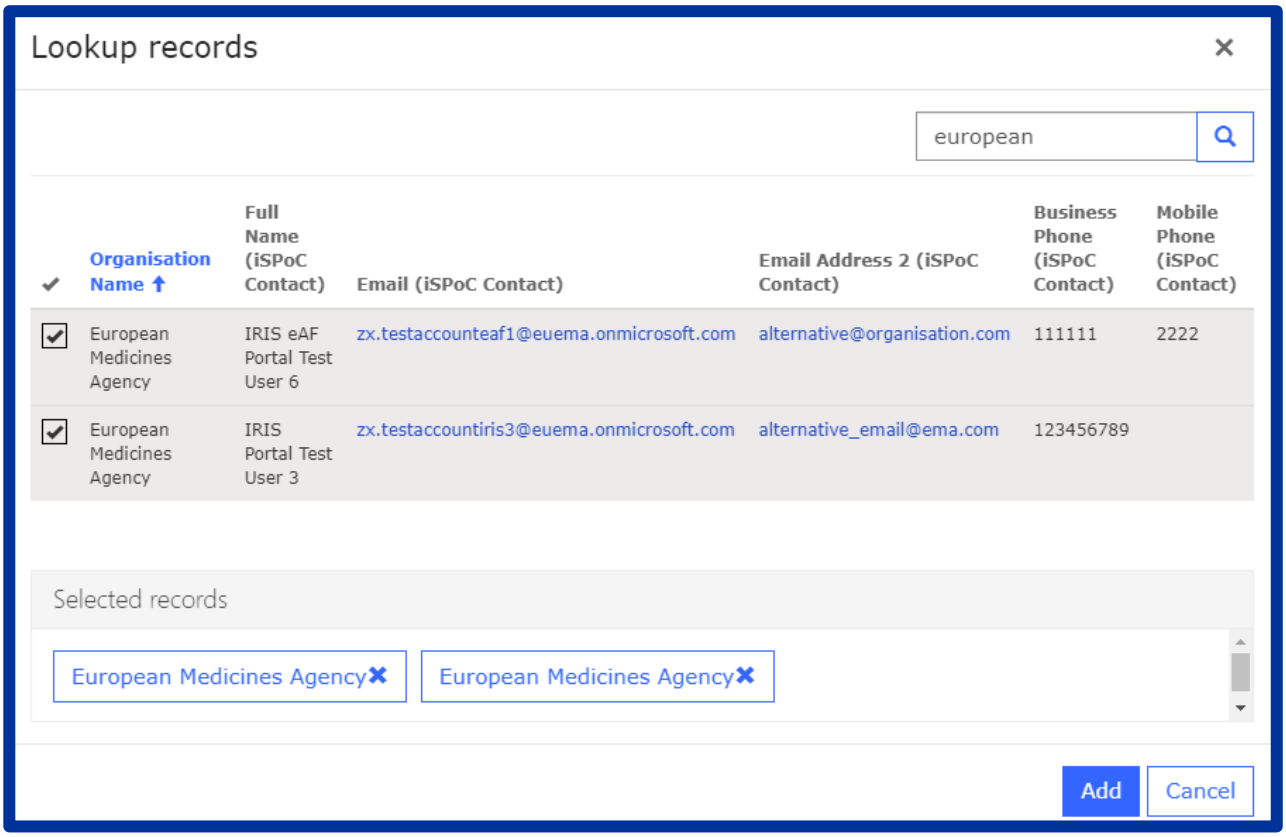
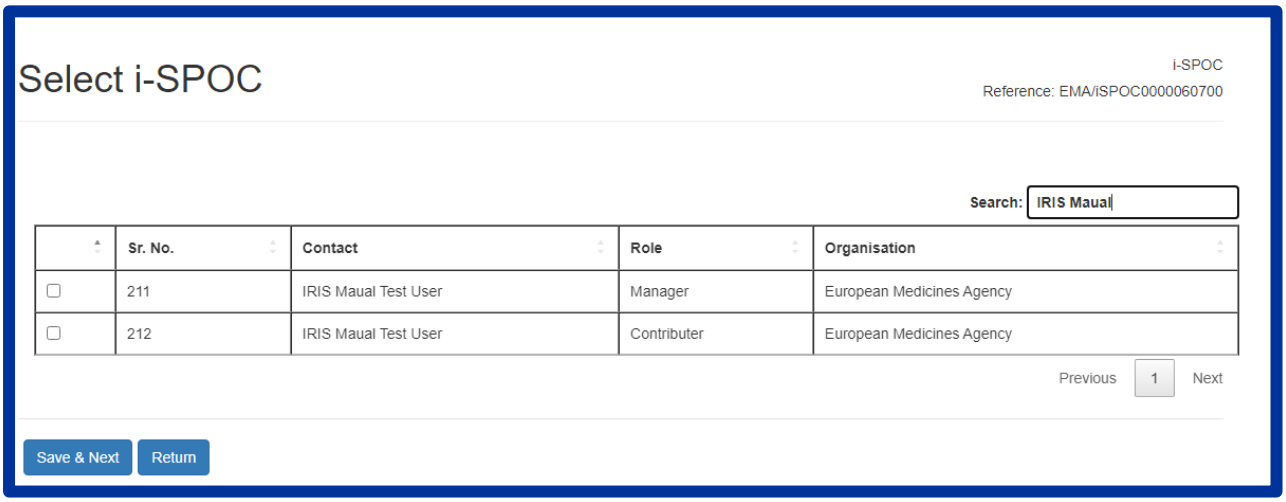



*Figure 51*



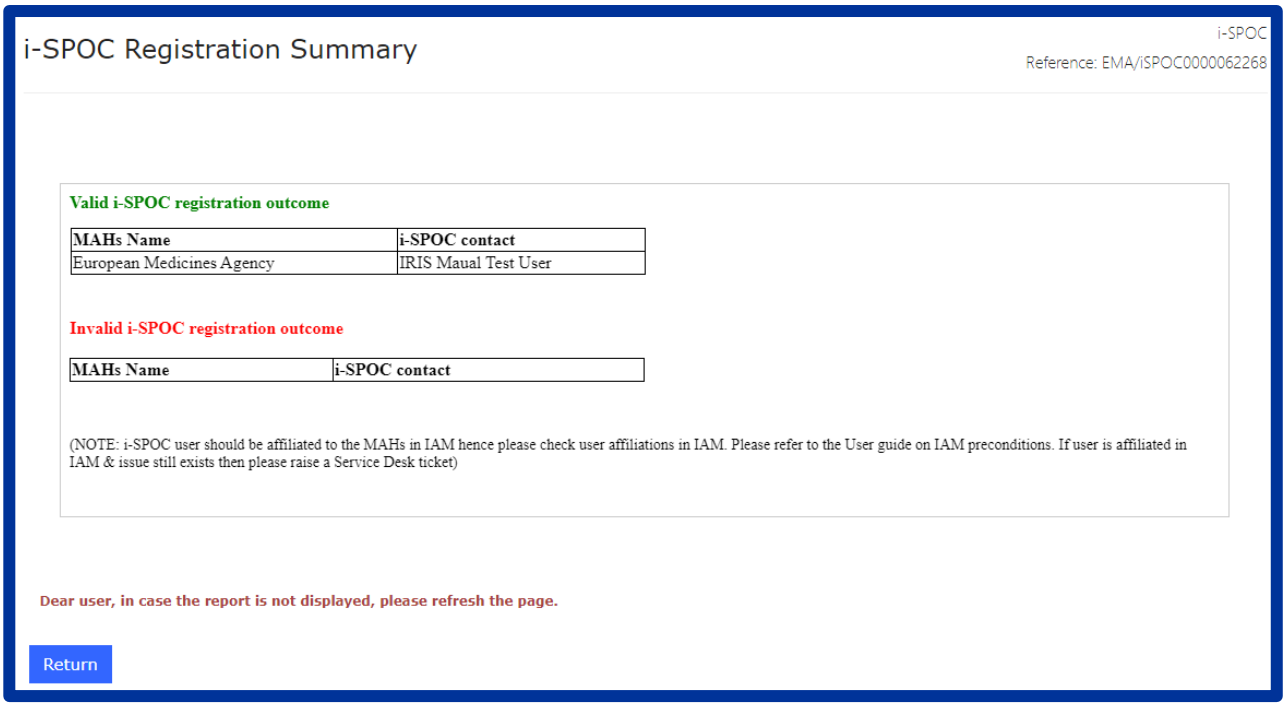

2. After the selection of the organisation(s), system will prompt you to select the i-SPOC. All the affiliated users with “MANAGER” or “CONTRIBUTOR” role can be selected as an i-SPOC. List displays all the affiliated users for selection. You can filter/search for i-SPOC user & select an individual record. Click on Save & Next button

