User Reference Guide - Individual Case Safety Reports (ICSRs) Submissions

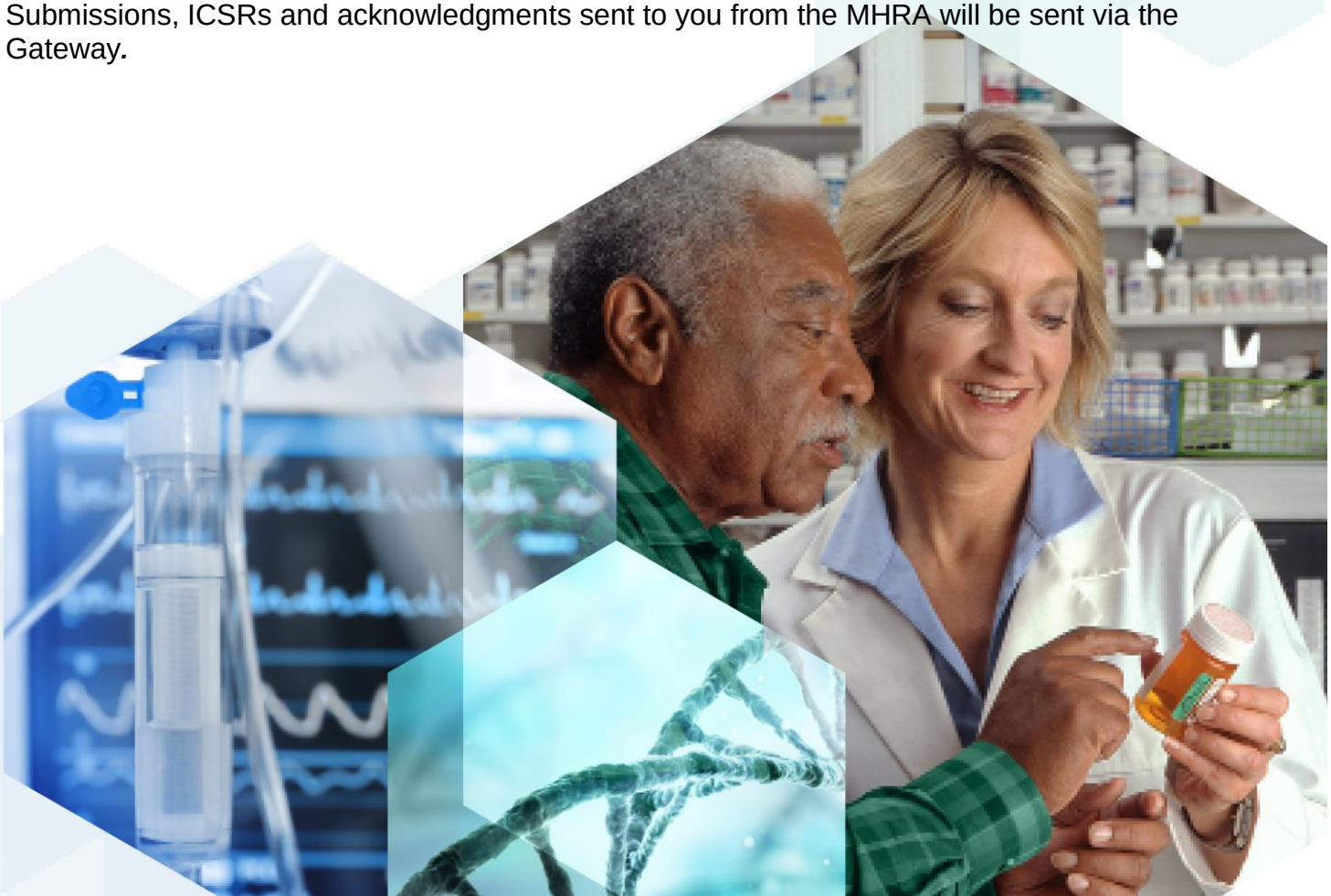
A step-by-step guide on using the ICSR Submissions platform to submit post-marketing and clinical trial ICSRs.

If you wish to submit and receive ICSRs to/from the MHRA (Medicines and Healthcare products Regulatory Agency) or submit suspected unexpected serious adverse reactions (SUSARs) to the MHRA, but do not have the capability to use the MHRA Gateway, you can do so by using ICSR Submissions.

The following user guide provides guidance on how to use the different functions of ICSR Submissions to manage, report and receive ICSRs or SUSARs.

If you wish to send and receive ICSRs, as well as submit SUSARs, via the MHRA Gateway please see the user reference guide.

Please note that if your organisation is registered to **both** MHRA Gateway and ICSR Submissions, ICSRs and acknowledgments sent to you from the MHRA will be sent via the Gateway**.**



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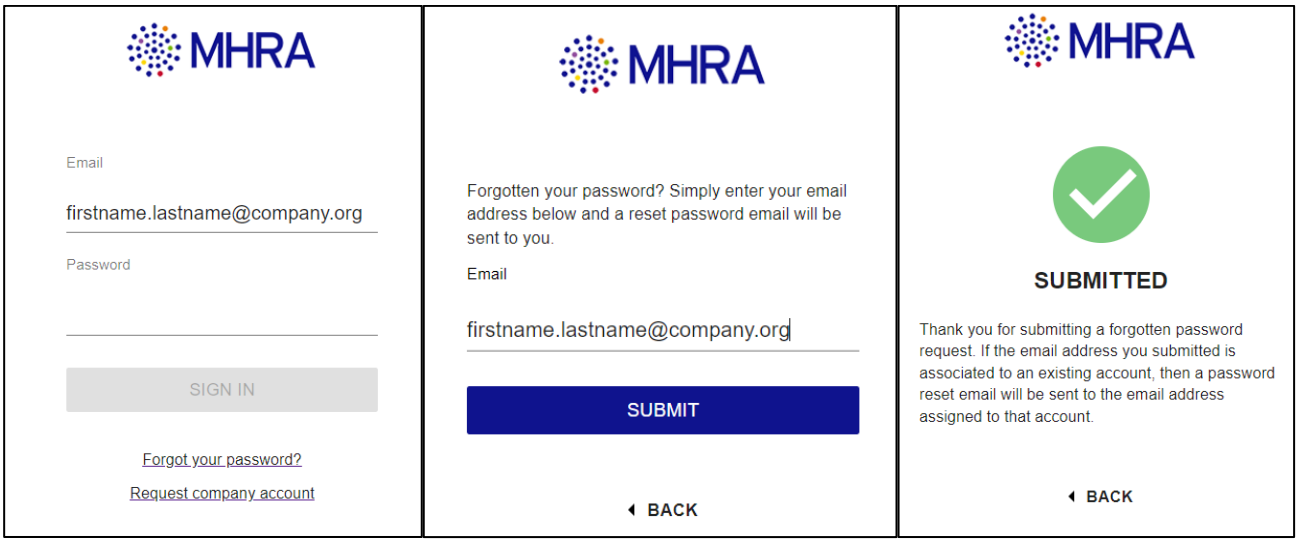
Section 1: Logging in to ICSR Submissions

Logging In

Once registration for ICSR submissions is completed, you can login to ICSR submissions via the login page at https://icsrsubmissions.mhra.gov.uk/login.

If you have forgotten your password, a reset password email can be sent by selecting the 'Forgot your password?' link on the login page and entering the email address associated with your account. If you do not receive an email, please check your spam, or junk mail folder.



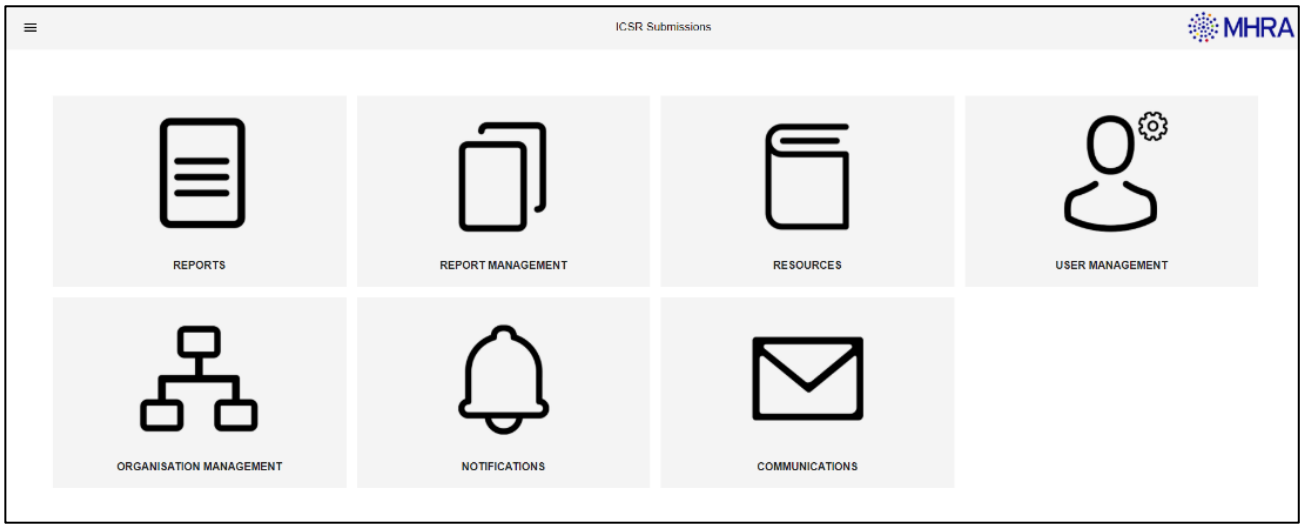
Choosing an Organisation

After logging in, if your account is linked to multiple organisations, you will be given the option to select which organisation you wish to view. After doing so, you will progress to the ICSR Submissions dashboard for the selected organisation where you can select the required functionality using the dashboard tiles as below.

