



**31 March 2022**

EMA/444925/2018

## IRIS guide for applicants

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

Version 2.7

<b>Table of abbreviations.....</b>	<b>3</b>
<b>1. Purpose and context.....</b>	<b>4</b>
1.1. Purpose of this guide.....	4
1.2. Preliminary requirement.....	4
1.3. Supported Browsers.....	4
<b>2. Common operations for all scientific submission types.....</b>	<b>4</b>
2.1. Display and sort submissions.....	4
2.2. Search for submissions.....	4
2.3. Create a new submission (general procedure for all submission types).....	5
2.4. Communication only to the Submission Contact (Portal contact) for a submission.....	8
2.5. Add managers to a draft/ongoing submission.....	9
2.6. Add contributors to a draft submission.....	10
2.7. Delete a draft submission.....	10
2.8. Withdrawal of a Submission.....	10
2.9. Automatic deletion of draft submissions.....	11
2.10. Respond to a notification email from EMA requesting changes.....	11
2.11. Respond to a List of Questions (LoQ) request.....	12
2.12. Check the current status of an ongoing Submission in the IRIS Portal.....	12
2.13. Regulatory Entitlements Affiliation.....	13
2.13.1. Regulatory Entitlements.....	13
2.13.2. My Individual Regulatory Entitlements.....	13
2.14. Products - Research Product Identifiers (RPI).....	14

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<b>3. Orphan submissions .....</b>	<b>15</b>
3.1. Create an application for orphan designation.....	15
3.2. Request a Pre-Submission Meeting (for OD).....	15
Request an Appeal (of a COMP Opinion) .....	16
3.3. Submit an Annual Report for an orphan designation.....	16
3.4. Other post-designation procedures for orphan-designated products .....	17
3.5. How to check if an Orphan Drug Sponsor (Location of an organisation) has associated Regulatory entitlements .....	17
<b>4. Scientific Advice .....</b>	<b>17</b>
4.1. Create an application for an Initial Scientific Advice (Human) .....	17
4.2. Create an application for other Scientific Advice procedures .....	18
4.2.1. Initial Scientific Advice – Veterinary .....	18
4.2.2. Initial Protocol Assistance.....	19
4.2.3. Initial Qualification Procedure.....	19
4.2.4. Follow up Scientific Advice – Human.....	19
4.2.5. Follow up Scientific Advice – Veterinary .....	19
4.2.6. Follow up Protocol Assistance.....	20
4.2.7. Follow up Qualification Procedure .....	20
4.2.8. Transfer a Scientific Advice.....	20
4.2.9. Clarification on Scientific Advice .....	21
4.2.10. Scientific Advice FAQ.....	22
<b>5. ITF Briefing Meeting Requests.....</b>	<b>22</b>
<b>6. Marketing Status .....</b>	<b>23</b>
6.1. Marketing Status Notification (Single) .....	24
6.2. Marketing Status Notification (Bulk Upload).....	27
6.3. Marketing Status Withdrawal Notification.....	31
6.4. Marketing Status Report .....	33
<b>7. Inspections.....</b>	<b>35</b>
7.1. GMP inspections.....	35
7.2. GCP Inspections .....	38
<b>8. Veterinary Signal Management.....</b>	<b>39</b>
8.1. Annual statements submission .....	40
8.2. Signal management submission .....	40

## Table of abbreviations

<b>Abbreviation</b>	<b>Explanation</b>
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
EU	European Union
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
IAM	Identity & Access Management
ITF	Innovation Task Force
LoQ	List of Questions
MS	Member State
OD	Orphan Designation
OMS	Organisation Management Service (part of SPOR)
PD	Parallel Distribution
RPI	Research Product Identifier
SA	Scientific Advice
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

1. 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;
2. 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);
3. 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

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

2. 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;
3. Click on the magnifying glass search symbol or press "Enter" on your keyboard to launch the search;
4. 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;
5. 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

The screenshot displays the IRIS 'Draft Submissions' interface. At the top, there is a navigation bar with 'Home', 'Forums', 'Submissions', and 'My Organisations Regulatory Entitlements'. Below this, the breadcrumb 'Home > Draft Submissions' is visible. The main heading 'Draft Submissions' is highlighted with a red box. A search bar and a 'Create new submission' button are located above the table. The table contains the following data:

Parent Submission ID	Submission ID	Submission Type	Sponsor	Subject	Modified On
EMA/SA/0000170821	EMA/SA/0000170821	Initial Scientific Advice - Human	Office of Health	(-)-(R)-3-(2-HYDROXYMETHYLINDANYL-4-OXY)PHENYL-4...	15/09/2020 11:19 AM
EMA/SA/0000171073	EMA/SA/0000171073	Initial Protocol Assistance	Office of Health		14/09/2020 3:56 PM
EMA/SA/0000171072	EMA/SA/0000171072	Initial Protocol Assistance	Office of Health		14/09/2020 3:49 PM
EMA/OD/0000171071	EMA/OD/0000171071	Application for Orphan Designation	Office of Health	(-)-(R)-3-(2-HYDROXYMETHYLINDANYL-	14/09/2020 3:22 PM

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

1. From the IRIS home page, click on "Draft submissions" sub-tab present under "Submission" tab;
2. 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];
3. 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";
4. Only if you are applying on behalf of an organisation:

- a) 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);
  - b) Pick the right organisation and (there may only be one) and click “**Select**”;
  - c) 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.**
5. “**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**”;
  6. 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;
  7. 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*

**Submission Form**

Initial Scientific Advice - Human  
Reference: EMA/SA/0000170821

Please make sure that the required sections have a green tick to the right (except “Documents from EMA”) before submitting the application.  
(Note: the “Documents from EMA” section is not relevant for Marketing Status Reporting submissions and therefore does not appear).

Customer Name : Office of Health  
Address : Åulestrasse 512 Vaduz 9490 Liechtenstein

- Administrative Information ✓
- Select Primary RPI ✓
- Additional information on product ✓
- Add Additional RPIs ✓
- Procedural Information ✓
- Scientific Information ✓
- Parallel Consultation EMA / EUnetHTA ✓
- Documents from Applicant ✓
- Documents from EMA
- Declaration ✓
- Submit Application

[Return](#) [Generate Application Form](#)

8. Click on **“Select RPI”** to bring up **“Research Product Identifier (RPI)”** screen:
  - a. Click the **magnifying glass** search symbol to bring up a list of RPI names;
  - b. In the pop-up window, pick an RPI name from the list and click **“Select”**;
  - c. 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](mailto:ITFSecretariat@ema.europa.eu) or [SA\\_Submissions@ema.europa.eu](mailto:SA_Submissions@ema.europa.eu) beforehand (depending on your intended procedure type). You will be requested to complete a specific Word form. Upon receipt of the form the secretariat will create an RPI for you. These ‘special’ RPIs cannot be requested via IRIS.
9. Click on **“Additional product information/update”**:
    - a. Make sure that the list of innovation/enabling technologies includes at least one term; if not, choose at least one with the **“Add”** button;
    - b. Click **“Save and return”**.
  10. 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;
  11. Back in the main **“Submission Form”** Screen, click on **“Documents from Applicant”**:

- a. In the next screen that appears, you can directly upload documents and create subfolders in 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. A Zip file is acceptable only as the container for the literature references;
  - b. Click **“Save and Return”** when you have finished uploading documents;
12. 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;
13. 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”**;
14. When you are ready to submit your final application, click on **“Declaration and re(submission)”**:
- a. **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;
  - b. Click on the **“Declaration and submission”** button;
  - c. 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;
  - d. 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.