*Figure 52*




3. Complete the remaining steps
4. System will notify you of the registration outcome (i.e., successful/unsuccessful) by displaying an outcome summary screen. Summary screen contains 2 sections:
    a. Valid i-SPOC registration outcome
    b. Invalid i-SPOC registration outcome
    c. If the user selects an i-SPOC who is not affiliated (in IAM/IRIS) to all the selected organisations, then these will marked as erroneous & listed under "Invalid i-SPOC registration outcome" section for re-registration

*Figure 53*



## 10. PRIME Eligibility

For general information on PRIME Eligibility procedures, please consult the PRIME: Priority medicines section of the EMA website.

For specific information on how to submit an application for PRIME Eligibility, including the supporting documentation) please refer to the European Medicines Agency Guidance for applicants seeking access to PRIME on the EMA website.

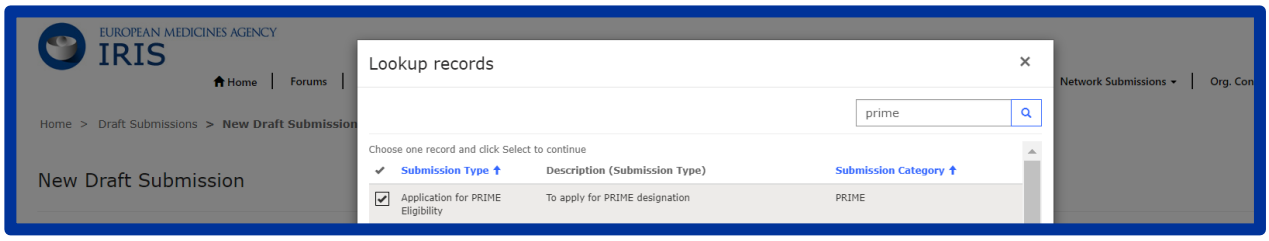
### *10.1 Create an application for PRIME Eligibility*

Step-by-step guidance on how to create a submission, please refer to the generic steps described in section 2.3.

For process specific step, please follow the steps below:

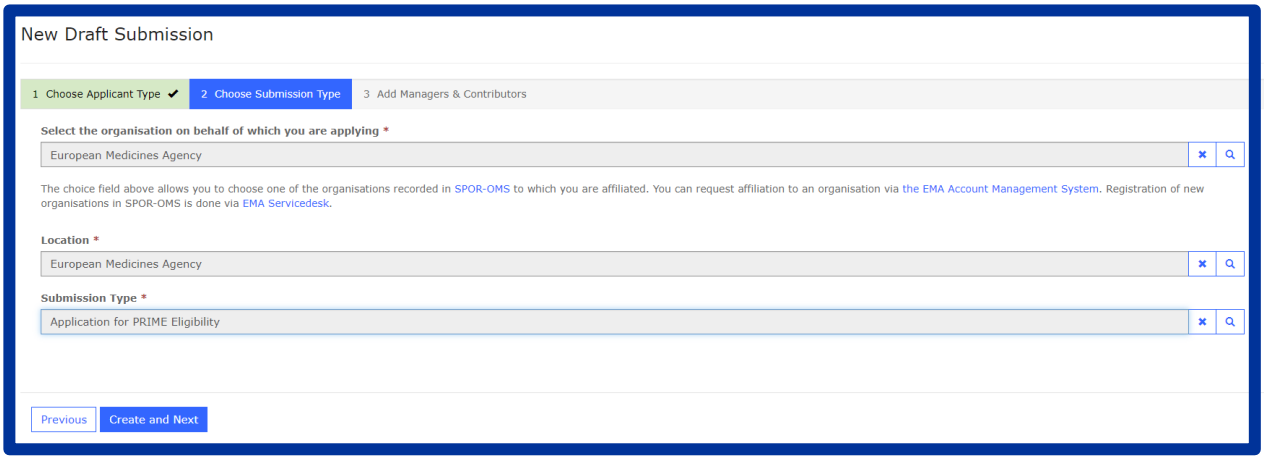
1. When choosing the submission type, **"2. Choose Submission Type"** click on the magnifying glass symbol in the drop-down list and type in a keyword (e.g., PRIME) or the process type you wish to apply for (e.g. **Application for PRIME eligibility**).

*Figure 54: Select Submission Type*



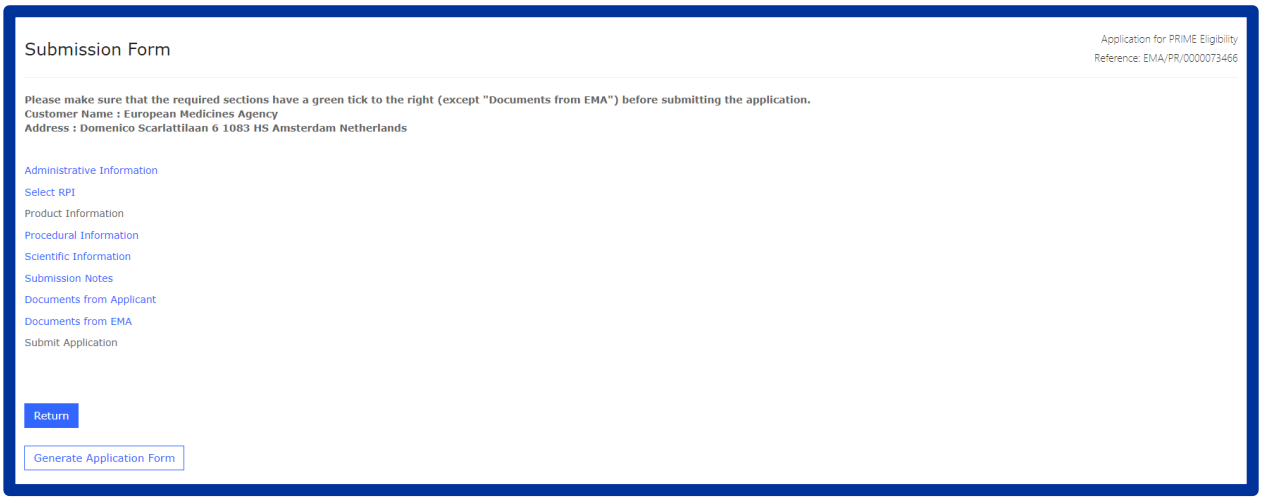

2. Once all three fields in step 2 are selected click "Create and Next".

*Figure 55: Submit Submission Type*



3. In the Submission form there is a list of nine steps (tabs) starting with "**Administrative Information**" and ending with "**Submit Application**" relating to the PRIME Eligibility Application displayed on the left-hand side of your screen.