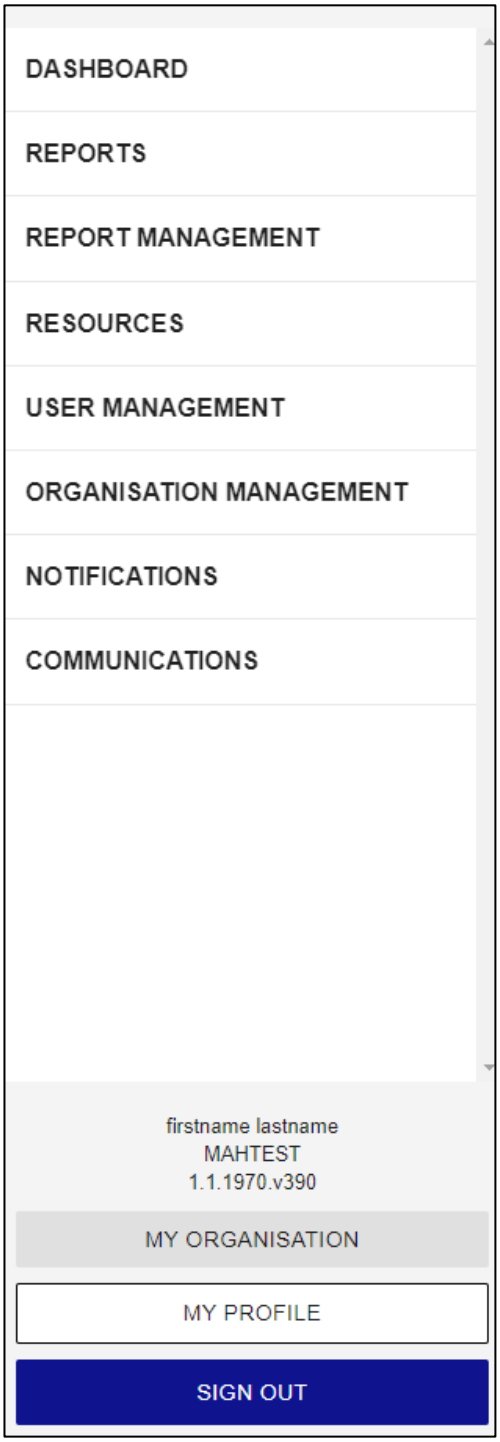
If your account is associated with a single organisation, you will progress directly to the ICSR Submissions dashboard after logging in.

Dashboard

Once logged in you will be taken to the dashboard. The tiles that appear on the dashboard will depend on your level of access, with organisation leads having the full display as below.



Select the burger menu ☰ at the top left of the screen to see the tiles in an alternative view.



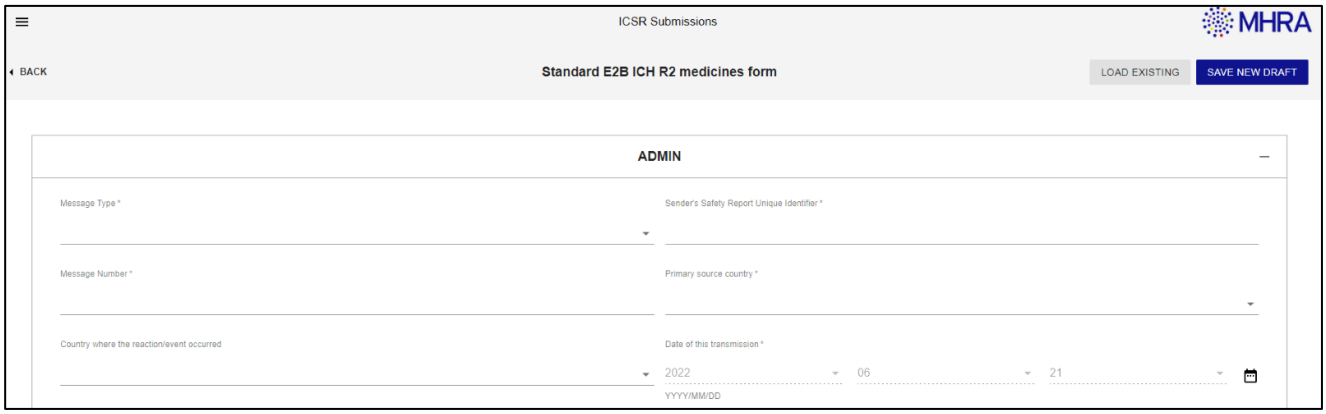
Section 2: Sending Reports

You can send both ICSRs and SUSARs to the MHRA in two ways; by creating new R2 reports or by posting R2 or R3 XML files. These two options can be found by selecting the ‘Reports’ tile from the dashboard or burger menu on the left-hand side of the dashboard.

New R2 Report

To create a new R2 report, you should select the ’New Report‘ tile which will provide the option to complete an E2B compliant R2 reporting form.

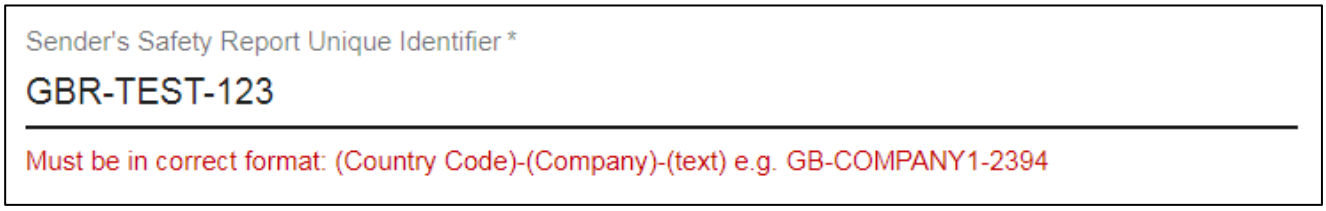
You will then be able to create an ICSR or SUSAR from scratch or you can create a report based on an existing E2b R2 XML. You can import this into the form using the 'Load Existing' option in the top right-hand corner of the form. For more information on this please see the 'Loading reports' section.



You will then be able to progress through the form to complete details about the ICSR or SUSAR. The form uses E2b R2 fields and generates R2 ICSRs and SUSARs that are sent directly to the MHRA.

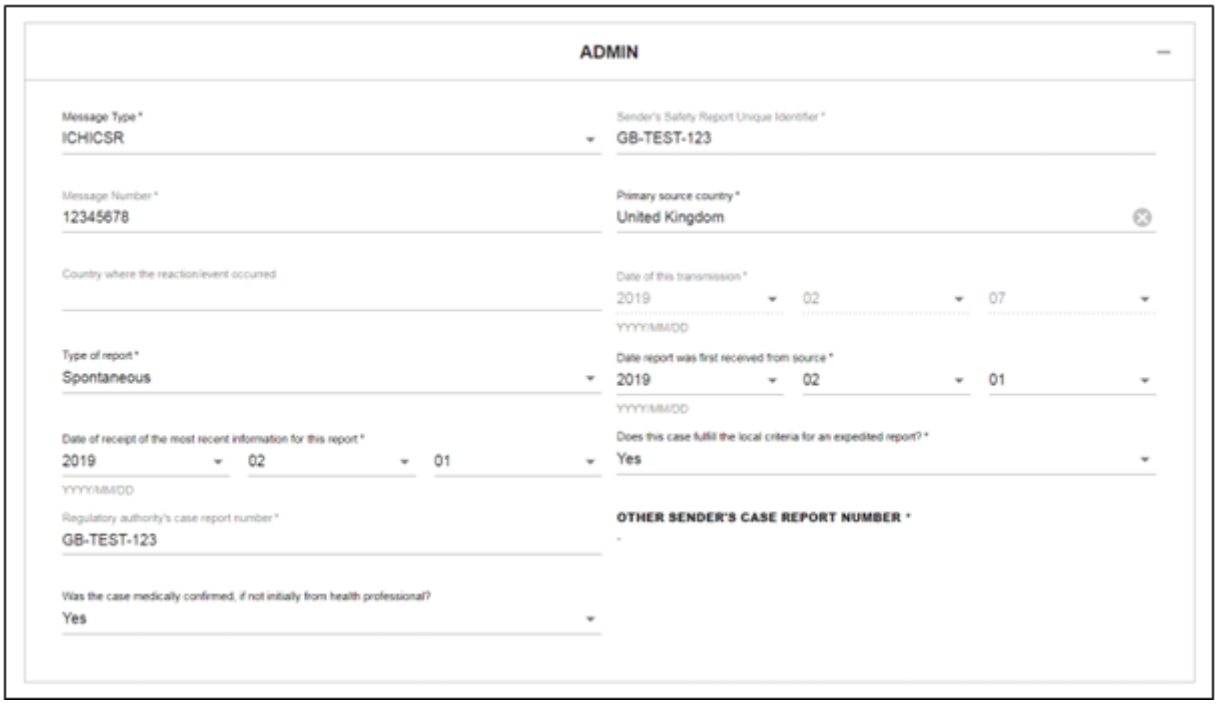
For reporters who have previously used the eSUSAR website to submit SUSARs, please note that the ICSR Submissions does not auto create worldwide reference numbers. These will need to be provided by your organisation and entered in the 'Sender's Safety Report Unique Identifier' field following the format of (Country Code)-(Company)-(text) e.g. GB-COMPANY1-2394.

Follow-up information for all reports must continue to consistently use the same worldwide reference number. Reporters must enter this in the 'Sender's Safety Report Unique Identifier' field. SUSARs previously submitted via the eSUSAR website should use the worldwide reference number auto created by the eSUSAR website.