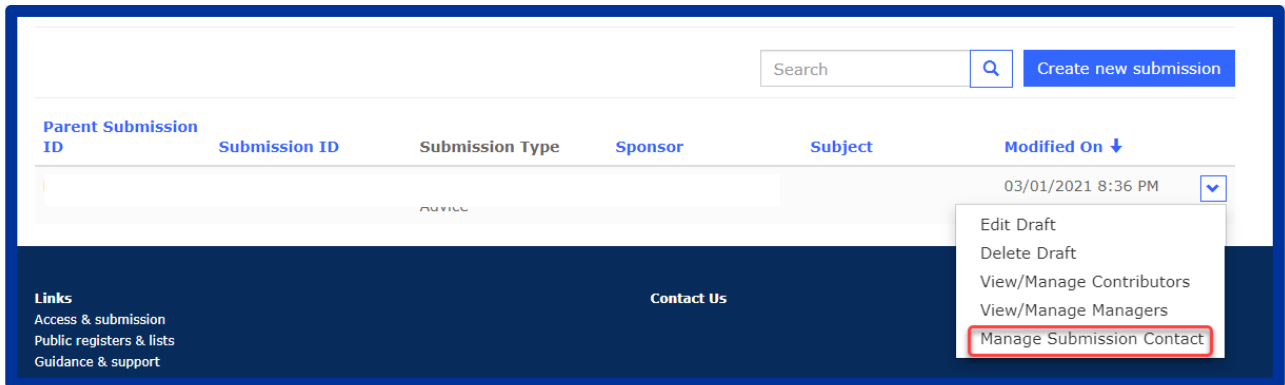
Applicants can nominate additional Industry managers and reassign the "submission contact" role as required, for example before a period of leave of the "submission contact". This can be done in IRIS, by clicking on the V to the right of the submission and selecting "Manage submission contact", as shown 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;
6. 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):

1. Click on **“Draft submissions”** 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 Contributors”**;
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 **“Continue to submission form”**;
6. 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*

Home > Ongoing Submissions > **Submission Form**

Annual Report  
Reference: EMA/OD/0000056341

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**Submission Form**

Customer Name : European Medicines Agency  
Address : 30 Churchill Place London E14 5EU United Kingdom

Regulatory Entitlement ✔

Scientific Content ✔

Submission Notes ✔

Documents from Applicant

Documents from EMA

Declaration and (re)submission ✔

[Return](#)

[Withdraw Submission](#) [Generate Application Form](#)

### **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*

<b>Submission Status</b>	<b>Notes</b>
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

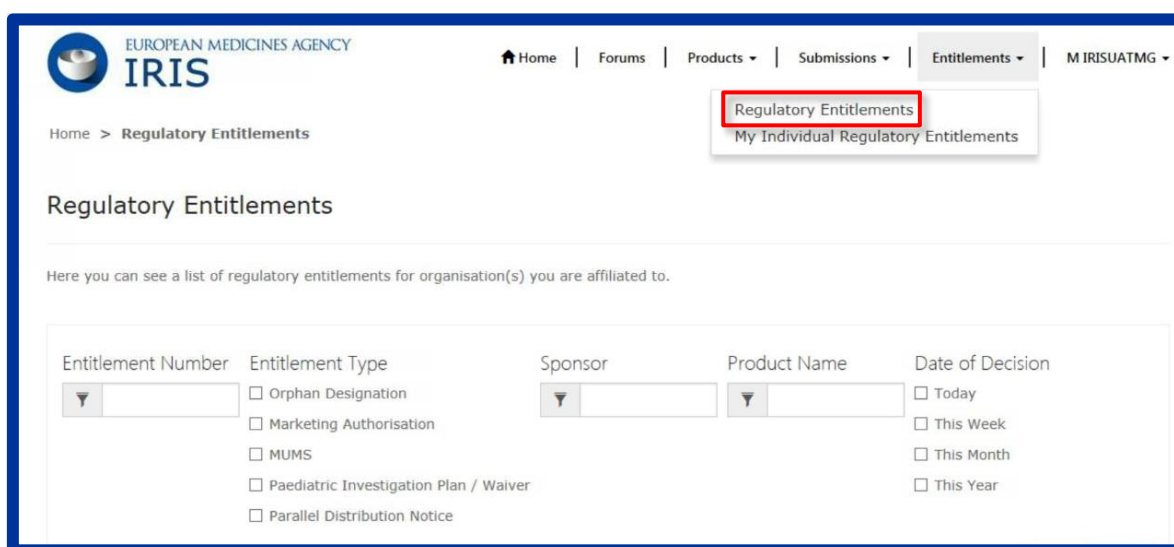
Withdrawal Requested	The applicant has requested a withdrawal, which is being assessed at EMA.
Completed-Positive	Case closed, positive outcome
Completed-Negative	Case closed, negative outcome
Completed-Withdrawn	Case closed as withdrawn, at the applicant's request.
Completed -Cancelled	Inspection request 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).