*Figure 56: Submission Form steps*



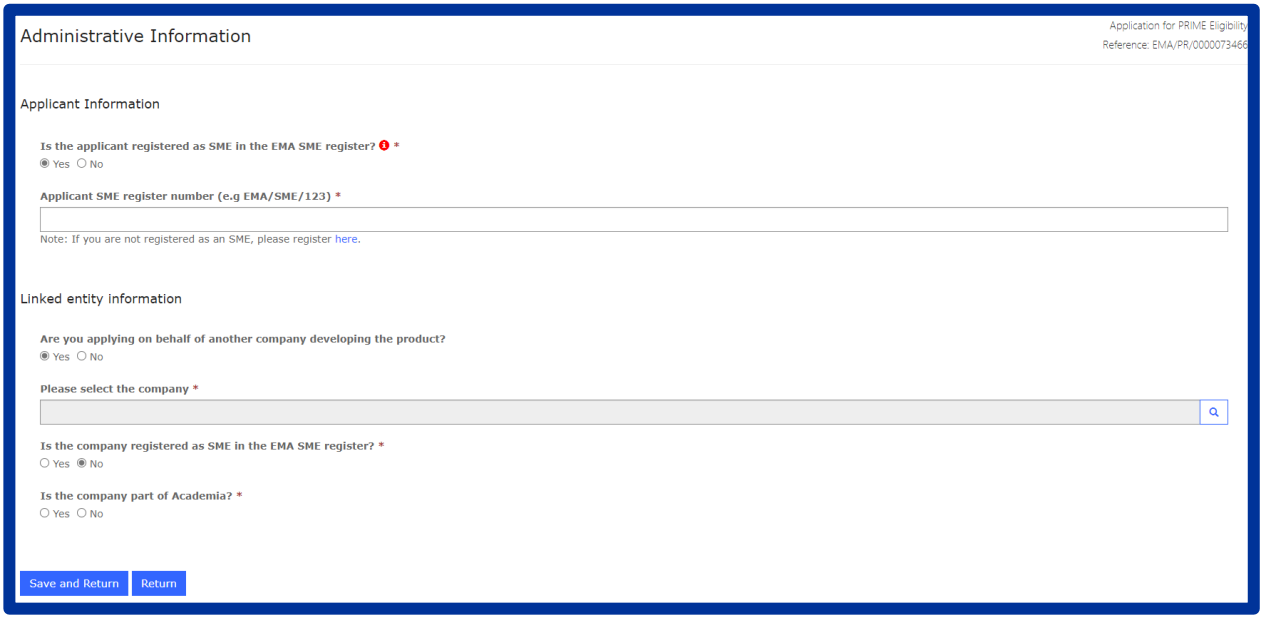

Note the following additional points:

- the reference number follows the format EMA/PR/0000001234, which is assigned automatically for your draft submission displayed on the upper right-hand side of the screen.
- the two sections "Administrative Information" and "Select RPI" must be completed, before the section (tab) "Product Information" becomes available (turns from grey to blue);
- the section (tab) "Submit Application" becomes available (turns from grey to blue) only when all mandatory sections, including "Documents from Applicant" are completed.
- all the mandatory field(s) marked with a red asterisk "*" should be completed.

4. In section "**Administrative information**", you need to indicate the registered SME status or if you are part of Academia.

- If the applicant is registered as SME, enter the "Applicant SME register number" (e.g., EMA/SME/123). If an SME applicant is not yet registered, please consult the "Applying for SME status" section of the EMA website.
- If you are applying on behalf of another company developing the product, please select the relevant company in the "Linked entity information" section.
- Click "Save and Return".

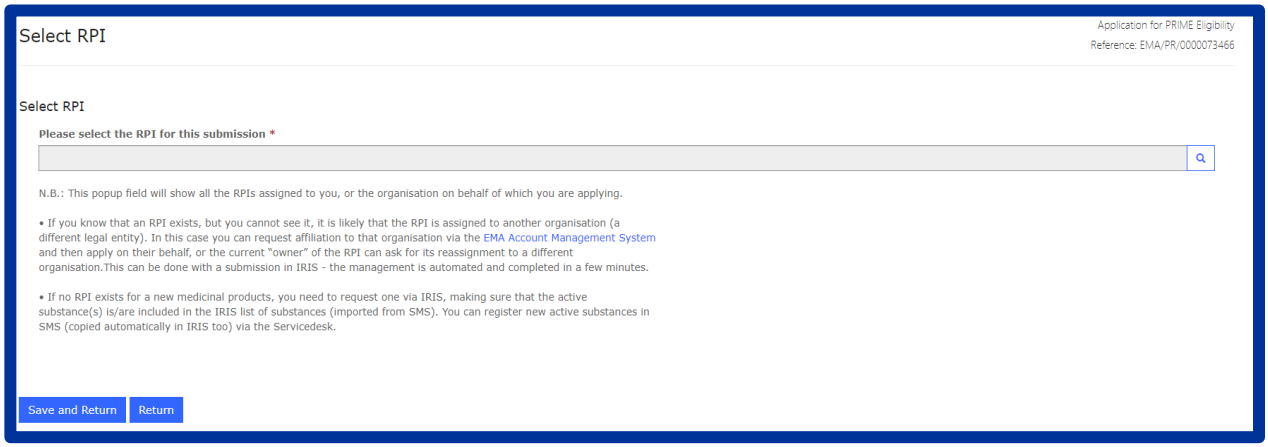
*Figure 57: Administrative Information*




5. In section "**Select RPI**", please note that only RPIs "owned" by the applicant, or by the organisation on behalf of which he is applying, can be added.

- Use the magnifying glass search symbol to look up and select the correct RPI.
- If you know that an RPI exists, but it does not appear in the records, it is likely that the RPI is assigned to another organisation (a different legal entity). In this case you can request affiliation to that organisation via the EMA Account Management System and then apply on their behalf, or the current "owner" of the RPI can ask for its reassignment to a different organisation. This can be done with a submission in IRIS - the management is automated and completed in a few minutes.
- If no RPI exists for a new medicinal product, you should request one via IRIS, making sure that the active substance(s) is/are included in the IRIS list of substances (imported from SMS). New active substances can be registered in SMS (and registered automatically also in IRIS) via the ServiceDesk.

*Figure 58: Select RPI*



6. In section "**Product Information**" the system displays relevant information on the selected RPI, such as product name, type of product and mechanism of action. Additionally, can provide other information which you find relevant of the submission about this product.

*Figure 59: Product Information*


7. In this section the system also displays **submission pipeline information** that is recorded on PRI "Information on Submission Pipeline". Please check this information and, if needed, update in the "Update Information on Submission Pipeline" section and provide explanation for the proposed change in the free text box. Please note that any changes made in these fields will result in updating also the information of the RPI record.