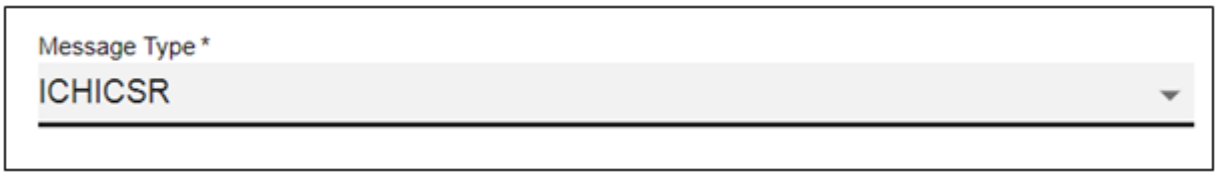


Likewise, the Message Number is not auto created and will also need to be input by the reporter. However, this field has no specific requirements and will accept any alphanumeric and special characters in any order.

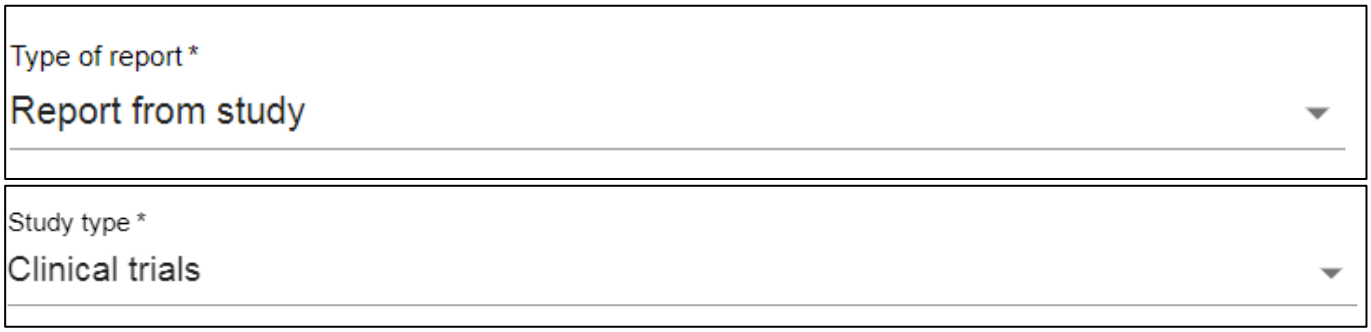
Mandatory fields are highlighted by an Asterix (*). If you do not complete these fields, you will not be able to progress.



'ICHICSR' should be selected from the 'Message type' drop down menu for creating both ICSRs and SUSARs. 'Backlog' should only be used after confirmation from the MHRA.



SUSARs are differentiated from ICSRs by selecting 'Report from study' in the 'Type of report' field, which can be found in the 'Admin' section, and by selecting 'Clinical trials' as 'Study Type' which can be found in the 'Reporter' section as below.



The field for 'Does this case fulfil the local criteria for an expedited report?' in the 'Admin' section should always be selected to 'yes' as SUSARs are to be reported in an expedited manner.

Please note, that to align with the use of the Clinical Trials Information System (CTIS), the ‘Study Name’ field in the ‘Reporter’ section must follow the format below where any of the three reference numbers must precede the abbreviated study name:

‘IRASID/EudraCT/EUCT number#abbreviated study name’.

NB. For ICSRs there are two report numbers that can be populated, ‘Regulatory authority's case report number’ or ‘Other sender's case report number’. Please fill in the correct field as per the table below:

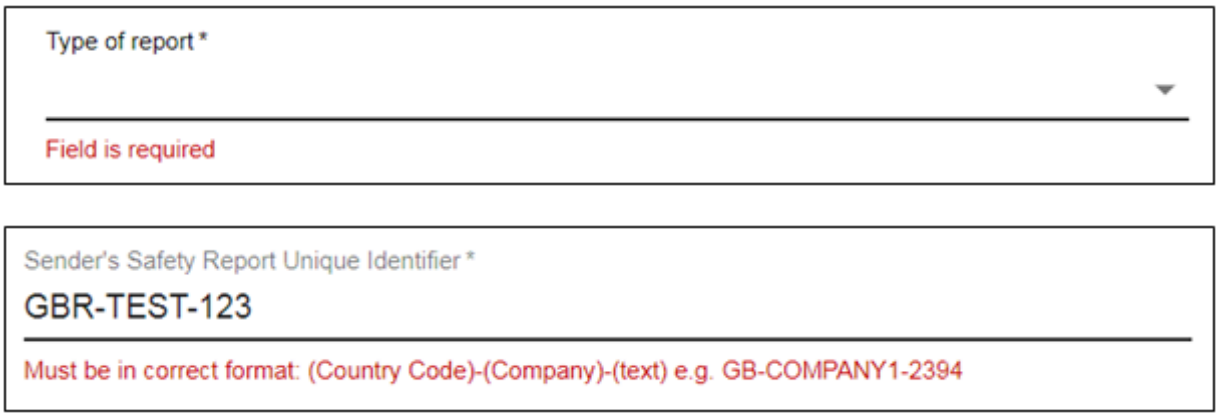
Field	Report type
Regulatory authority's case report number	Regulatory Authority Report
Other sender's case report number’	Company Report

Full details about the fields in the form, the permitted values and field lengths can be found in the International Conference on Harmonisation E2B R2 schema: ICH ICSR Specification.

Follow-up information for SUSARs previously submitted via the eSUSAR website must refer to the eSUSAR report’s XML file field ‘authoritynumb’ where the number has been auto created. This value must be entered in the ICSR field 'Regulatory authority case report number'.

For initial SUSAR reports submitted using ICSR Submissions, please complete the field 'Other sender's case report number' with the value created by your organisation.

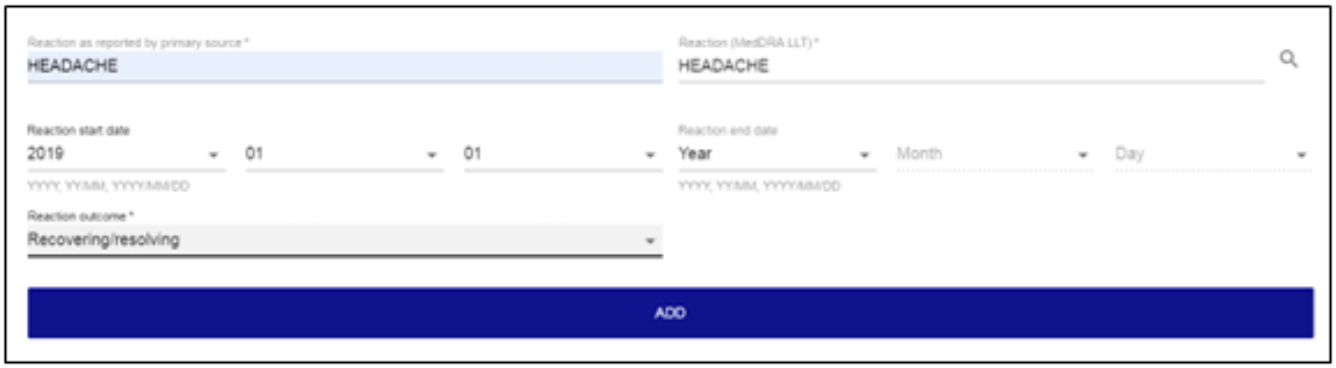
As you complete the form, validations will be applied to fields. If the information entered in the field fails the validations, you will see a message highlighting this in red underneath the field in question. Examples of such validation warnings include the following:



As you scroll through the form you can expand and minimise different sections using the +/- icon on the right-hand side of the section title bar.

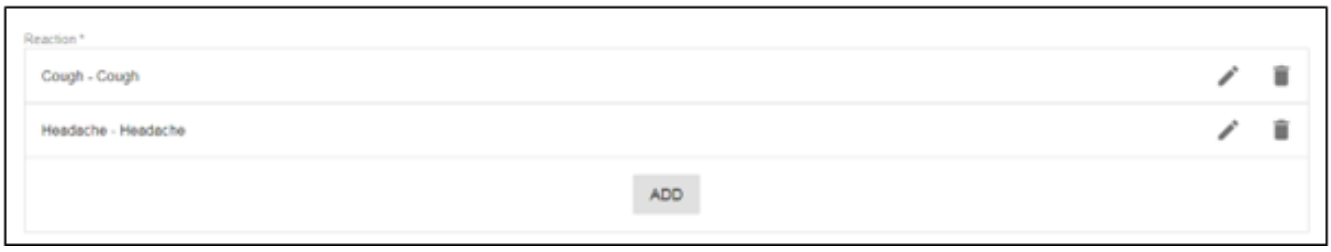
Some aspects of the form are repeatable (e.g. reaction), so should be edited/expanded by selecting ‘add’ which will load a series of fields relating to that section.

Once the required fields are completed, you can select ‘add’, which will add the section and take you back to the main form.