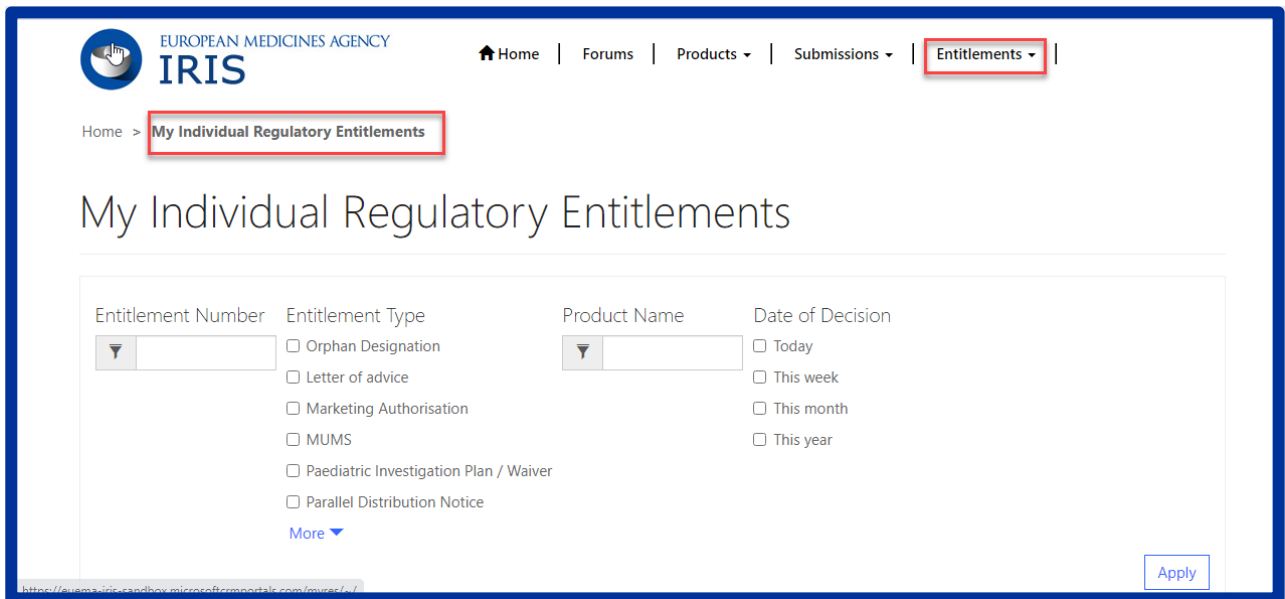
Figure 6: Regulatory Entitlements



### 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

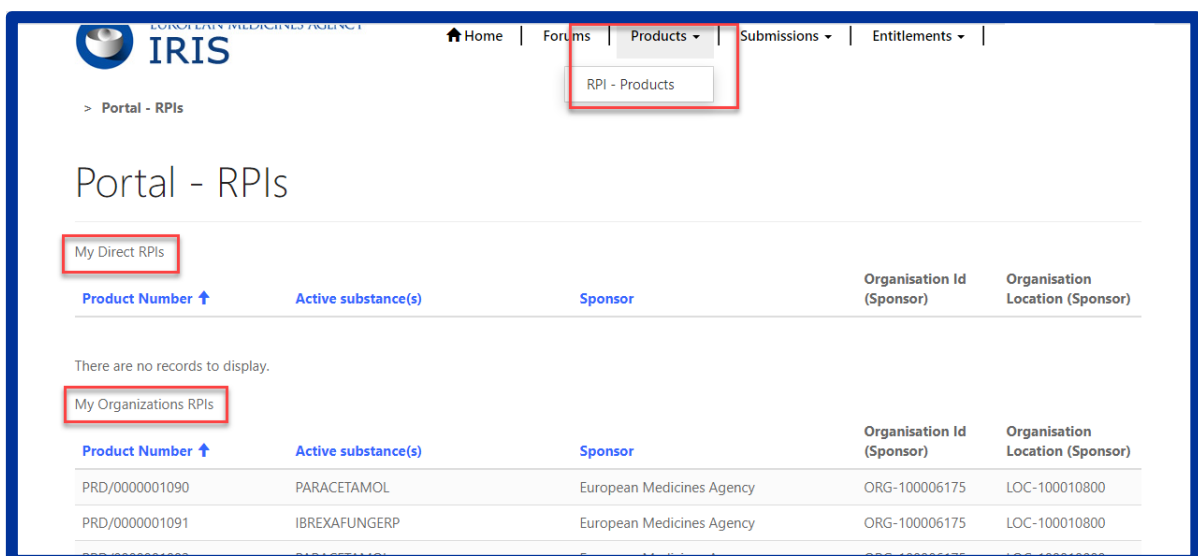


#### 2.14. Products - Research Product Identifiers (RPI)

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).

1. “**My Direct RPIs**”, which displays all active RPIs for which you are a direct sponsor.
2. “**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

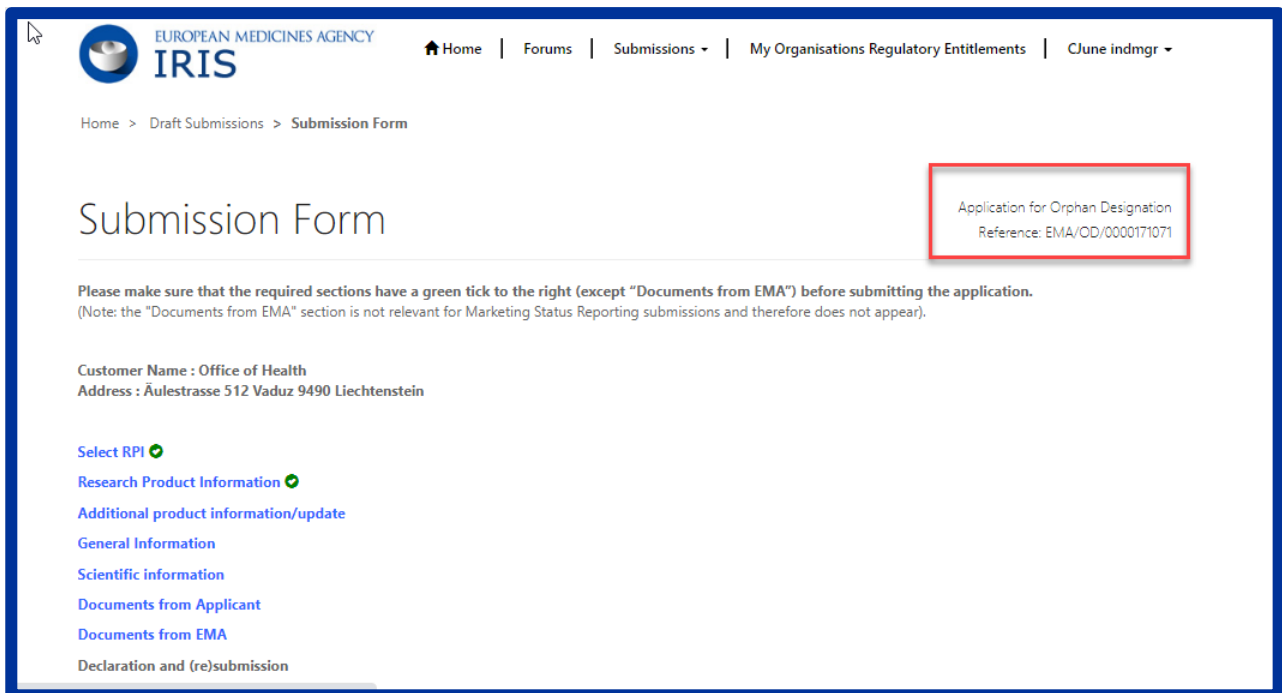
For general information on orphan designation and allied procedures, please consult the Orphan Designation page of the EMA website. For specific information on how to prepare a specific Orphan submission, including how to prepare the Scientific Document, please see the specific sections on the Orphan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