*Figure 60: Information on Submission Pipeline*

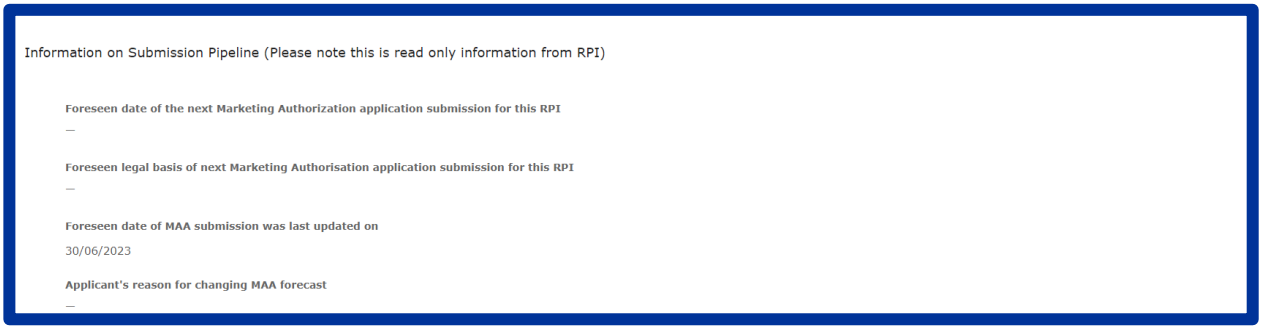
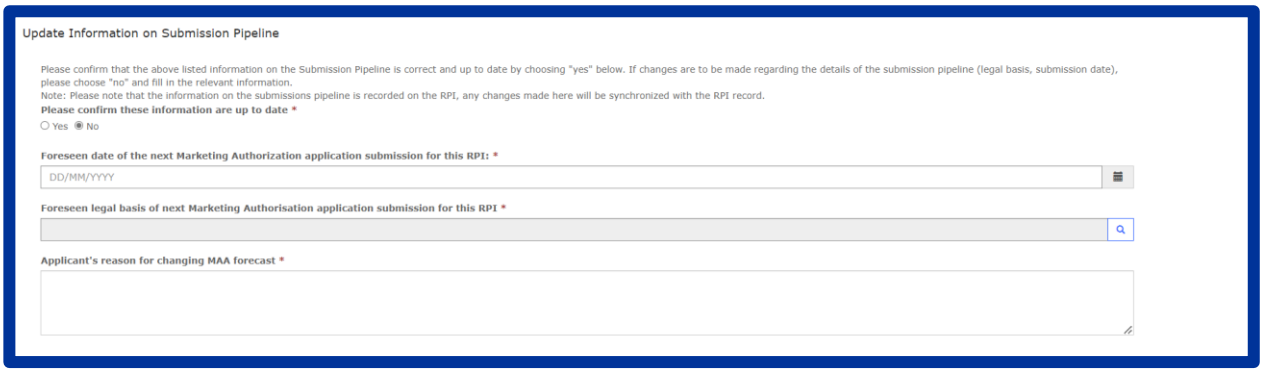
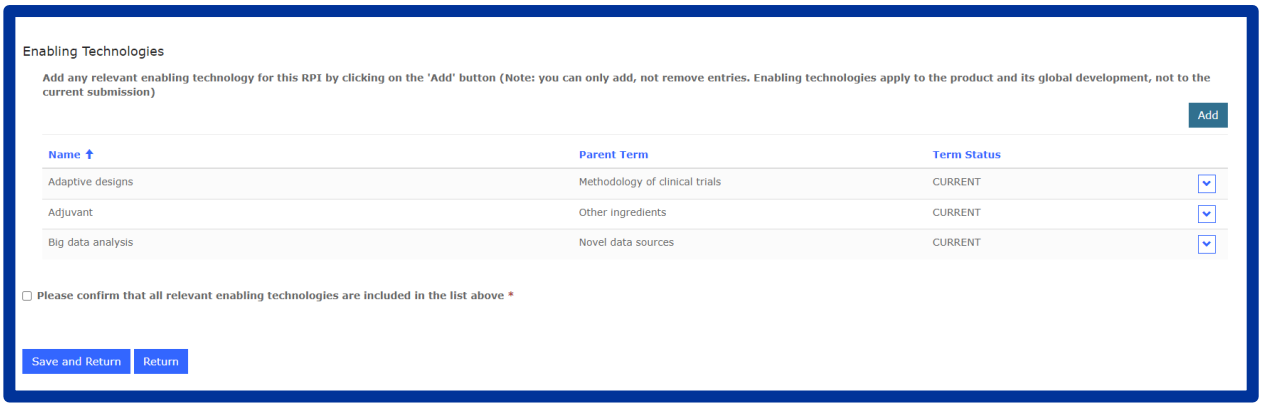



*Figure 61: Update Information on Submission Pipeline*



8. Add any relevant "Enabling technology" for this RPI by clicking on the "Add" button. Enabling technologies apply to the product and its global development, not to the current submission. Please confirm that all relevant enabling technologies are included in the list by ticking the box.

*Figure 62: Enabling Technologies*




9. In section "**Procedural Information**", please complete all mandatory fields.

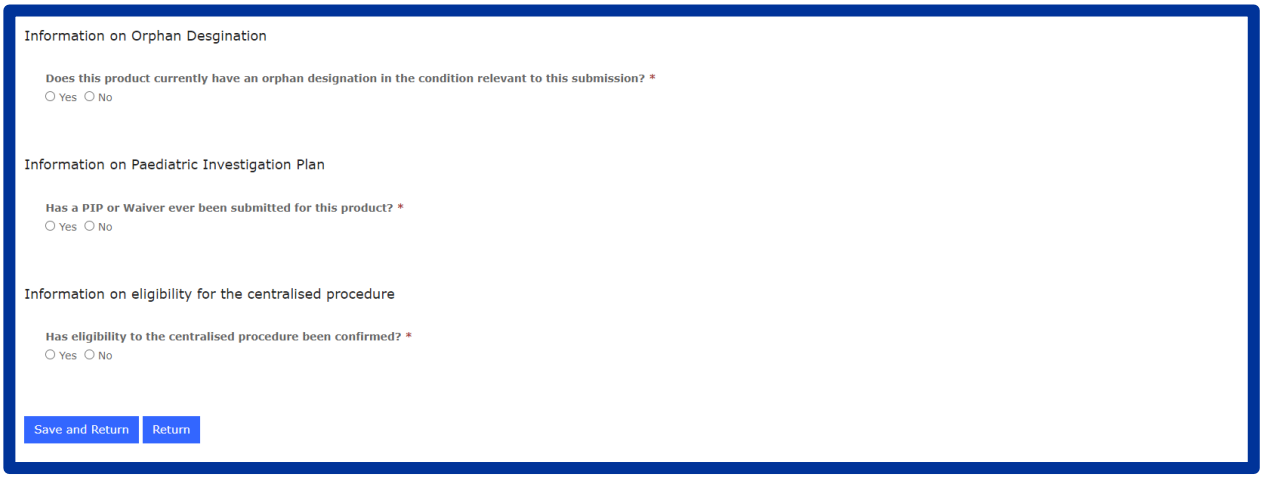
- If the product currently holds an "Early-Entry PRIME designation", please choose the PRIME designation number using the magnifying glass search symbol.
- If the current application is a "resubmission of a previously denied/withdrawn PRIME eligibility request", please choose the previous PRIME eligibility submission number.
- If a PRIME eligibility "pre-submission meeting" was held prior to the current submission, please enter the Pre-submission meeting date.
- If "National Scientific Advice" has been provided in the past, please add the relevant information by clicking on the "Add" button.

*Figure 63: Procedural Information*


- If the product holds an "Orphan Designation" in the condition relevant to this submission, please choose the Orphan Designation Number.

- If a "PIP or Waiver" has been submitted for this product, please enter the PIP/Waiver procedure number (e.g. EMEA-xxxxxx-PIPxx-xx). If a PIP or Waiver has not been submitted, please enter the date of planned PIP submission.
- If eligibility to the "centralised procedure" been confirmed for this product, please enter the corresponding Product Number (H000xxxx).

*Figure 64: Procedural information*

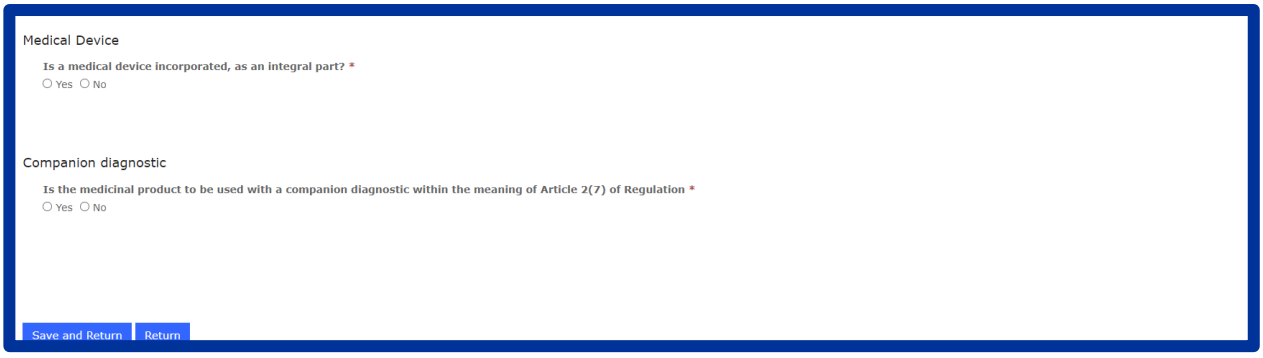



10. In section "**Scientific information**", please complete information on the condition to be treated by entering the "Proposed scope" (Treatment, Diagnosis or Prevention), the "Proposed Condition/Indication" and select all types of "data supporting the PRIME application".