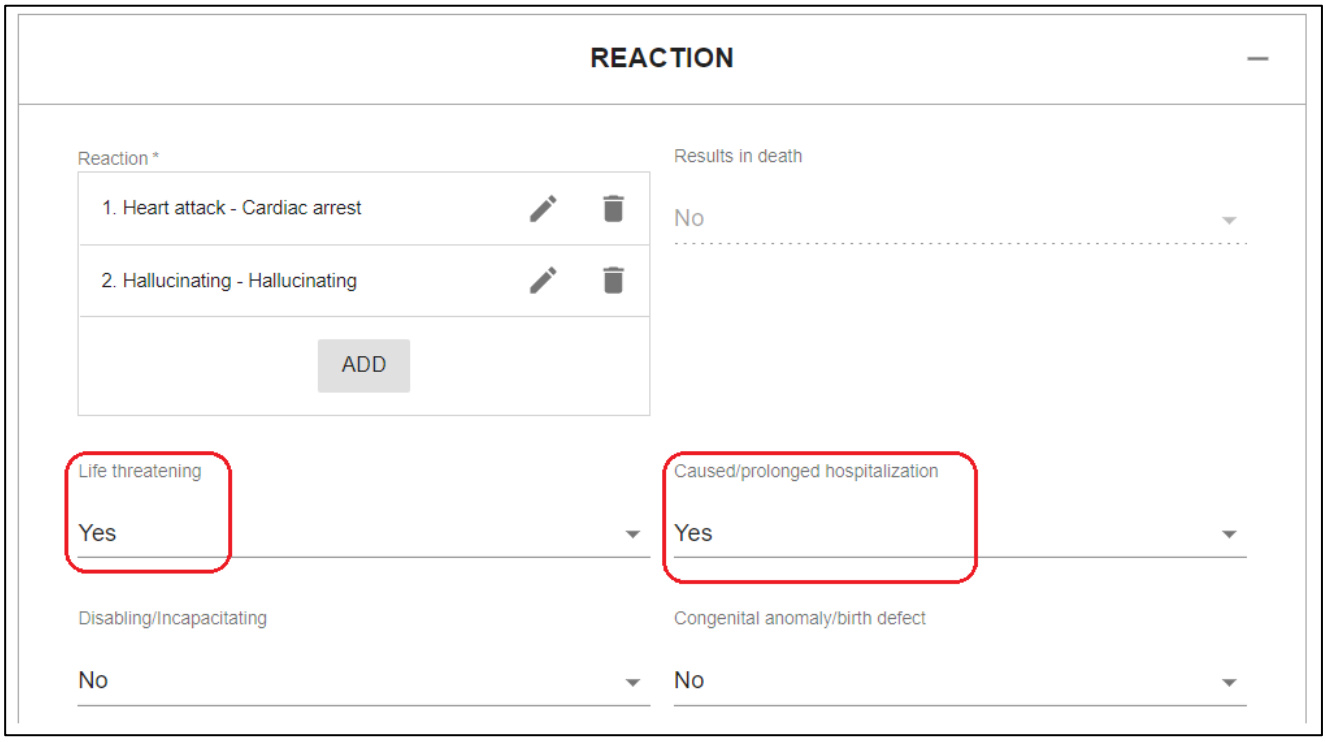
You can then add repeats of the section if required.

If you want to edit or delete a previously completed section, this can be done by clicking the pencil or bin icon found at the right-hand side of the section.

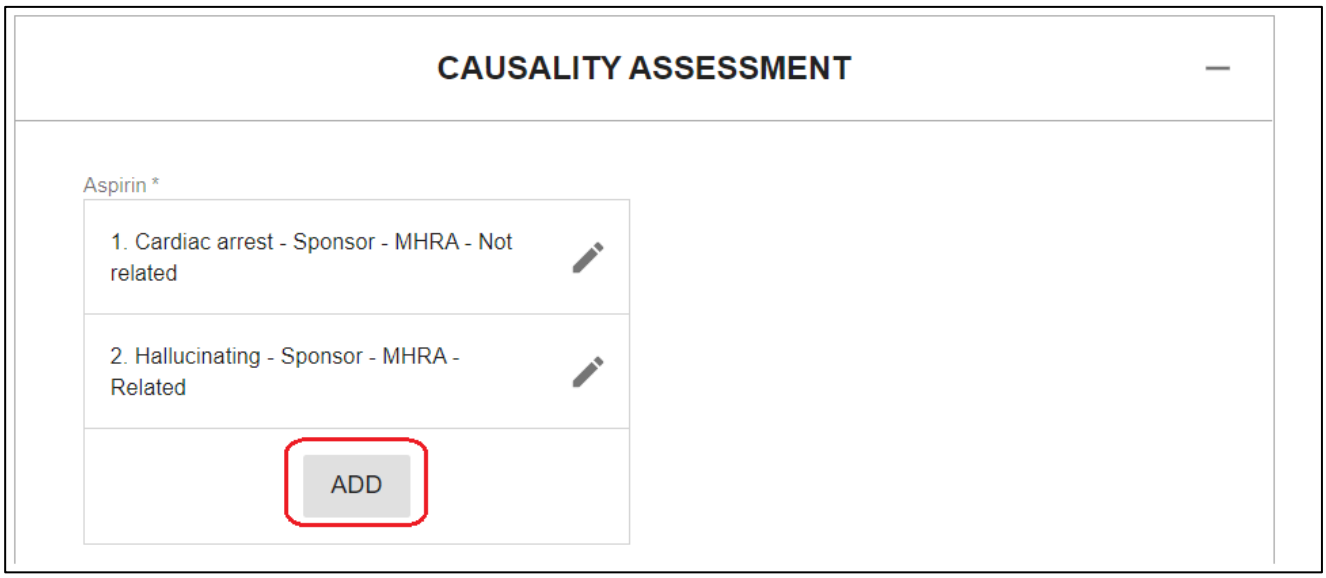


Please note, for Drugs not found in the MHRA drug list using the search function, please enter the drug as free text. On submission, the MHRA will add the drug to our internal drugs list to be included in the next periodic update.

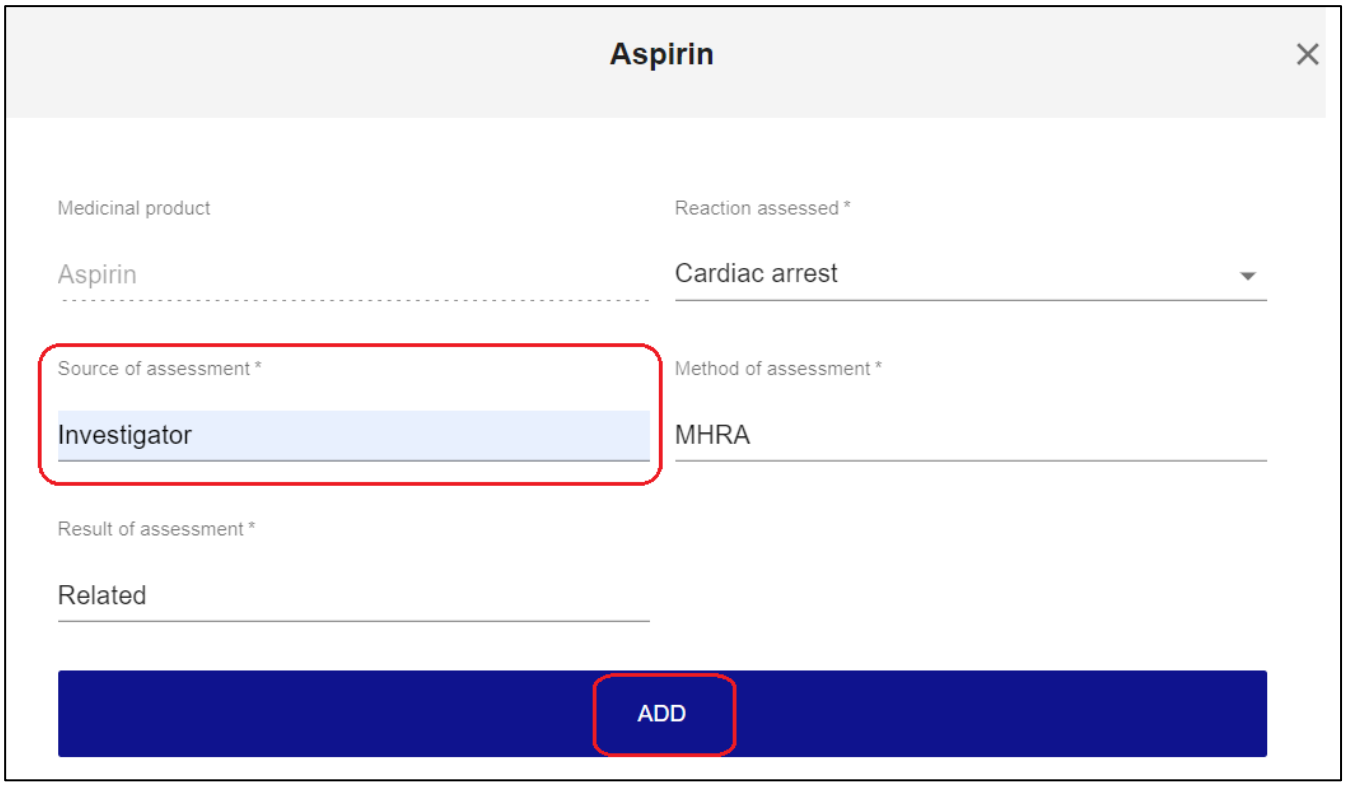
For SUSAR reports, the seriousness criteria listed in the ‘Reports’ section must have at least one selected as ‘yes’ to align with the definition of a SUSAR:



When reporting SUSARs, causality assessments for each drug/reaction must be provided by both Sponsor and investigator. The ‘Causality Assessment’ section can also be edited by selecting ‘add’ which will enable the reporter to provide further assessments per drug/event:



Once all fields have been completed with assessments from both Sponsor and investigator for each drug/reaction you can select ‘add’, which will add the section and take you back to the main form:



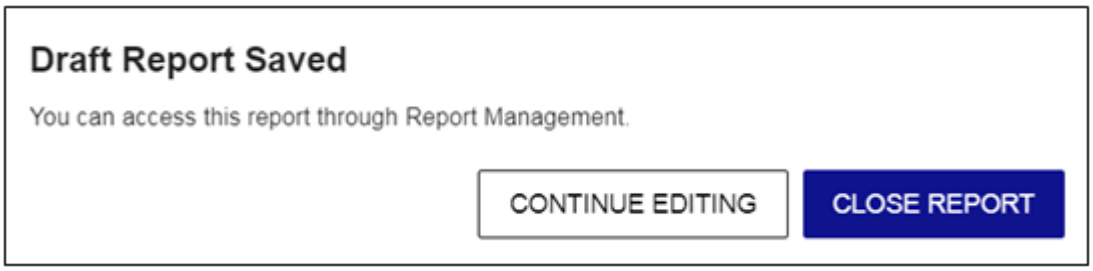
Once the form is completed, you should select ‘Validate & Send’ at the bottom of the form. This will send the ICSR or SUSAR to the MHRA. If the validate and send option is greyed out, then a mandatory field is missing, or a field has failed a validation thereby preventing submission. In this situation you should go through the form to complete the required information.