1. 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 screenshot shows the 'Submission Form' page in the IRIS system. At the top, there is a navigation bar with the EMA logo, 'EUROPEAN MEDICINES AGENCY', and 'IRIS'. The navigation menu includes 'Home', 'Forums', 'Submissions', 'My Organisations Regulatory Entitlements', and 'Clune indmgr'. Below the navigation bar, the breadcrumb trail reads 'Home > Draft Submissions > Submission Form'. The main heading is 'Submission Form'. A red box highlights the text 'Application for Orphan Designation' and 'Reference: EMA/OD/0000171071'. Below this, there is a note: 'Please make sure that the required sections have a green tick to the right (except "Documents from EMA") before submitting the application. (Note: the "Documents from EMA" section is not relevant for Marketing Status Reporting submissions and therefore does not appear)'. The customer information is 'Customer Name : Office of Health' and 'Address : Åulestrasse 512 Vaduz 9490 Liechtenstein'. The form sections are listed on the left: 'Select RPI' (with a green tick), 'Research Product Information' (with a green tick), 'Additional product information/update', 'General Information', 'Scientific information', 'Documents from Applicant', 'Documents from EMA', and 'Declaration and (re)submission'.

2. 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)

1. **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;

2. Select **“Request for Pre-Submission Meeting”** as submission type;
3. 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);
4. 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”**;
5. Follow steps 13 and 14 from Section 2.3. **“Create a new submission (general procedure for all submission types)”** above;
6. Your request for a Pre-Submission Meeting has now been submitted and will appear in your **“Ongoing Submissions”** list.

### ***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”**;

### ***3.3. 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**”.

### **3.4. 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.

### **3.5. 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](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:

1. 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;
2. 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);
3. 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;
4. 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).
5. 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

EUROPEAN MEDICINES AGENCY  
**IRIS**

Home | Forums | Submissions ▾ | My Organisations Regulatory Entitlements | Clune indmgr ▾

Home > Draft Submissions > Submission Form > Add Additional RPIs

Add Additional RPIs Initial Scientific Advice - Human  
Reference: EMA/SA/0000170821

Selected primary RPI for this submission \*

PRD/0000069803

Please select additional RPI(s) for any other product to be associated to this submission

**Add RPI**

Product Number ↑	Domain	Active substance(s)	Other names
There are no records to display.			

Please confirm that all additional RPI(s) have been associated with the submission \*

## 4.2. Create an application for other Scientific Advice procedures

### 4.2.1. 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.

#### 4.2.2. 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).

#### 4.2.3. 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:

1. Select “**Initial Qualification Procedure**” as submission type.

#### 4.2.4. 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:

2. Select “**Follow up Scientific Advice-Human**” as submission type;
3. 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;
4. 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);
5. 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.

#### 4.2.5. 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).

#### 4.2.6. 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 Advice”** 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).

#### 4.2.7. 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.

#### 4.2.8. 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:

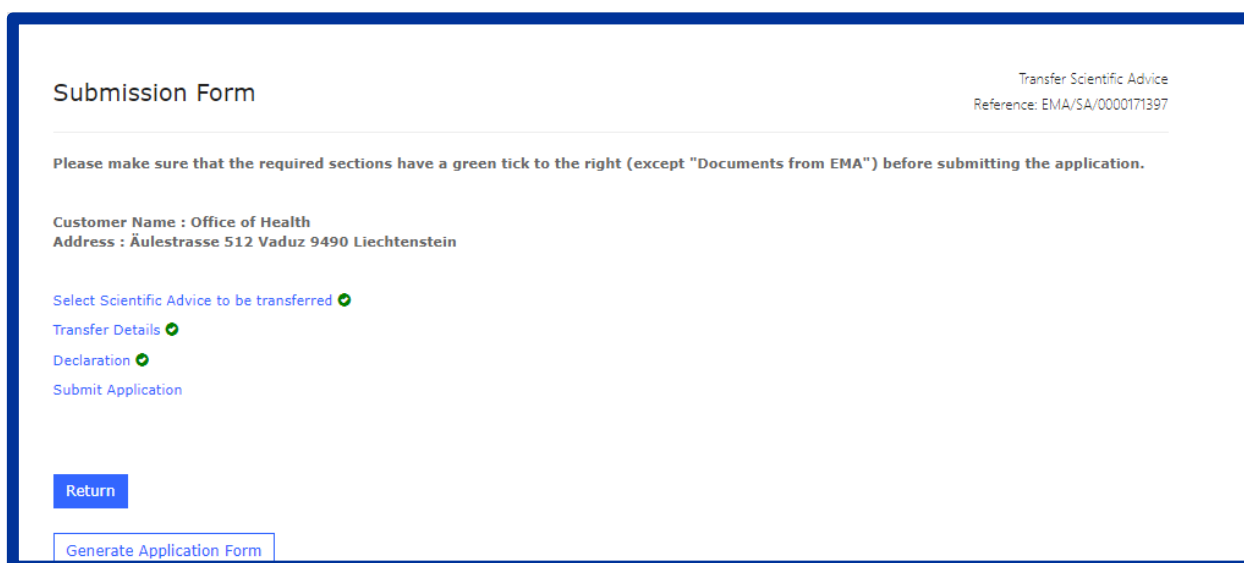
- Select **“Transfer a scientific Advice”** as submission type.
- The reference number will contain SA (e.g. EMA/SA/0000001234) for your draft submission displayed on the upper right-hand side of the “Portal – New Submission” screen;

The following four tabs will appear as shown in Figure 11:

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 11 Transfer Scientific Advice*



The screenshot shows a web interface for 'Transfer Scientific Advice'. At the top right, it displays 'Transfer Scientific Advice' and 'Reference: EMA/SA/0000171397'. Below this is a header 'Submission Form'. A message states: 'Please make sure that the required sections have a green tick to the right (except "Documents from EMA") before submitting the application.' Underneath, customer details are listed: 'Customer Name : Office of Health' and 'Address : Äulestrasse 512 Vaduz 9490 Liechtenstein'. A list of tabs is shown: 'Select Scientific Advice to be transferred' (with a green tick), 'Transfer Details' (with a green tick), 'Declaration' (with a green tick), and 'Submit Application'. At the bottom left is a blue 'Return' button, and at the bottom center is a 'Generate Application Form' button.

#### 4.2.9. 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 12). Once added, click on **“Save and Return”**;

*Figure 12 adding notes for clarification*

The screenshot shows a web form titled "Grounds for Clarification". In the top right corner, it says "Clarification on Scientific Advice" and "Reference: EMA/SA/0000171401". Below the title, there is a sub-header "Grounds for Clarification" followed by a prompt: "Please state grounds for clarification below \*". A large text input area contains the word "testing". At the bottom left of the form, there is a blue button labeled "Save and Return".

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.

#### 4.2.10. 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

1. **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.
2. **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.
3. **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 6.3.