*Figure 65: Scientific information*


11. Notes relating to medical devices and companion diagnostics should also be answered in this section.

*Figure 66: Information on Medical Device and Companion diagnostics*




12. Any additional comments on the submission can be included in section **"Submission Notes".**

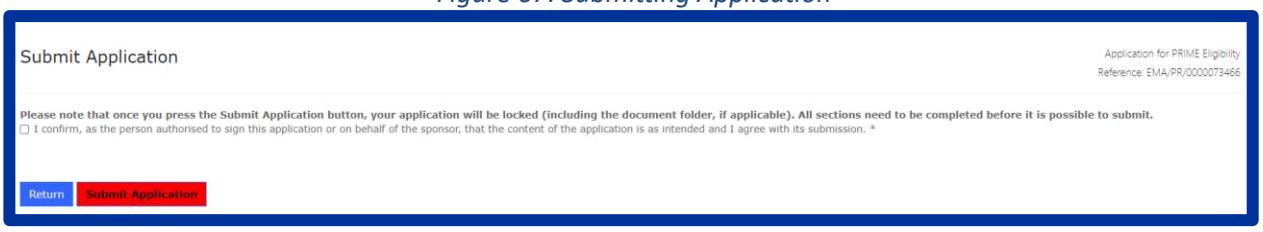
13. In section **"Documents from Applicant"**, the following documentation should be uploaded, named according to the naming conventions below:

- PRIME eligibility request – Applicant's justification: the file name should be composed as follows: PRIME eligibility submission number (e.g., EMA/PR/0000001234) – RPI number – request justification.
- References: the file (Zip) name should be composed as follows: PRIME eligibility submission number (e.g., EMA/PR/0000001234) – RPI number – references
- Any additional documentation may be submitted by clicking on the "Add" button.
- You may wish to generate a Word file copy of the Application Form by clicking on the "Generate Application Form" button at the bottom of the "Submission Form" page. The file will appear automatically in the "Documents from Applicant" section.
- Please confirm that you have uploaded all documents that may be relevant to the submission.

After the outcome of the PRIME eligibility application is finalised, the Outcome Letter will become available in the section **"Documents from EMA".**

14. Please make sure that the required sections have a green tick to the right (except from "Documents from EMA") before **submitting the application**.

*Figure 67: Submitting Application*




You may review your draft application before submitting by clicking on the "Review Application" button in the pop-up box.

To see the status of your PRIME Eligibility applications (draft and submitted), go to the IRIS home page, click on the **"Submission"** tab and choose one of the three sub-tabs:

- on the "**Draft submissions**" sub-tab you can see a list of all your draft applications; from here you can edit, delete, view/manage the managers, contributors and contact person for each draft application before finalising the submission.

- on the "**Ongoing submissions**" sub-tab you can see a list of all your ongoing submissions and the evaluation status of the submitted case; from here you can edit, view/manage the managers, contributors, and contact person for each submission.
- on the "**Completed Submissions**" sub-tab you can view of all your completed submissions, the outcome and change the submission contact person.

Click on the drop-down arrow tab to perform all above modifications.

### *10.2 Transfer of a PRIME Regulatory Entitlement*

Step-by-step guidance on how to create a submission, please refer to the generic steps described in section 2.3.

For process specific step, please follow the steps below:

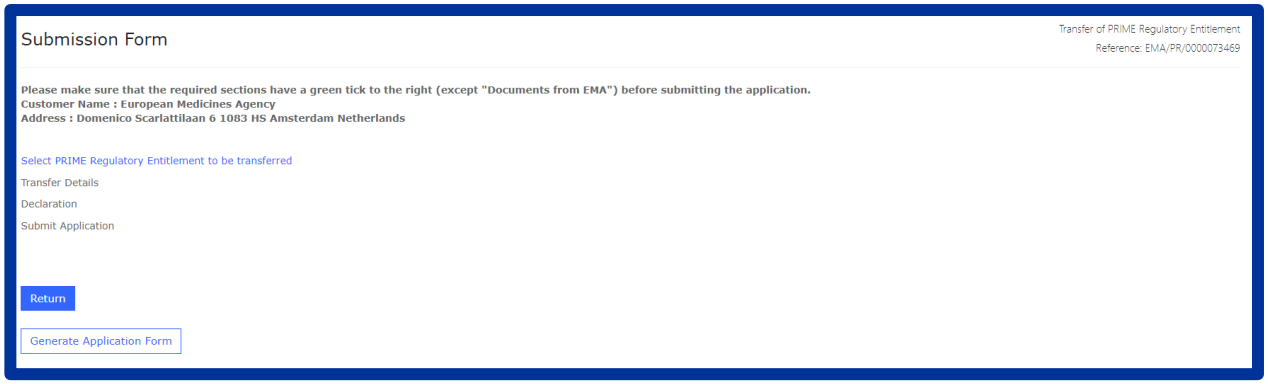
1. When choosing submission type, click on the magnifying glass symbol in the drop-down list and type in a keyword (e.g., PRIME) or the process type you wish to apply for (**e.g. Transfer of PRIME Regulatory Entitlement**) and then on "Select"; click "Create and Next".

*Figure 68: New Draft Submission*


2. Click "**Continue to Submission Form**".

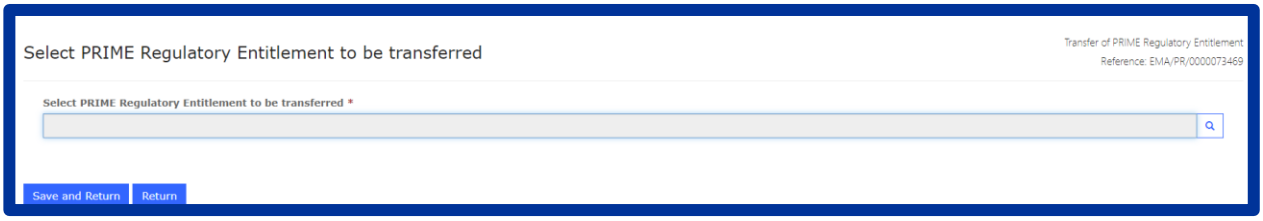
There is a Submission form list of four steps (tabs) starting with "**Select PRIME Regulatory Entitlement to be transferred**" and ending with "**Submit Application**" relating to your **"Transfer of PRIME Regulatory Entitlement"** application; the application reference number will contain PR (e.g., EMA/PR/0000001234) and displayed on the upper right-hand side of your screen;

*Figure 69: Submission Form steps*




3. In section "**Select PRIME Regulatory Entitlement to be transferred**", use the search symbol to look up the number of the PRIME Regulatory Entitlement to be transferred and then click on "Select"; click "Save and Return".

*Figure 70: Select PRIME Regulatory Entitlement to be transferred*




4. In section "**Transfer Details**", use the search symbol to look up the details of the new organization to which the PRIME Regulatory Entitlement will be transferred.

*Figure 71: Transfer Details*


5. In section "**Declaration**", tick the box to confirm as the person authorised to submit this application or on behalf of the applicant, that the content of the application is accurate and agree to the submission.

*Figure72: Declaration*


6. Please make sure that all the required sections have a green tick to the right before submitting the application.

You may generate a Word file copy of the Application Form by clicking on the "**Generate Application Form"** button at the bottom of the "**Submission Form**" page. The file will appear automatically in the

Please note that once you press the Submit Application button, your application will be locked.

Should you wish to **withdraw** your "**Transfer of PRIME Regulatory Entitlement**" application, you may do so from the "**Ongoing submissions**" sub-tab by clicking on the drop-down arrow tab on the right-hand side of your application (View/Edit Submission option).