ICSRs and SUSARs submitted via ICSR submissions can be tracked via the ‘Report Management’ page including acknowledgement status (please refer to section 3).

Saving Draft Reports

As you create a new report, you can save a draft as you go by selecting the ‘Save Draft’ option in the top right-hand corner of the form.

After doing this, a pop-up will appear giving you the option to either continue editing the report or to close the report and return to the ICSR submissions dashboard.



Saved drafts can be accessed via the ‘Report Management’ screen (please refer to section 3).

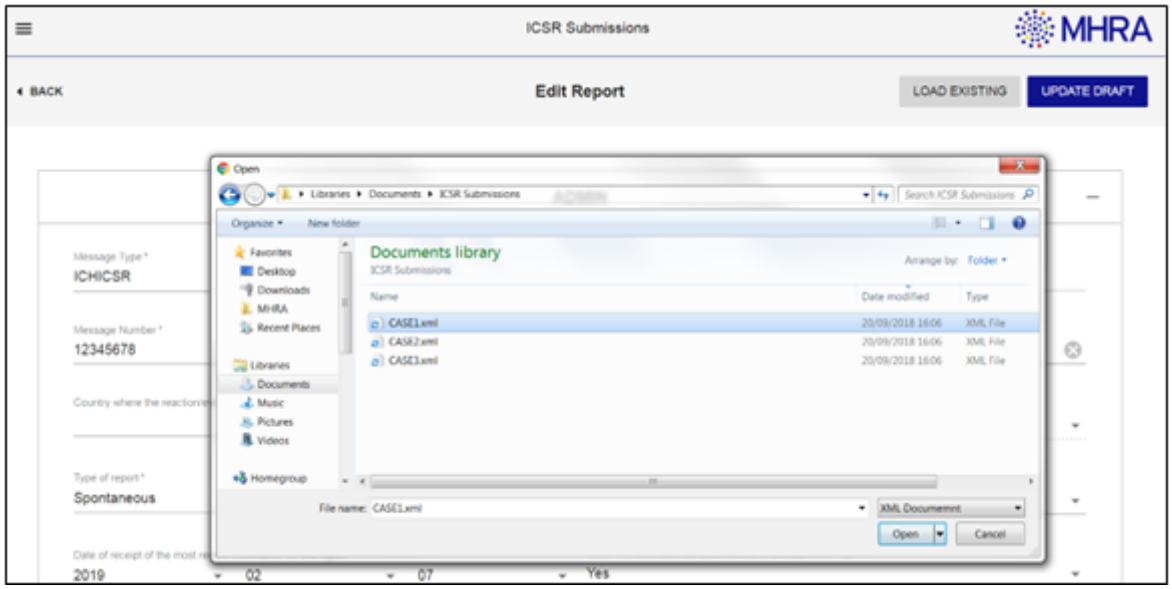
Loading Reports

If you wish to create a report based on an existing E2B R2 XML, you can import this into the form using the ‘Load Existing’ option in the top right-hand corner of the form.

Any XML which is imported into the from will automatically have the sender ID updated to match the organisation to which you are logged in. Therefore, if you have access to multiple organisations, please ensure you are logged in to the correct one before loading.

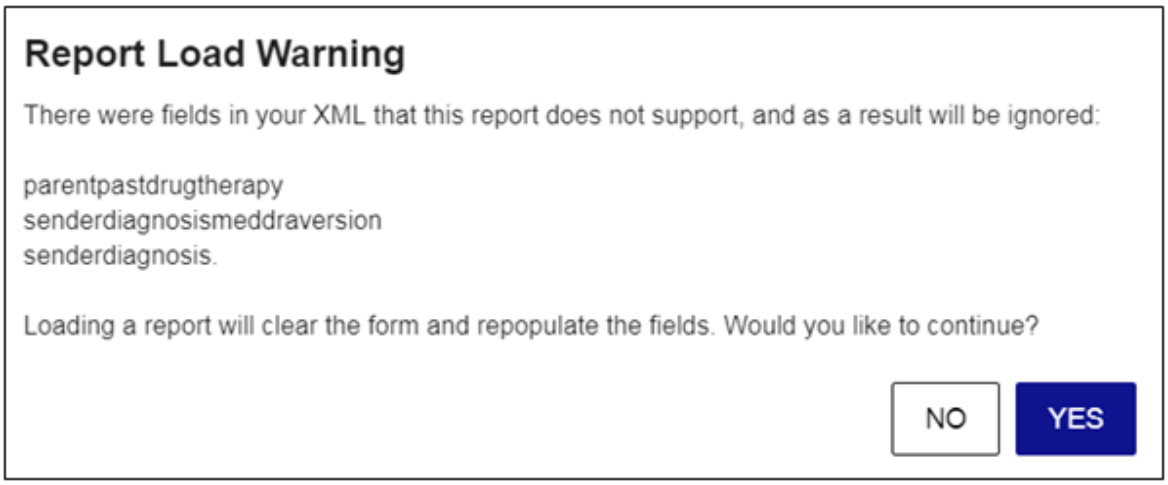
If using this option to follow up a previously submitted report via the eSUSAR website, please ensure the sender ID matches to your new ICSR organisation account prior to loading.

On selecting this option, you will be able to select a file from your file browser.

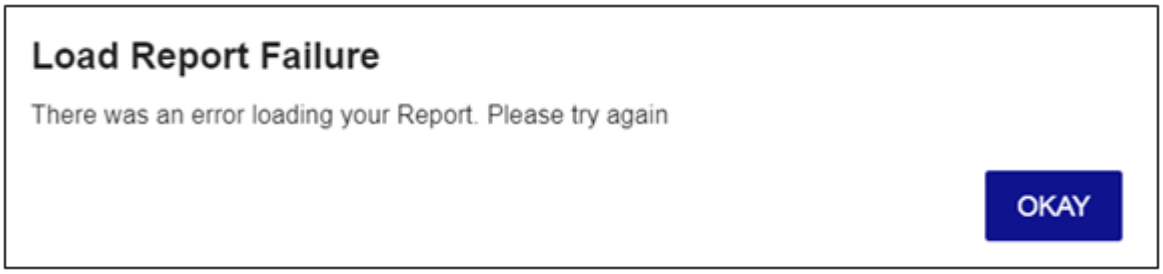


Loading a report will clear the form and repopulate fields.

Note: A small number of E2B R2 fields are not supported in the R2 report form, and if these are present in the XML you are attempting to load, a warning will appear to alert you to this. If present, the fields in question will be highlighted in the warning message and will be ignored if loaded.



If you attempt to upload a file that is not a valid E2B R2 XML file (e.g. an E2B R3 XML), an error message will be displayed, and the report will not be loaded.



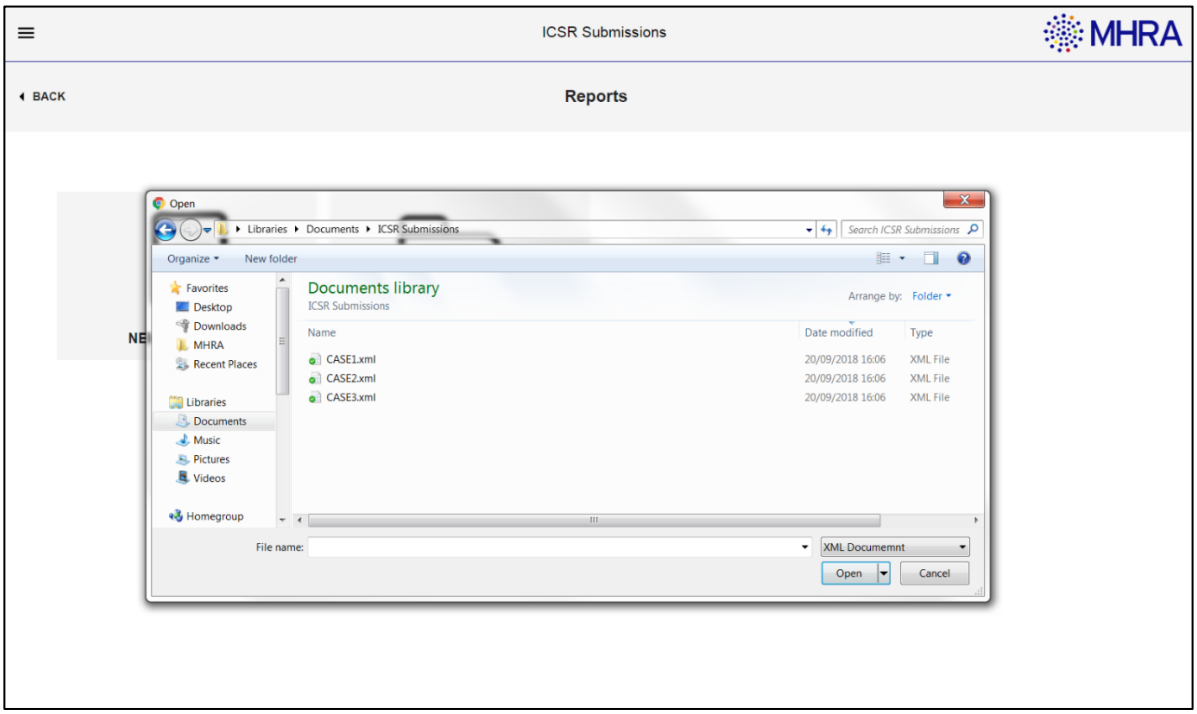
Exporting Reports

You can export an R2 XML as you complete the form. This can be exported both when the form is incomplete, and when the form is ready to submit.