### 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) Alternatively, you can also use Marketing Status Notification (Bulk)
How to report <b>temporary</b> marketing cessation of all presentations in all EU MS	Marketing Status Notification (Single) 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) 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
How to report the <b>permanent</b> cessation of all presentations in all EU/EEA MS. (Sunset clause will be triggered)	Marketing status Withdrawal notification
How to report the <b>temporary</b> cessation of all presentations in all EU/EEA MS. (Sunset clause will be triggered)	Marketing Status Notification (Single) 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 13);

*Figure 13 Marketing Status Single Notification*

The screenshot shows a web interface for a 'Submission Form'. At the top, there is a breadcrumb trail: 'Home > Draft Submissions > Submission Form'. The main title is 'Submission Form' and the subtitle is 'Marketing Status Notification (Single)'. A reference number 'EMA/PA/0000056130' is displayed. Below this, a message states: 'Please make sure that the required sections have a green tick to the right (except "Documents from EMA") before submitting the application.' The user's details are listed as 'Customer Name : European Medicines Agency' and 'Address : 30 Churchill Place London E14 5EU United Kingdom'. A list of steps is provided: 'Select Authorised Product' (highlighted in blue), 'Register Marketing Status', 'View Proposed Marketing Status', 'Declaration', and 'Submit Application'. A 'Return' button is located at the bottom left.

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 14.

*Figure 14 - How to add Product Presentations*

Home > Draft Submissions > Submission Form > Current Market Report

Current Market Report Marketing Status Notification (Single)  
Reference: EMA/PA/0000056130

<b>Product *</b> PRD/0000003234	<b>Product Status (SIAMED)</b> Valid
<b>EU Number</b> EU/1/17/1181	<b>Reference Number (SIAMED)</b> PRD/0000003234
<b>Product Name</b> Spherox	<b>Active substance(s)</b> SPHEROIDS OF HUMAN AUTOLOGOUS MATRIX-ASSOCIATED CHONDROCYTE

**Current Market Report** Search

Name ↑	Nickname (Authorised Product)	Strength (Product Presentation)	Pharmaceutical form (Product Presentation)	Pack Size (Product Presentation)	Country ↑	Marketing Status	Date of Marketing Status Change	Reason for Cessation	Estimated date of Reintroduction
There are no records to display.									

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](#)

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

*Figure 15 Adding product presentation, Marketing Status & Member states*

Register Marketing Status Marketing Status Notification (Single)  
Reference: EMA/PA/0000056130

**Authorised Product \***  
PRD/0000003234

**Product \***  
PRD/0000003234

**EU Number**  
EU/1/17/1181

**Product Name**  
Spherox

**Marketing Status \***  
Not marketed

**Date of Marketing Status Change \***  
26/05/2021

**Product Status (SIAMED)**  
Valid

**Reference Product Identifier**  
PRD/0000003234

**Active substance(s)**  
SPHEROIDS OF HUMAN AUTOLOGOUS MATRIX-ASSOCIATED CHONDROCYTE

**Reason for Cessation \***  
01. Safety - Medicinal product is harmful (Articles 116 and 117)

**Does Cessation lead to Shortage? \***  
Yes

**Product Presentations** Add

EU Number ↑	Nickname	Marketed Country List	Not Marketed Country List	Temporarily Unavailable Country List
EU/1/17/1181/001	Spherox 10-70 spheroids/cm <sup>2</sup> - Implantation suspension			

**Member State** Add

Name ↑

Austria

Belgium

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 16 Viewing proposed presentations Figure 16 below. Click on **'Return'** after checking all information;

Figure 16 Viewing proposed presentations

Home > Draft Submissions > Submission Form > View Proposed Marketing Status

Marketing Status Notification (Single)  
Reference: EMA/PA/0000056130

View Proposed Marketing Status

Product  
PRD/0000003234

Proposed Marketing Status

	Nickname (Product Presentation)	Strength (Product Presentation)	Pharmaceutical form (Product Presentation)	Pack Size (Product Presentation)	Country	Marketing Status ↑	Date of Marketing Status Change	Reason for Cessation	Does cessation lead to Shortage?	Estimated date of Reintroduction
001	Spherox 10-70 spheroids/cm <sup>2</sup> - Implantation suspension	10-70 spheroids cm <sup>2</sup>	Implantation matrix	1 to 10 sterile tubes with up to 2 applicators each + 1 syringe per applicator	Austria	Marketed	26/05/2021	01. Safety - Medicinal product is harmful (Articles 116 and 117)	Yes	
001	Spherox 10-70 spheroids/cm <sup>2</sup> - Implantation suspension	10-70 spheroids cm <sup>2</sup>	Implantation matrix	1 to 10 sterile tubes with up to 2 applicators each + 1 syringe per applicator	Belgium	Marketed	26/05/2021	01. Safety - Medicinal product is harmful (Articles 116 and 117)	Yes	

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 [Service Desk Ticket](#) by selecting software 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:

1. Select the Authorised product in the section **“Select Authorised Product”**, click **‘Save & Return’**.
2. 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.
3. 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 1

Please note that the values in each column must be provided in a standardised format; refer to Figure 17 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 17 Format/Values for Fields in csv*

Data columns	format and allowed values
Marketing Status	Marketed Not marketed Temporarily unavailable Never marketed
Date of Marketing Status Change (format)	DD-MM-YYYY
Reason for Cessation	01. Safety - Medicinal product is harmful (Articles 116 and 117) 02. Efficacy - Medicinal product lacks therapeutic efficacy (Articles 116 and 117) 03. Benefit/risk - risk-benefit balance is not favourable (Articles 116 and 117) 04. Quality - Quantitative and qualitative composition of the medicinal product is not as declared (Articles 116 and 117) 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) 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) 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)

	08. Commercial reasons (excluding any ground of art 116 or 117)
Does Cessation lead to Shortage	Yes No
Country	ISO code (2 digit) AT,BE,BG,HR,CY,CZ,DK,EE,EL,FI,FR,DE,EL,HU,IS,IE,IT,LV,LI,LT,LU,MT,NL, NO,PL,PT,RO,SK,SI,ES,SE,XI

Figure 18 Download Excel

Home > Draft Submissions > Submission Form > Download Current Marketing Status

Download Current Marketing Status Marketing Status Notification (Bulk Upload)  
Reference: EMA/PA/00000252874