### *10.3 Withdrawal of a PRIME Regulatory Entitlement*

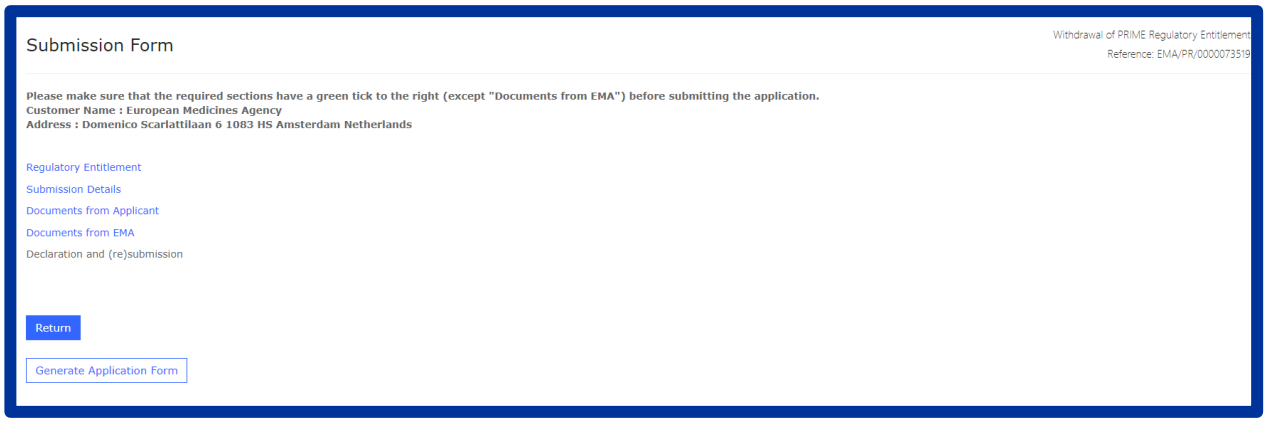
Step-by-step guidance on how to create a submission, please refer to the generic steps described in section 2.3.

For process specific step, please follow the steps below:

1. When choosing submission type, click on the magnifying glass symbol in the drop-down list and type in a keyword (e.g., PRIME) or the process type you wish to apply for (**e.g., Withdrawal of PRIME Regulatory Entitlement**) and then on "Select"; click "Create and Next".

There is a Submission form, list of five steps (tabs) starting with "**Regulatory Entitlement**" relating to your "Withdrawal of PRIME Regulatory Entitlement" application.

*Figure 73: Submission Form steps*




2. In section "**Regulatory Entitlement**", use the search symbol to look up the number of the PRIME Regulatory Entitlement to be withdrawn and then click on "Select"; click "Save and Return".
3. In section "**Submission Details**", it is mandatory to provide a brief explanation detailing the reasons for the submission of the withdrawal of this regulatory entitlement.

4. In section “**Documents from Applicant**”, please upload any documents that may be relevant to the submission.
5. Please make sure that all the required sections (except from "Documents from EMA") have a green tick to the right before submitting the application.

You may generate a Word file copy of the Application Form by clicking on the “Generate Application Form” button at the bottom of the “**Submission Form**” page. The file will appear automatically in the “**Documents from Applicant**” section.

Please note that once you press the Submit Application button, your application will be locked (including the document folder, if applicable). You may review your draft application before submitting by clicking on the “Review Application” button in the pop-up box.

Should you wish to **withdraw** your “**Withdrawal of PRIME Regulatory Entitlement**” application, you may do so from the “**Ongoing submissions**” sub-tab by clicking on the drop-down arrow tab on the right-hand side of your application (View/Edit Submission option).

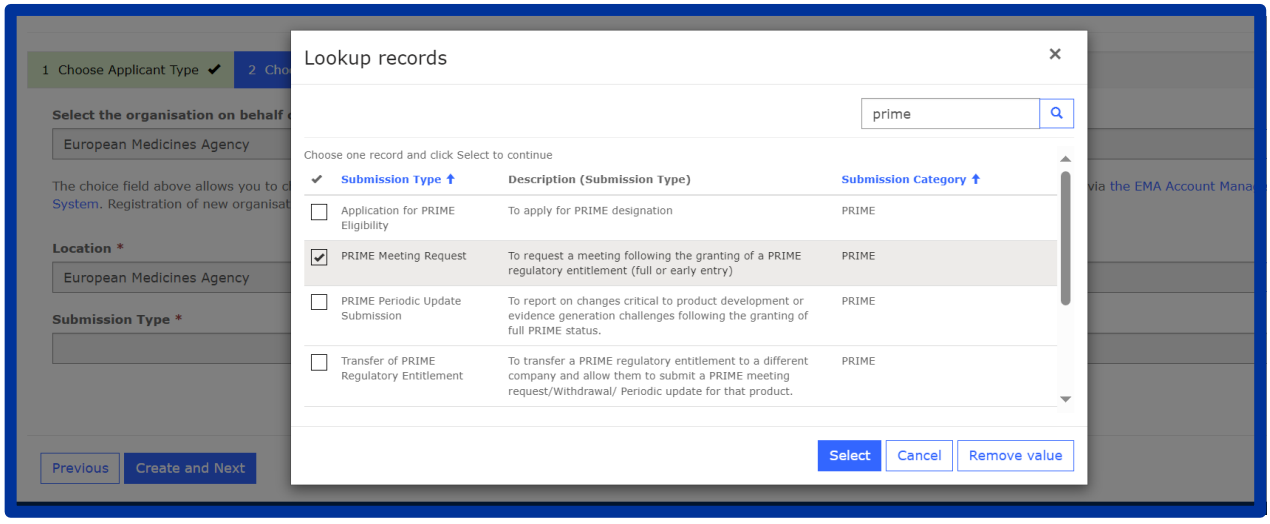
### *10.4 Submission of a PRIME Meeting Request*

Step-by-step guidance on how to create a submission, please refer to the generic steps described in 2.3.

For process specific step, please follow the steps below:

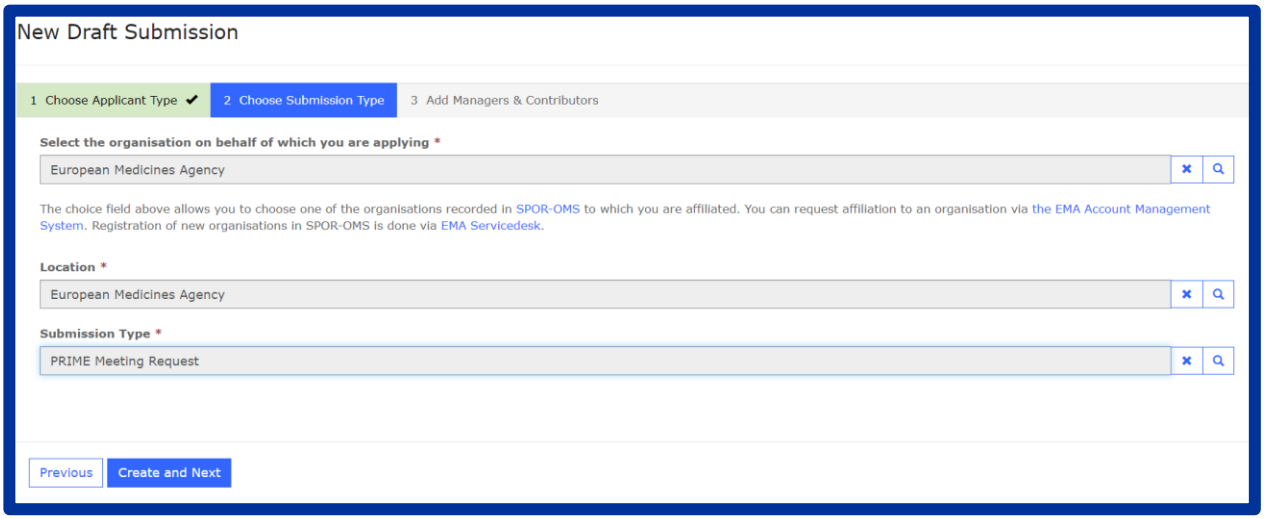
1. When choosing the submission type, **“2. Choose Submission Type”** click on the magnifying glass symbol in the drop-down list and type in a keyword (e.g., PRIME) or the process type you wish to apply for (e.g. **PRIME Meeting request**).

*Figure 74: Select Submission Type*




2. Once all three fields in step 2 are selected click “Create and Next”.

*Figure 75: Submit Submission Type*




3. In the Submission form there is a list of four steps (tabs) starting with **"Meeting Information"** and ending with **"Submit Application"** relating to the PRIME Meeting Request displayed on the left-hand side of your screen.