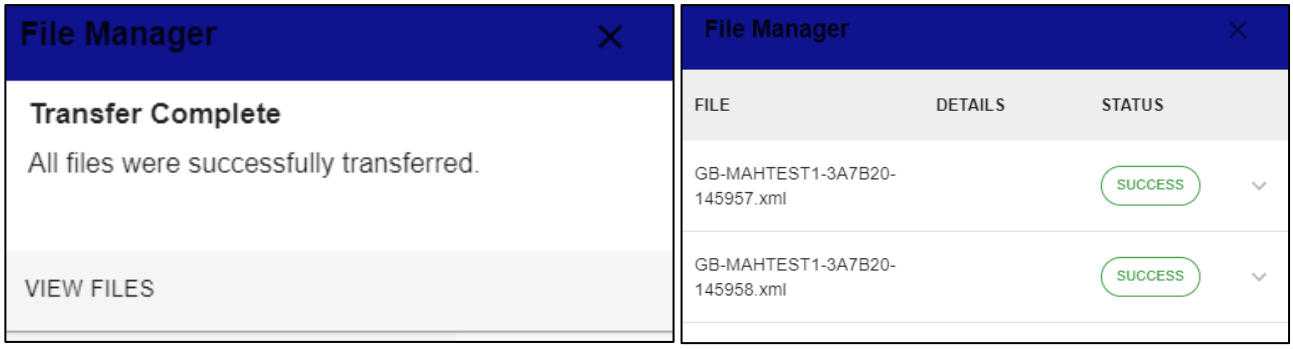
Post XML Reports

If you have an existing E2B R2 or E2B R3 XML that you would like to send to the MHRA, you should select the 'Post XML Reports' tile.

On selecting this option, you will be able to select a file or multiple files from your file browser.

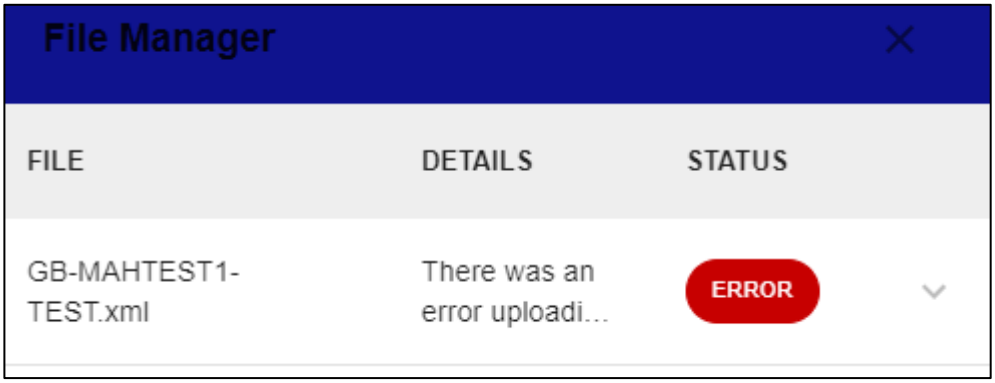


Once you select the file you wish to post, a success message will be displayed to confirm it has been sent.



ICSRs and SUSARs posted via ICSR submissions can be tracked via the 'Report Management' page, including acknowledgement status (please refer to section 3).

If your file does not follow E2B formatting guidelines, the file will fail to send, and an error message will be generated.

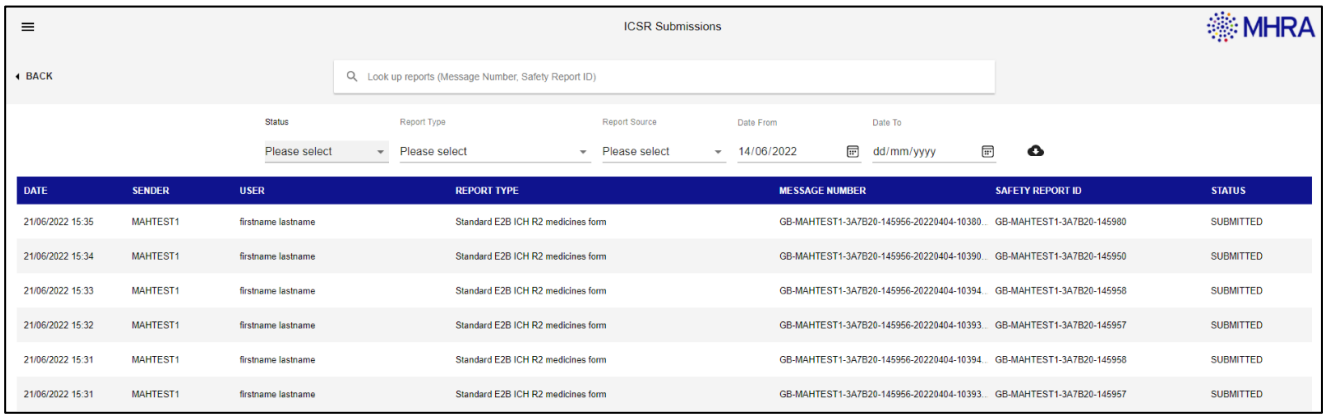


You cannot upload a report for an organisation you are not logged in to. If the sender ID in the XML does not match the sender ID associated with the organisation on ICSR Submissions, an error message will be displayed.

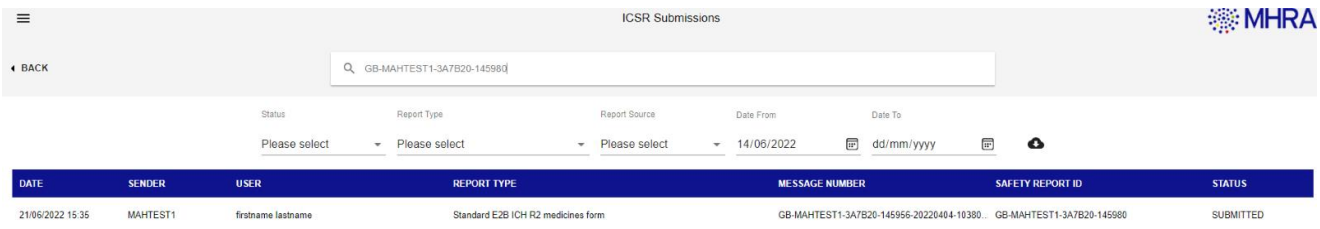
Section 3: Managing Reports

ICSRs and SUSARs sent to the MHRA

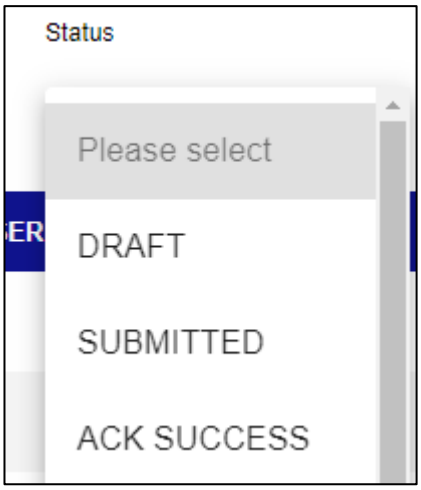
Reports sent to the MHRA, and draft reports can be tracked in the ‘Report Management’ screen.



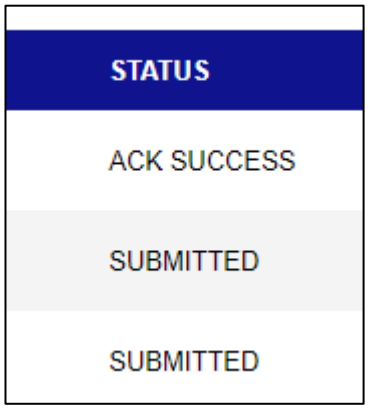
You can look up specific reports by searching for either ‘message number’ or ‘safety report ID’ using the search function.



You can filter reports on ‘status’, ‘report type’, ‘report source’, ‘date from’ and ‘date to’. As a standard the ‘date from’ filter will automatically have one week prior selected. Please remove or edit this if searching for cases outside of this window.



The acknowledgement status of a report can be seen in the ‘Status’ column.



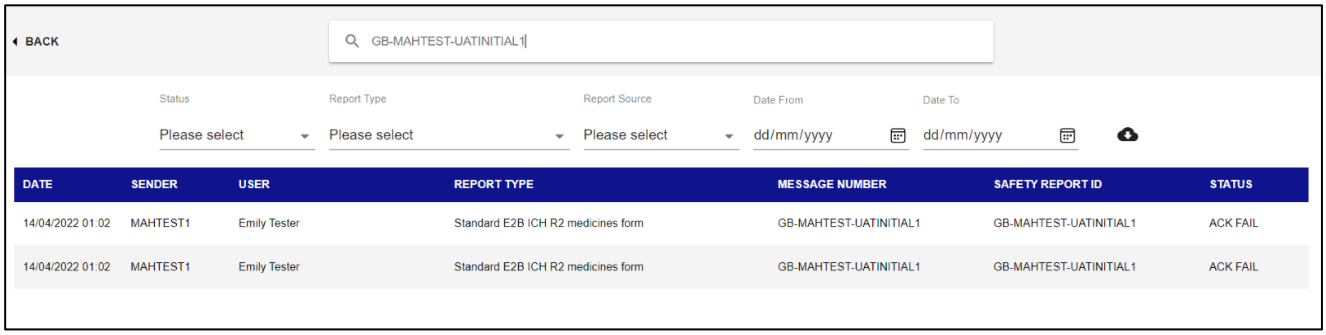
See the table below for information on the four different options found in the ‘status’ column:

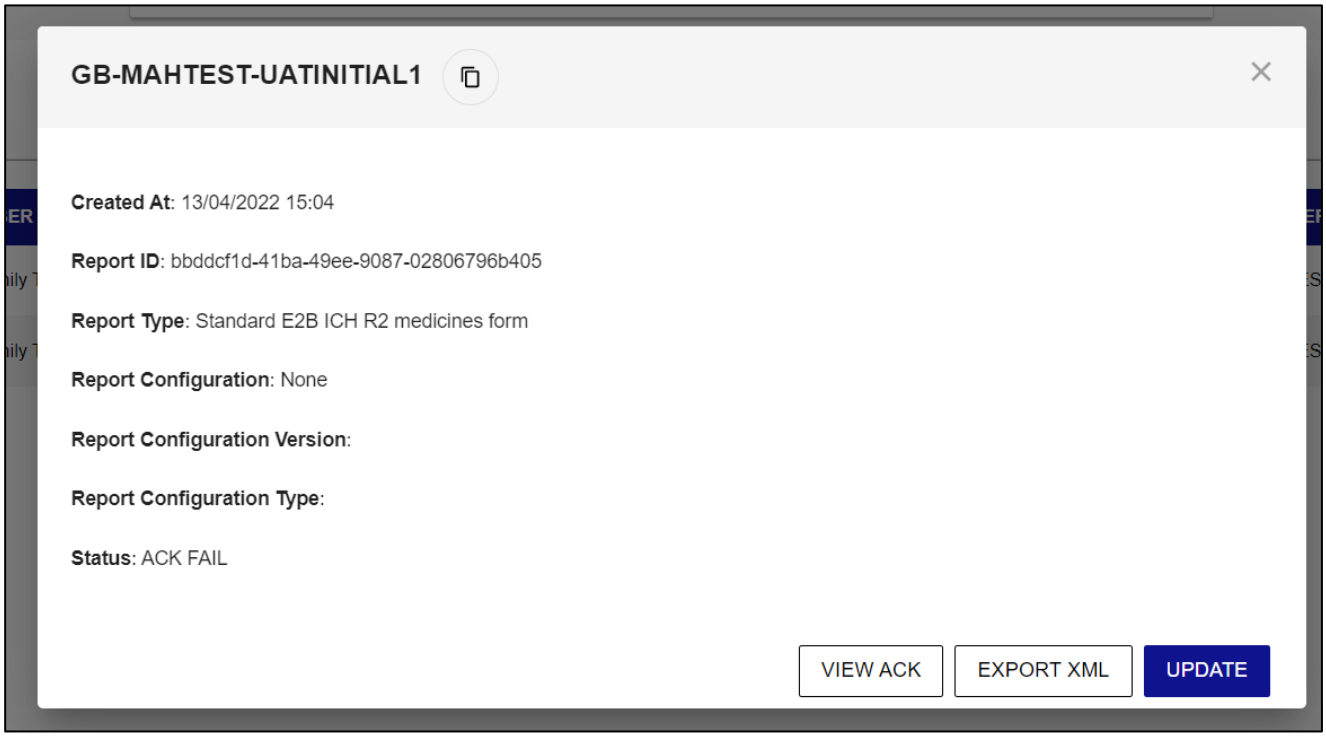
Status	Explanation
Submitted	Report submitted to the MHRA. No acknowledgement received yet
Ack Success	Report submitted to the MHRA. Positive acknowledgement (01 ack) received
Ack Fail	Report submitted to the MHRA. Negative acknowledgement (02 ack) received
Draft	Draft report saved from the new report form

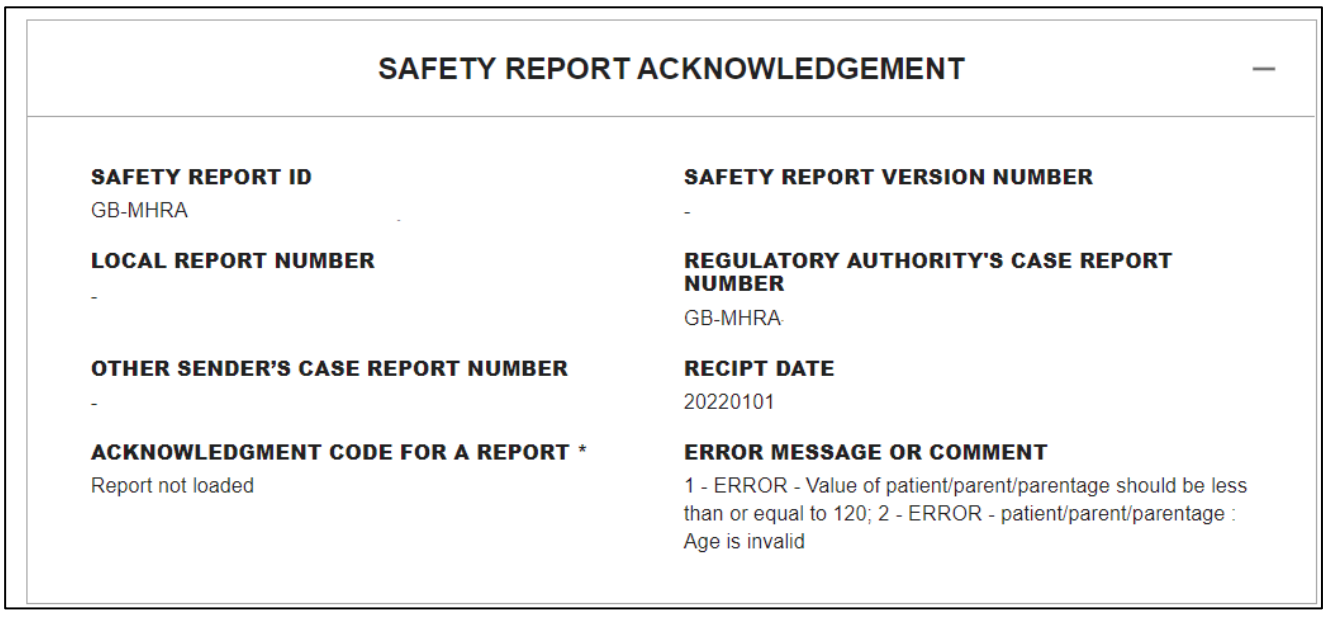
If you have not received an acknowledgment within 72 hours of submitting an ICSR or SUSAR, contact E2B.support@mhra.gov.uk, including information on the filename, message number and senderreportID, as well as attaching the XML file.

For reports with the status ‘Ack Fail’ please click ‘view ack’ and then ‘open’. Under ‘error message or comment’ the reason/s for the submission failure can be seen. The error will

need to be addressed by ‘updating’ the report and manually correcting the field referred to in the error message, before re-validating and sending the report to the MHRA.







You can also view saved draft reports by filtering status to ‘Draft’. If you want to continue editing a draft report, select the report and select ‘update’ to view the editable draft form. You will then need to select ‘Update’ in the top right-hand corner of the report form.

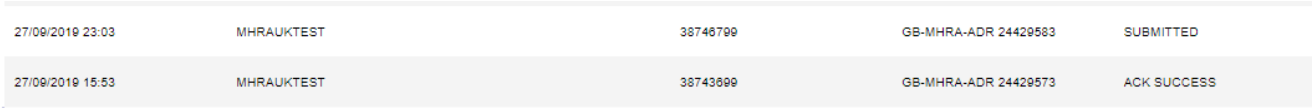
ICSRs received from the MHRA

ICSRs received from the MHRA can also be tracked in the ‘Report Management’ screen. Please note this section does not apply to SUSARs where only acknowledgements of receipt should be expected following submission of the report.

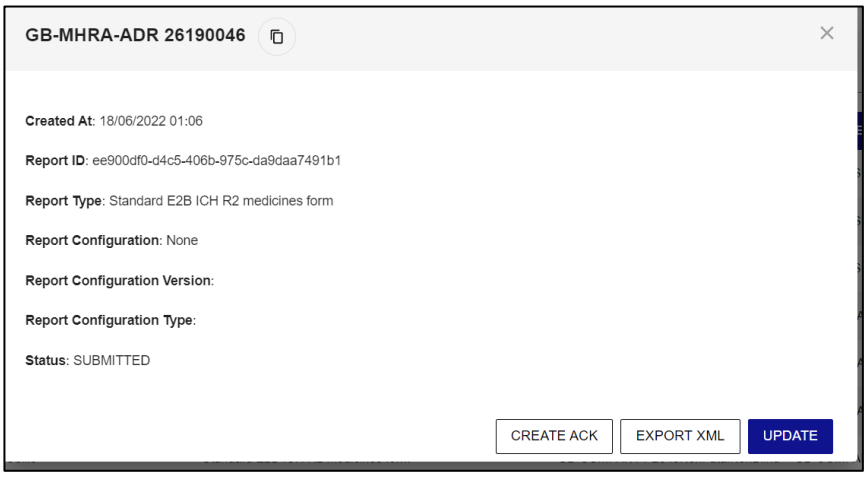
ICSRs sent by the MHRA, which are Anonymised Single Patient Reports (ASPRs), can be identified by the sender column ‘MHRAUK’. An organisation will need to manually acknowledge each ICSR successfully received which will send an ack back to the MHRA. It is expected that all ICSRs sent by the MHRA will be acknowledged within 2 business days.

We suggest that companies check for cases daily to weekly to ensure that where cases need to be forwarded on timelines are met.