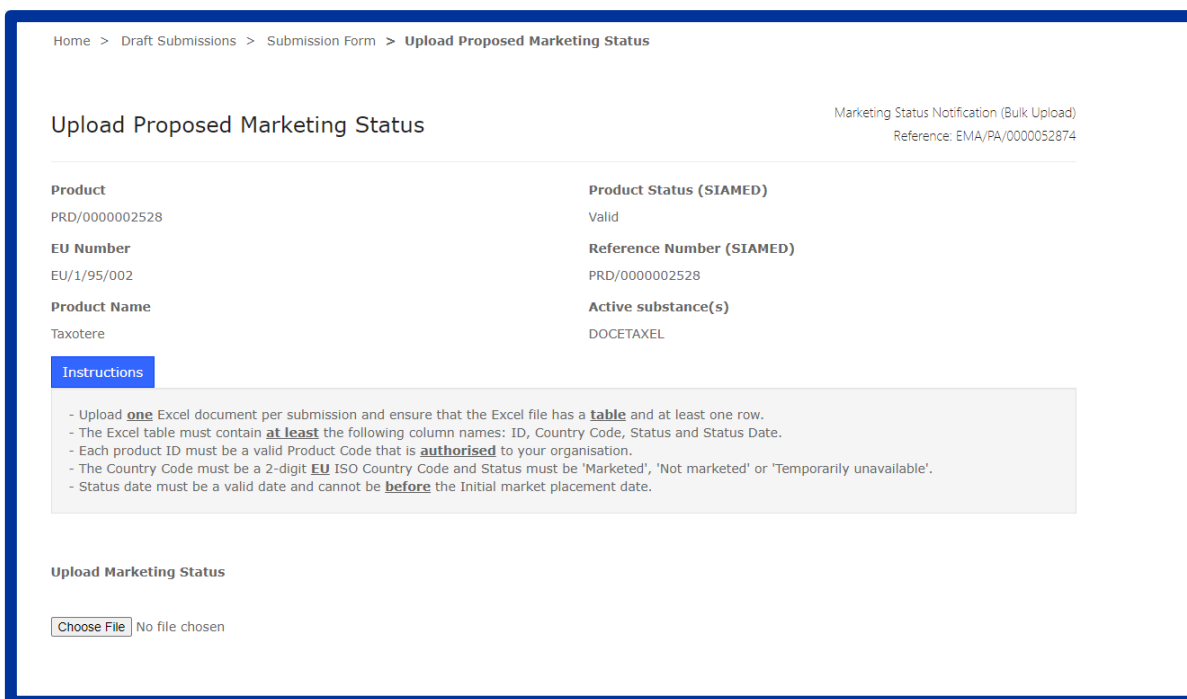
<b>Product *</b> PRD/0000002528	<b>Product Status (SIAMED)</b> Valid
<b>EU Number</b> EU/1/95/002	<b>Reference Number (SIAMED)</b> PRD/0000002528
<b>Product Name (Calculated)</b> Taxotere	<b>Active substance(s)</b> DOCETAXEL

Current Marketing Status Search  [Download](#)

EU Number	Product Nick Name	Strength	Pharmaceutical form	Pack Size	Member State ↑	Marketing Status	Date of Marketing Status Change	Reason for Cessation	Estimated Date of Reintroduction	Does Cessation lead to Shortage?
EU8613	Taxotere 80 mg/2 ml - Concentrate and solvent for solution for infusion	80 mg/2 ml	Concentrate and solvent for solution for infusion	1 vial + 1 vial	Austria	Marketed	27/05/2021			
EUUUU27773	Taxotere 20 mg/1 ml - Concentrate	20 mg/1 ml	Concentrate for solution for infusion	1 vial	Austria	Not marketed	25/05/2021	01. Safety - Medicinal product is		

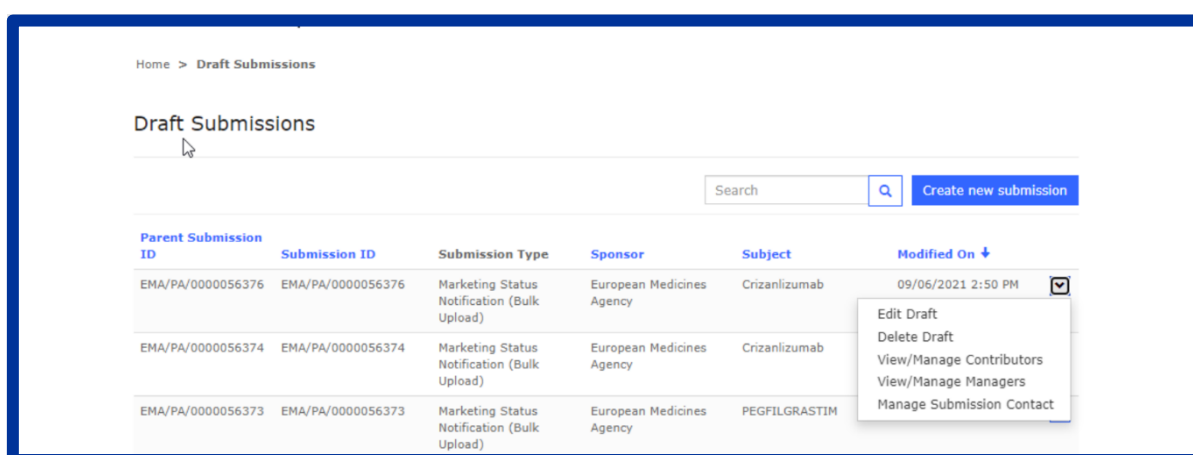
4. The **'Upload Proposed Marketing Status'** section is now enabled to upload the Excel file. Please do not use the excel downloaded from the Marketing Status Report since it has a different format, use only the excel downloaded as explained in this section (above points). Click on the **'Notification'** button to read the instructions on uploading the file. Upload the file by clicking on the **'Choose file'** (Figure 19) button. Once the file is uploaded, click on **'Save and Return'**.

Figure 19 Upload CSV file



5. 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.
6. 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.
7. Your submission is shown in the **“Submissions/Ongoing”** sub-tab.
8. 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 in **“edit draft”** mode by clicking on **“V”** shaped button present on the right end corner of the record.

*Figure 20 Opening the submission in edit mode*



9. Click on the **‘Upload Proposed Marketing Status’** section. Errors will be shown under section **‘Input File Validation’** as shown in Figure 22

*Figure 21 Excel Validation Errors*

Submission Form Marketing Status Notification (Bulk Upload)  
Reference: EMA/PA/0000052874

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Please make sure that the required sections have a green tick to the right (except "Documents from EMA") before submitting the application.  
**Customer Name : Stanton Inc and Sons**  
**Address : 63284 MY Kita 862 Lemke Fall Japan**

[Select Authorised Product](#) ✓  
[Download Current Marketing Status](#) ✓  
[Upload Proposed Marketing Status](#) ✗  
[View Proposed Marketing Status](#)  
[Declaration](#)  
[Submit Application](#)

Figure 22 Showing Validation errors and uploading file again

Upload Marketing Status

The record already contains data and re-uploading will overwrite its contents. [Download](#)

No file chosen

Input File Validation

Name ↑	Description
EU613	Row4:Country is invalid,Marketing Status does not exists
EU8613	Row2:Country is invalid
EUUUU27773	Row3:Country is invalid,Does Cessation Lead to shortage does not exists

- Download the file again by clicking on **‘Download’**, correct the data, upload the file and submit again. This process must be repeated until the system accepts the uploaded file. You will then receive an email stating that your submission is valid, and submission has moved to **‘Completed’** tab.