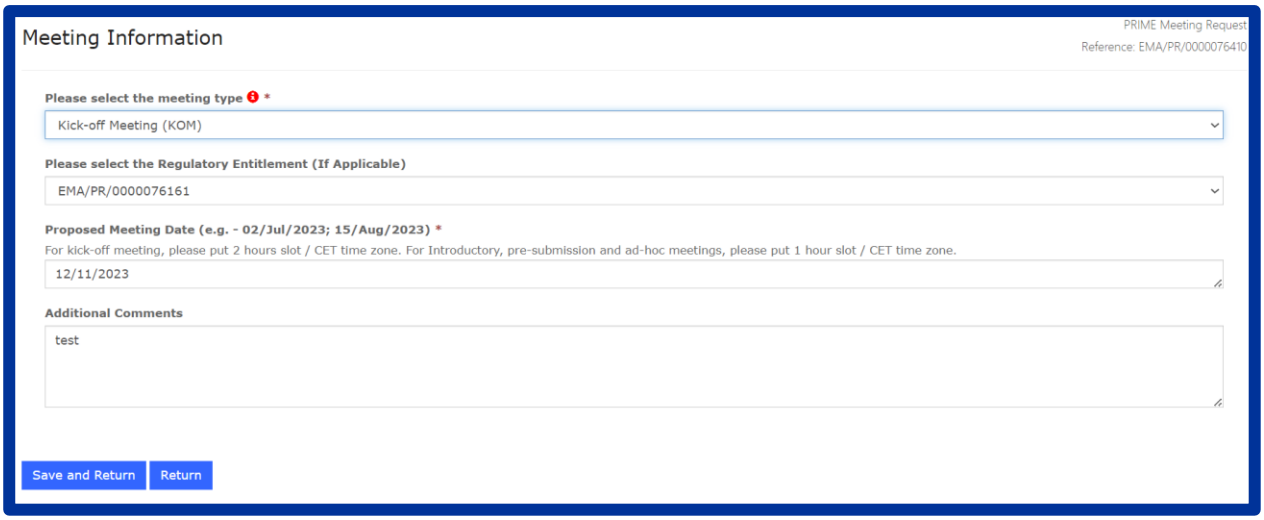
*Figure 76: Submission from steps*


4. In the "**Meeting Information"** tab, you need to choose the correct meeting type (Kick Off Meeting (KOM), Introductory meeting, Ad-hoc meeting, Submission readiness meeting and Pre-submission meeting).

*Figure 77: Submission from steps - Meeting information*

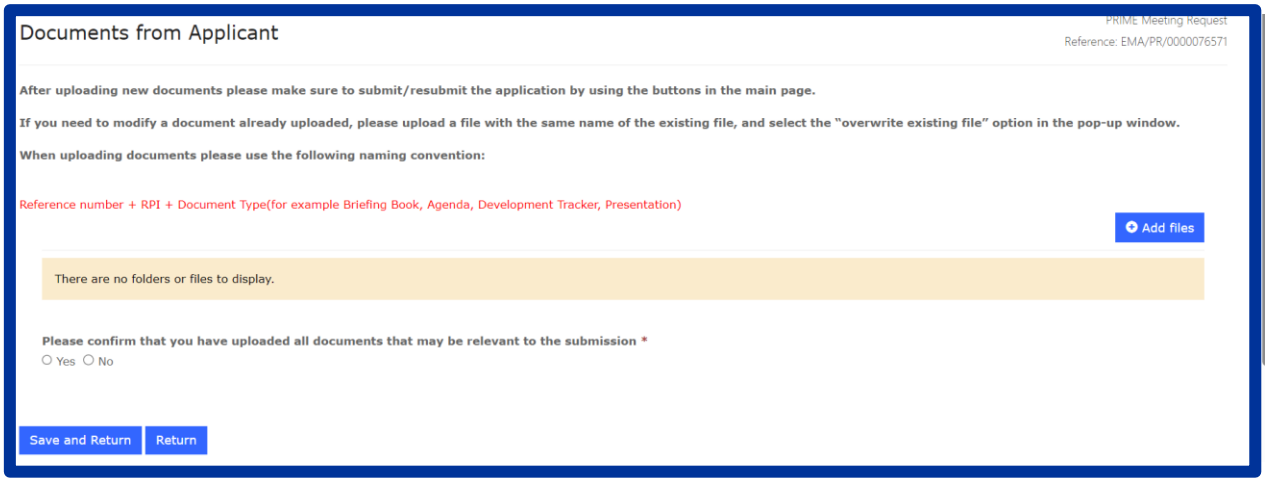

5. In the next steps, you need to first select the relevant (if any) **PRIME Regulatory Entitlement**, propose up to 5 possible **dates** for the meeting and add any **additional comments**. Kick-Off meeting and submission readiness meeting can only be requested if there is a full PRIME designation on the product. For early entry PRIME designations, please select Introductory meeting type. Ad-hoc meeting can be requested if the applicant has any type of PRIME regulatory entitlement, regardless of the type. Pre-submission meeting request is not inked to any regulatory entitlement.

*Figure 78: Submission From steps – Meeting information*




6. In the "**Documents from Applicants"** tab, you need to submit all relevant documentation for the requested meeting. Please follow the naming convention as Reference number + RPI + document type. For example: EMA/PR/0000076571 - PRD/0001234 – Briefing Book

*Figure 79: Submission from steps – Documents from Applicant*



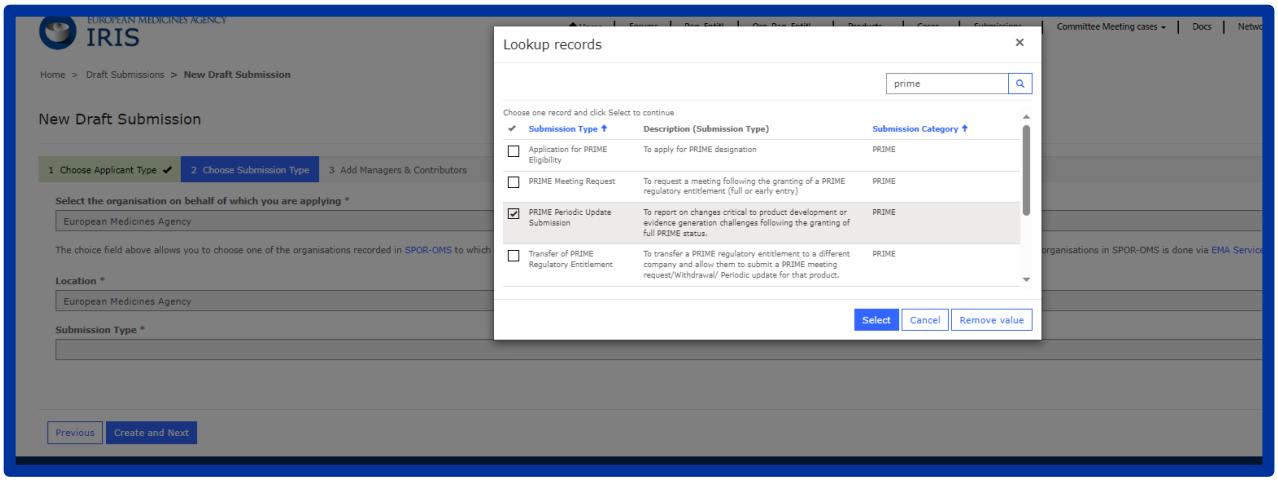

### *10.5 Submission of a PRIME Periodic Update*

Step-by-step guidance on how to create a submission, please refer to the generic steps described in section 2.3.

For process specific step, please follow the steps below:

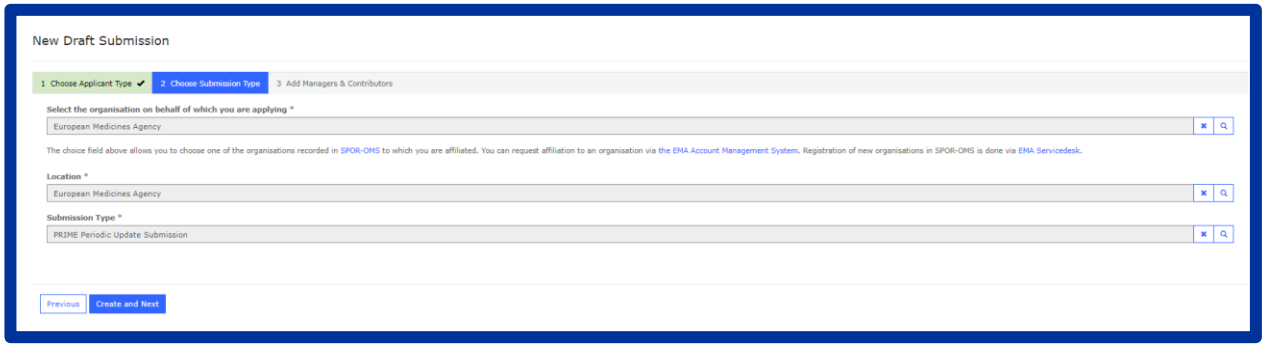
1. When choosing the submission type, **"2. Choose Submission Type"** click on the magnifying glass symbol in the drop-down list and type in a keyword (e.g., PRIME) or the process type you wish to apply for (e.g. **PRIME Periodic Update Submission**).

*Figure 80: Select Submission Type*



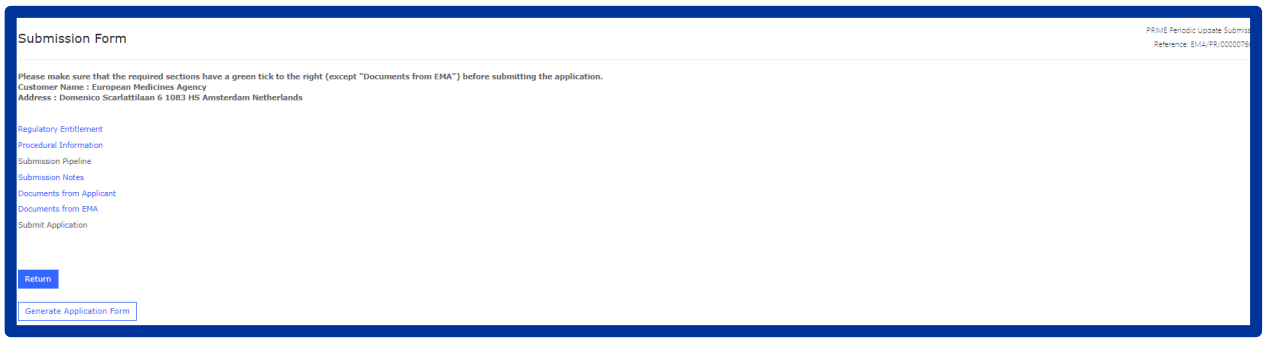

2. Once all three fields in step 2 are selected click "Create and Next".

*Figure 81: Submit Submission Type*



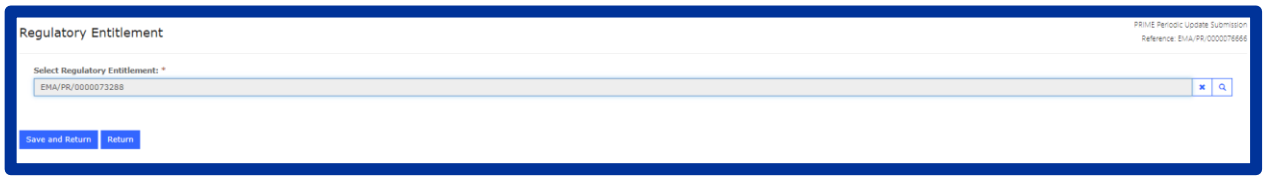

3. In the Submission form there is a list of seven steps (tabs) starting with **"Regulatory Entitlement"** and ending with **"Submit Application"** relating to the PRIME periodic update submission displayed on the left-hand side of your screen.

*Figure 82: Submission form steps*




4. In the "**Regulatory Entitlement"** tab, you need to choose the correct regulatory entitlement for which you wish to submit the periodic update and proceed to the next step by clicking on save and return.

*Figure 83: Submission form steps – Regulatory Entitlement*




5. In the "**Procedural Information"** tab, you need to indicate if *development is still ongoing* for the designated product/indication. In case the development is discontinued, the reasons must be explained in the next field called *"Reasons for discontinuation of development"*, which is a free text field. If PIP has been agreed the *PIP number* should be indicated in the next field. In case *scientific advice* has been received since the last periodic update, this must be recorded in the next section, by indicating the advice number. Finally, if *expedited advice* is requested with the submission of the periodic update, the area and some details must be explained in the last two free text fields. Please note that the expedited scientific advice referred to in the periodic update is a separate procedure and this request will have to be separately submitted.

*Figure 84: Submission form steps – Procedural Information*


6. In the "**Submission pipeline"** tab, the system displays **submission pipeline information** that is recorded on PRI "Information on Submission Pipeline (Please note this is read only from RPI)". Please check this information and, if changes are applicable to the either the MAA submission date or the legal basis, update in the "Update Information on Submission Pipeline" section and provide explanation for the proposed change in the free text box. Please note that any changes made in these fields will result in also updating the information of the RPI record.

*Figure 85: Information on Submission Pipeline*

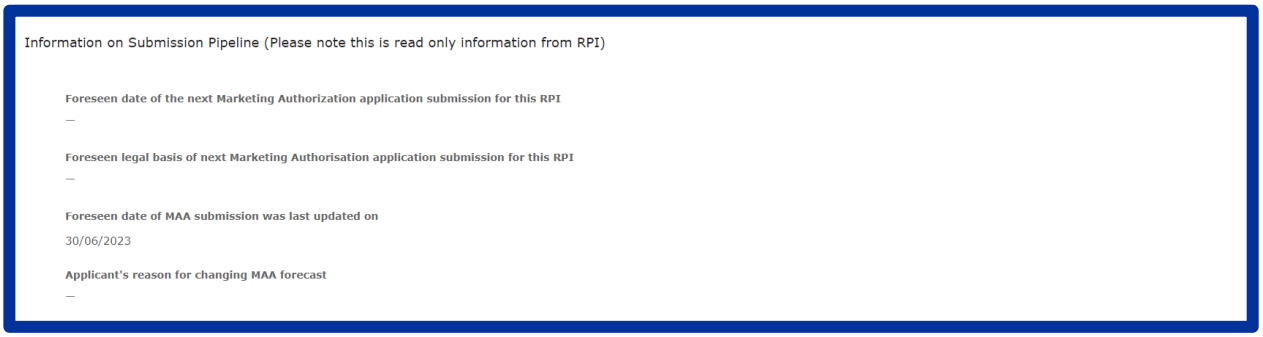
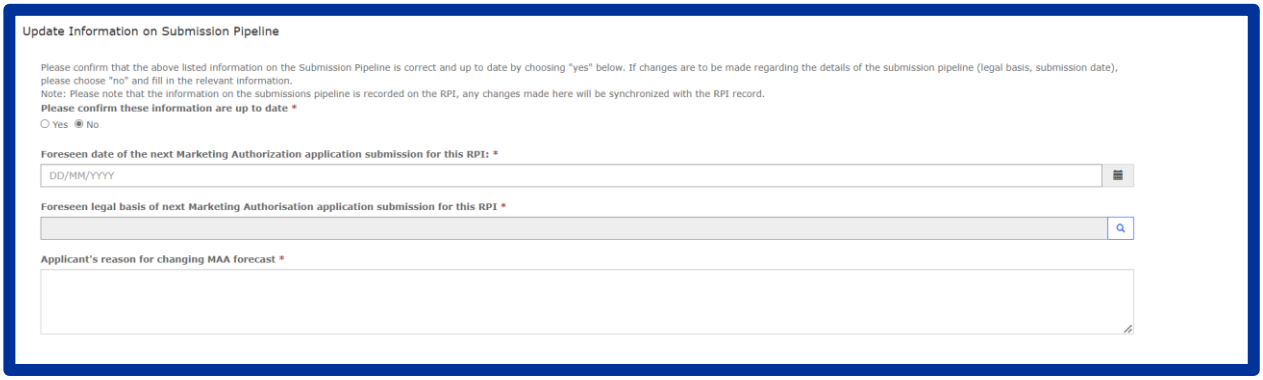


*Figure 86: Update Information on Submission Pipeline*




7. Once all the other steps have been completed the application can be submitted by the authorised person as for the other PRIME related procedures.

*Figure 87: Submitting the application*