### 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:

- 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 23). You have to delete this draft submission yourself (2.7. Delete a draft submission);

Figure 23 Withdrawal of one or more presentations

The screenshot shows a web form titled "Select Authorised Product" within a navigation bar "Home > Select Authorised Product". The form is for a "Marketing Status Withdrawal Notification" with reference "EMA/PA/0000056150". It displays the "Authorised Product" as "PRD/0000002528". A red warning message states: "Please note that the submission type 'Product Withdrawal Notification' is to remove all product presentations for all member states. If you would like to withdraw product presentations for certain member states only please select the submission type 'Marketing Status Notification' instead. Kindly navigate back to the draft submission page, delete this submission and create a new submission of type 'Marketing Status Notification (Single or Bulk)'." Below this, a question asks "Do you want to withdraw/suspend all presentations of the medicinal product? (Art. 14b)" with radio buttons for "Yes" and "No", where "No" is selected. A blue "Save and Return" button is at the bottom left.

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

Figure 24 Withdrawal of all presentations

This screenshot is identical to Figure 23, but the radio button for "Yes" is selected for the question "Do you want to withdraw/suspend all presentations of the medicinal product? (Art. 14b)".

Click on the section "Reasons for Product Withdrawal" and choose one of the options as shown in Figure 25 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 25 Adding Reason for withdrawal

Reasons for Product Withdrawal Marketing Status Withdrawal Notification  
Reference: EMA/PA/0000056150

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Authorised Product  
PRD/0000002528

Do you want to withdraw/suspend all presentations of the medicinal product? (Art. 14b)

Yes  No

If yes, Please choose:

A request for withdrawal of the central marketing authorisation of your product ⓘ  
 A decision not to apply for the renewal of a marketing authorisation  
 Permanent cessation of marketing of the product ⓘ

Please provide the intended date:

Please provide the reason for permanent marketing cessation:

Based on the grounds provided in Articles 116 and 117 of Directive 2001/83/EC  
 Not based on the grounds provided in Articles 116 and 117 of Directive 2001/83/EC

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<sup>1</sup> 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 26. 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.

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<sup>1</sup> Industry Portal users

Figure 26 Marketing Status Report

> View Marketing Status Report

Marketing Status Report provides an overview of current/future Marketing Status for all Authorised Medicinal Products for all Countries.

EU Number  Product Name  Strength  Pharmaceutical Form  Marketing Status

Future Marketing Status  Country  Shortage  Future Shortage  Date of Marketing Status Change

Future Date of Market Status Change

[Apply](#)

Report Date  [Apply](#) [Reset](#)

[Search](#) [Download](#)

EU Number ↑	Product Nickname	Strength	Pharmaceutical Form	Pack Size	Marketing Authorisation Holder	Country ↑	Marketing Status	Date of Marketing Status Change	Date of initial placing on the market	Reason for Cessation	Es da Re
EU/1/95/002/001	Taxotere 20 mg/0.5 ml - Concentrate and solvent	20 mg/0.5 ml	Concentrate and solvent for solution for infusion	1 vial + 1 vial	Sanofi Mature IP	Austria	Marketed	01/06/2021	01/06/2021		

## 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 received, if any of the information given has changed or is incorrect and if there are any problems with the proposed timing. 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<sup>2</sup> 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.

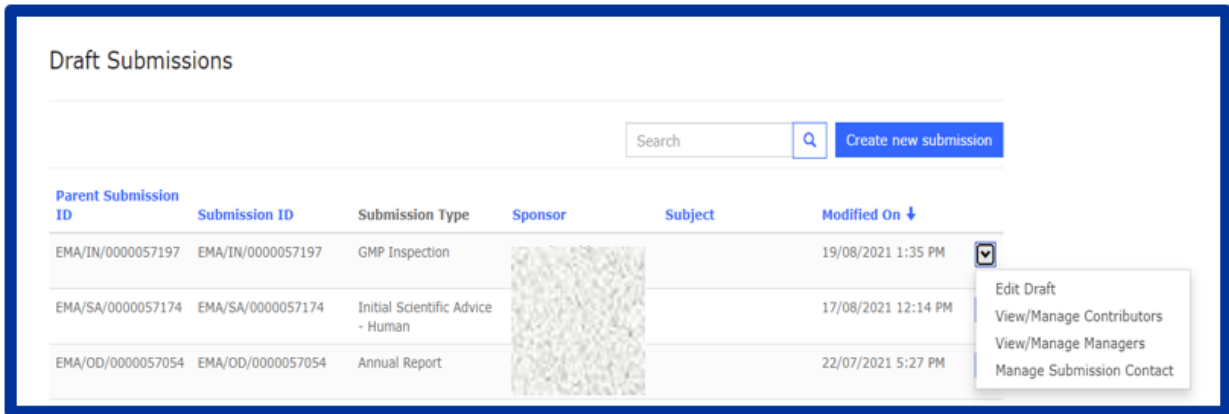
At that point, you must update the submission with the necessary information (e.g. Purchase Order number) and submit it via the IRIS Portal, within 10 working days of the inspection announcement. Please follow the steps below to submit the required information.

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/0000XXXXX**’ 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 27);

---

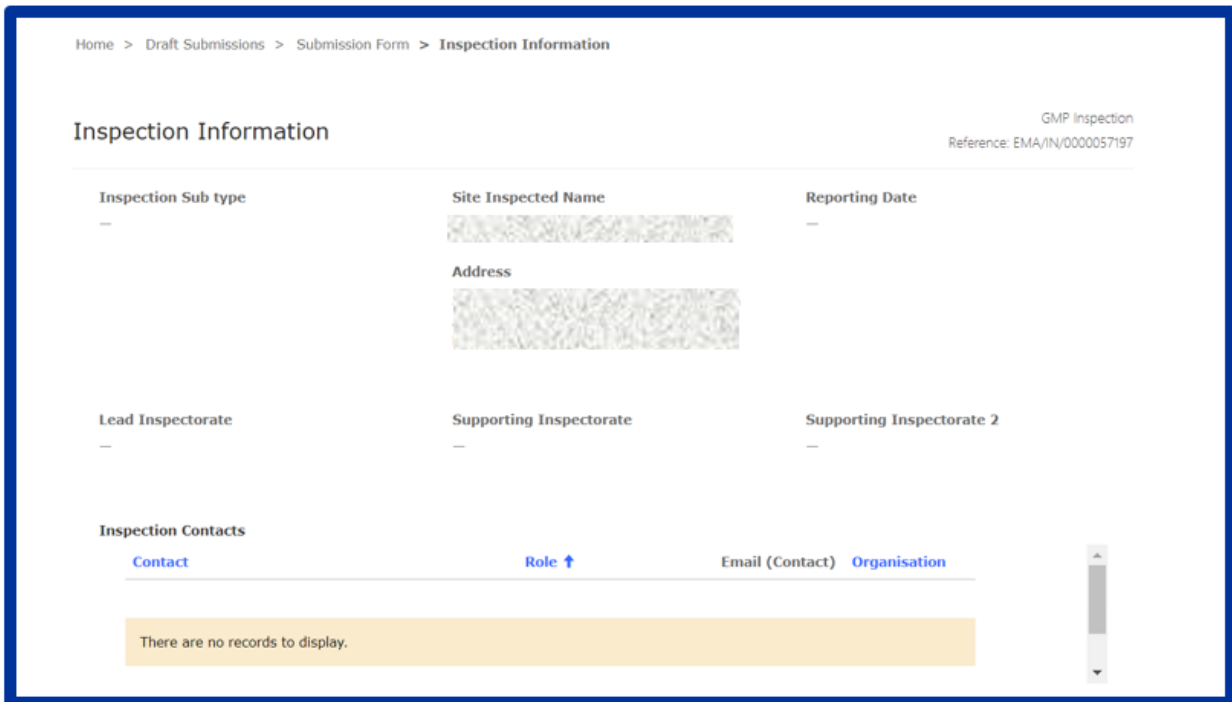
<sup>2</sup> The notified user is the existing Product Contact as already notified to EMA (integrated from SIAMED2); this user becomes the Portal Contact (a.k.a. Submission Contact) for the ongoing submission. To change the product contact, use the [existing procedure](#).

Figure 27 : Edit Mode



3. Click on the **'Inspection Overview'** section as shown in Figure 28. 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 28



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 29 To Edit Purchase Order and fees

Inspection details

Reference: EMA/IN/0000057369

Please note that you can only submit the data for this inspection if the purchase order number is provided for each product. If you do not have a purchase order number for a product, please include the text n/a instead.

Authorized Products

Invented name (Product)	EMA Number (Product)	Domain (Product)	Active substance(s) (Product)	Number of fees ↑	Inspection Scope	Purchase Order number

Product Details

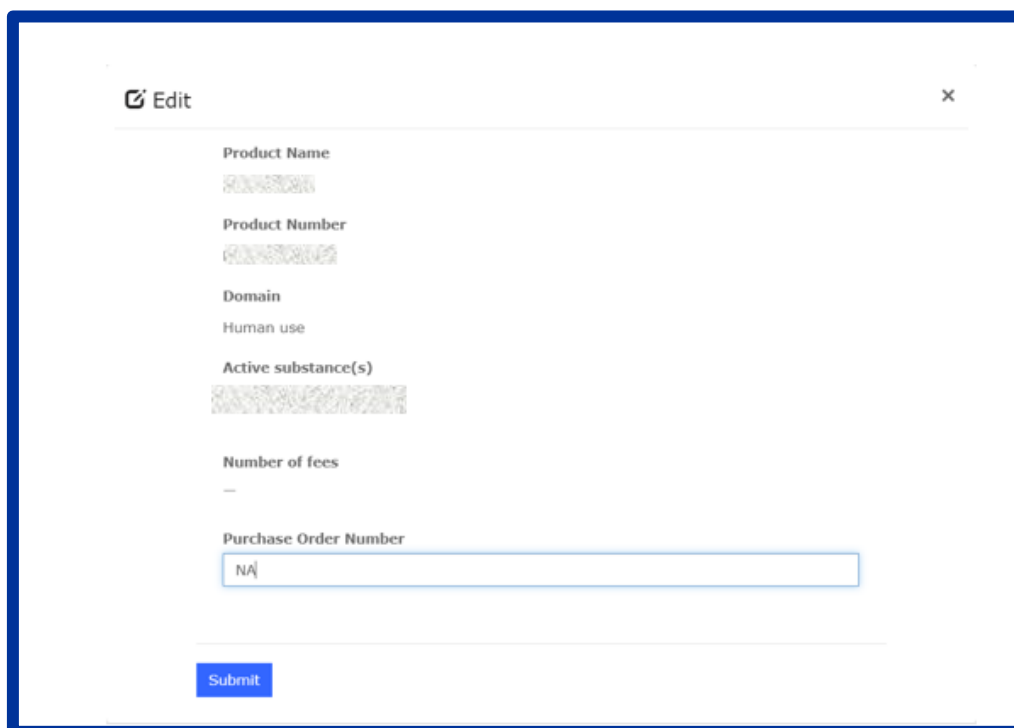
Invented name (Product)	Strength (Product)	Pharmaceutical form (Product)	Manufacturing Operation ↑	Active substance in scope for inspection

< 1 2 3 4 5 6 7 8 ... 16 >

Click on edit as shown in Figure 30, 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 30 Adding Purchase Order Number



The screenshot shows a web form titled 'Edit' with a close button (X) in the top right corner. The form contains several fields: 'Product Name', 'Product Number', 'Domain', 'Human use', 'Active substance(s)', and 'Number of fees'. The 'Purchase Order Number' field is highlighted with a blue border and contains the text 'NA'. A blue 'Submit' button is located at the bottom left of the form.

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 “**Outgoing**” 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<sup>2</sup> 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. At that point, you must update the submission with the necessary information (i.e. Purchase Order (PO) 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/0000XXXXX**' 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.
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.

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.

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**" 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 31 Submission Form):

Figure 31 Submission Form



The screenshot shows the 'Submission Form' interface. At the top right, it indicates 'Annual statements submission' with a reference number 'EMA/VS/0000082122'. Below this, a message states: 'Please make sure that the required sections have a green tick to the right (except "Documents from EMA") before submitting the application.' The customer information is listed as 'Customer Name : European Medicines Agency' and 'Address : Domenico Scarlattilaan 6 1083 HS Amsterdam Noord-Holland Netherlands'. A list of sections is provided: 'Select Authorised Products', 'Submission Details', 'Documents from Applicant', 'Documents from EMA', and 'Declaration and Submission'. A 'Return' button is located at the bottom left.

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**”, add all corresponding documents (if applicable) by clicking on “**Add files**” and then 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 VeDDRA**", select the concerned VeDDRA PT term(s) and then click on "**Add**".
  - e. Indicate if any of the VeDDRA terms concerned in the signal is a **Medically Important (MI) term**. Please consult the document "[Guideline on veterinary good pharmacovigilance practices \(VGVP\) Module: Signal Management](#)" for the complete list of MI Terms.
  - f. Click on "**Add Species**" and select the concerned animal species, then click "**Add**".
  - g. 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.
  - h. Under proposal for action, click on "**Add**" and select the appropriate regulatory action(s), then click on "**Add**".
  - i. 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.
  - j. 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.