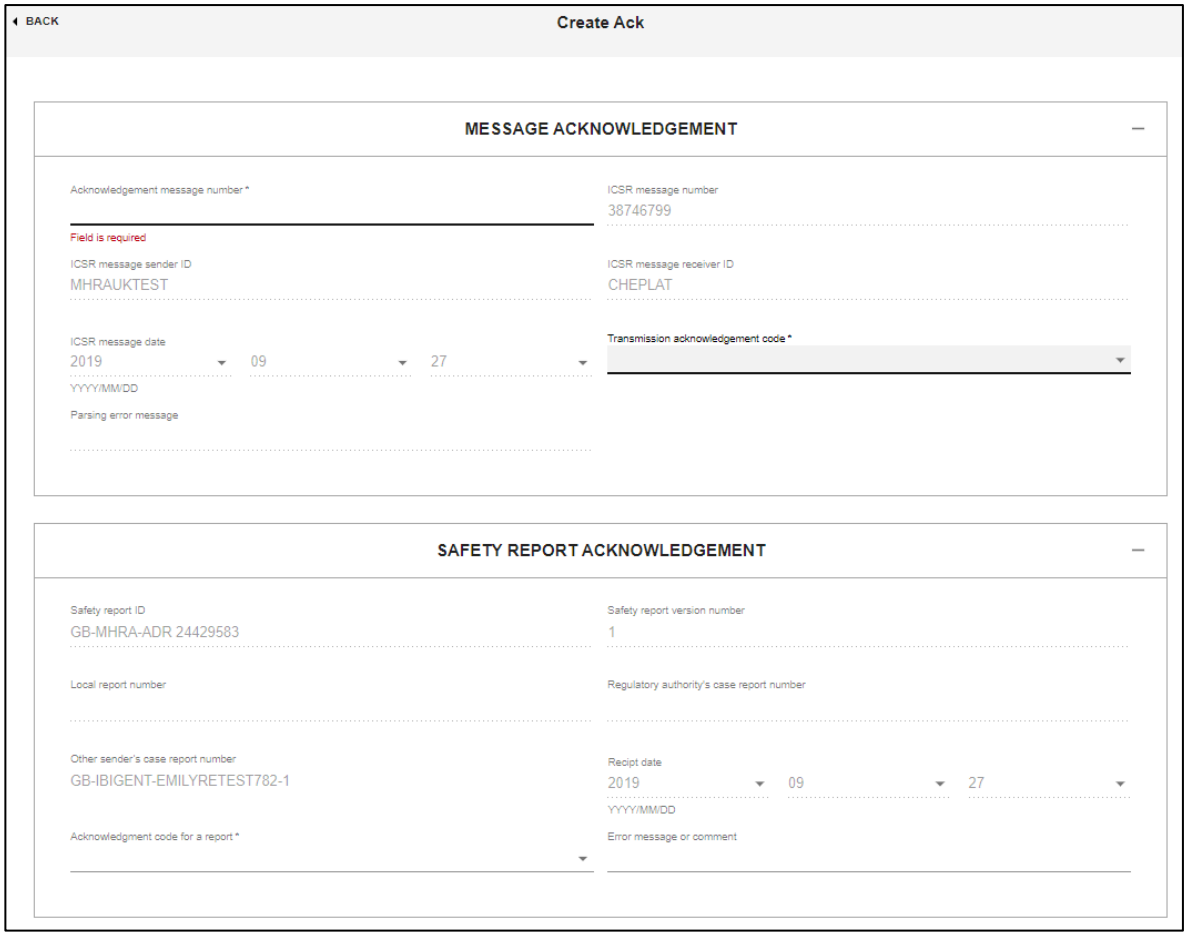
To acknowledge an ICSR you must first select the report.



This will provide the option to ‘Create ack’ which you should then select.

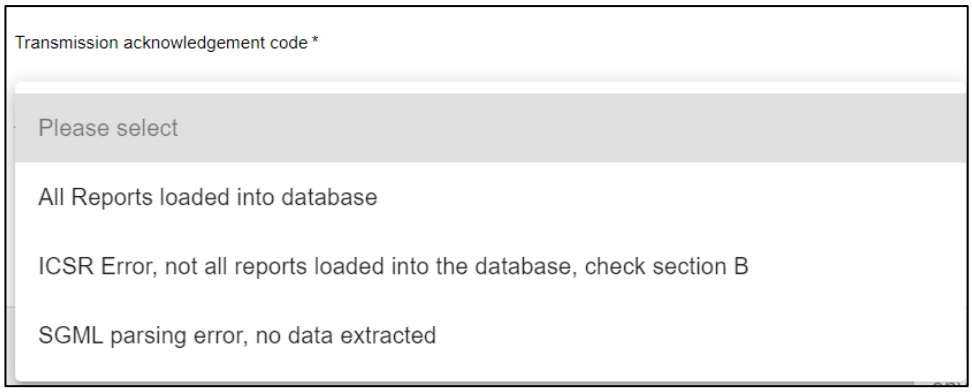


The ack will then need to be completed.



Some of the fields will be pre-populated. You will need to enter details for the acknowledgement message number, transmission acknowledgement code, acknowledgement code for a report. If the report failed, then an error message or comment should also be added.

- Acknowledgement message number: This field is up to the discretion of the MAH and is often filled with your internal reference number.
- Transmission acknowledgement code: This is a drop down where you acknowledge whether or not you received the ICSR correctly. See the table below for the different options available.



Status	Explanation
All reports loaded into database	Have been able to successfully download the ICSR received from MHRA and have successfully loaded onto pharmacovigilance (PV) database
ICSR error, not all reports loaded into the database, check section B	Have been able to successfully download the ICSR received from the MHRA however, have not loaded onto PV database (provide reason in error message or comment field)
SGML parsing error, no data extracted	Unable to download or load into PV database (provide reason in error message or comment field)

- Acknowledgment code for a report: Confirm whether the ICSR has been successfully loaded onto the PV database. If selecting 'Report not loaded' please leave a concise reason as to why the report has not been loaded as this is what the MHRA will use to review the failed ack.

Once you have completed the ack you can select 'Validate and Send'.

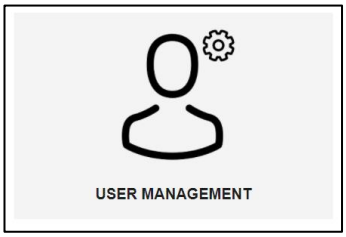
Section 4: Resources

You can access resources relating to ICSR submissions via the ‘Resources’ tile on the dashboard or burger menu.

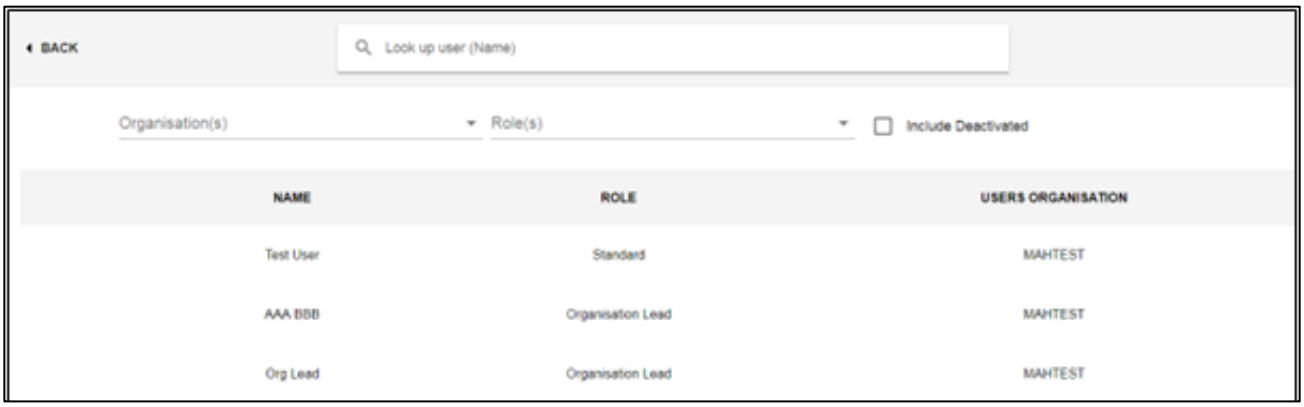
Resources will host documents, such as guidance materials to support using ICSR Submissions. Select ‘View’ to download the document.

Section 5: User Management

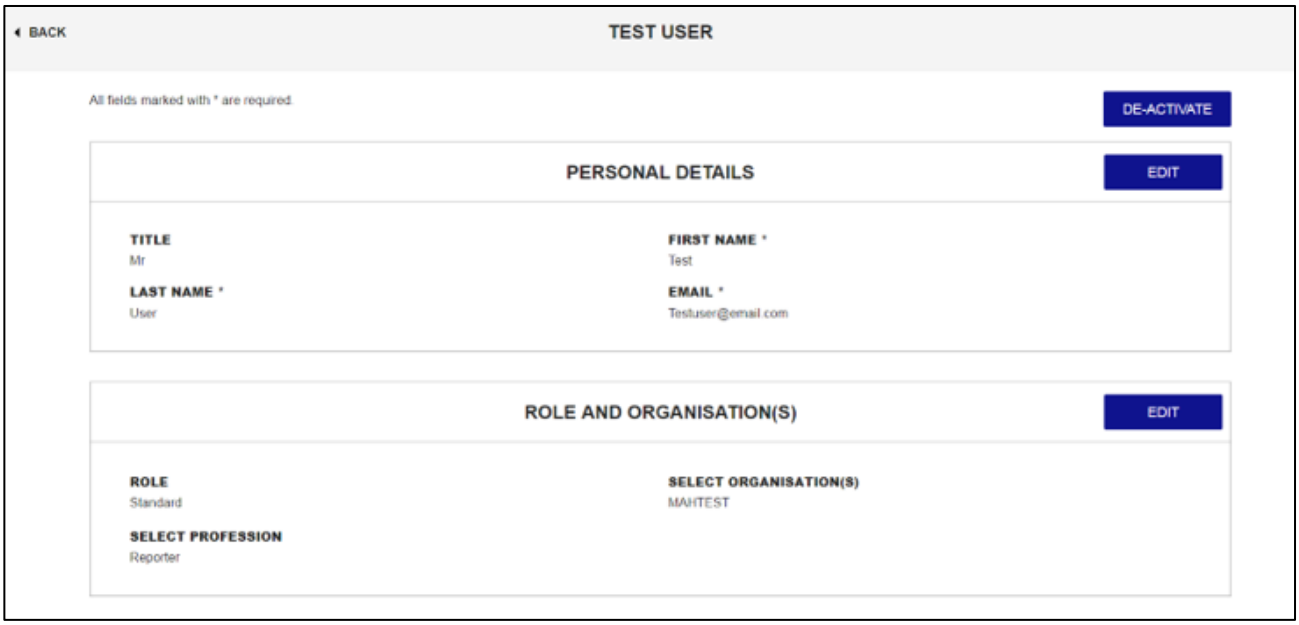
If you are an organisation lead, users associated with your organisation can be viewed by selecting the ‘User Management’ from the dashboard or burger menu.



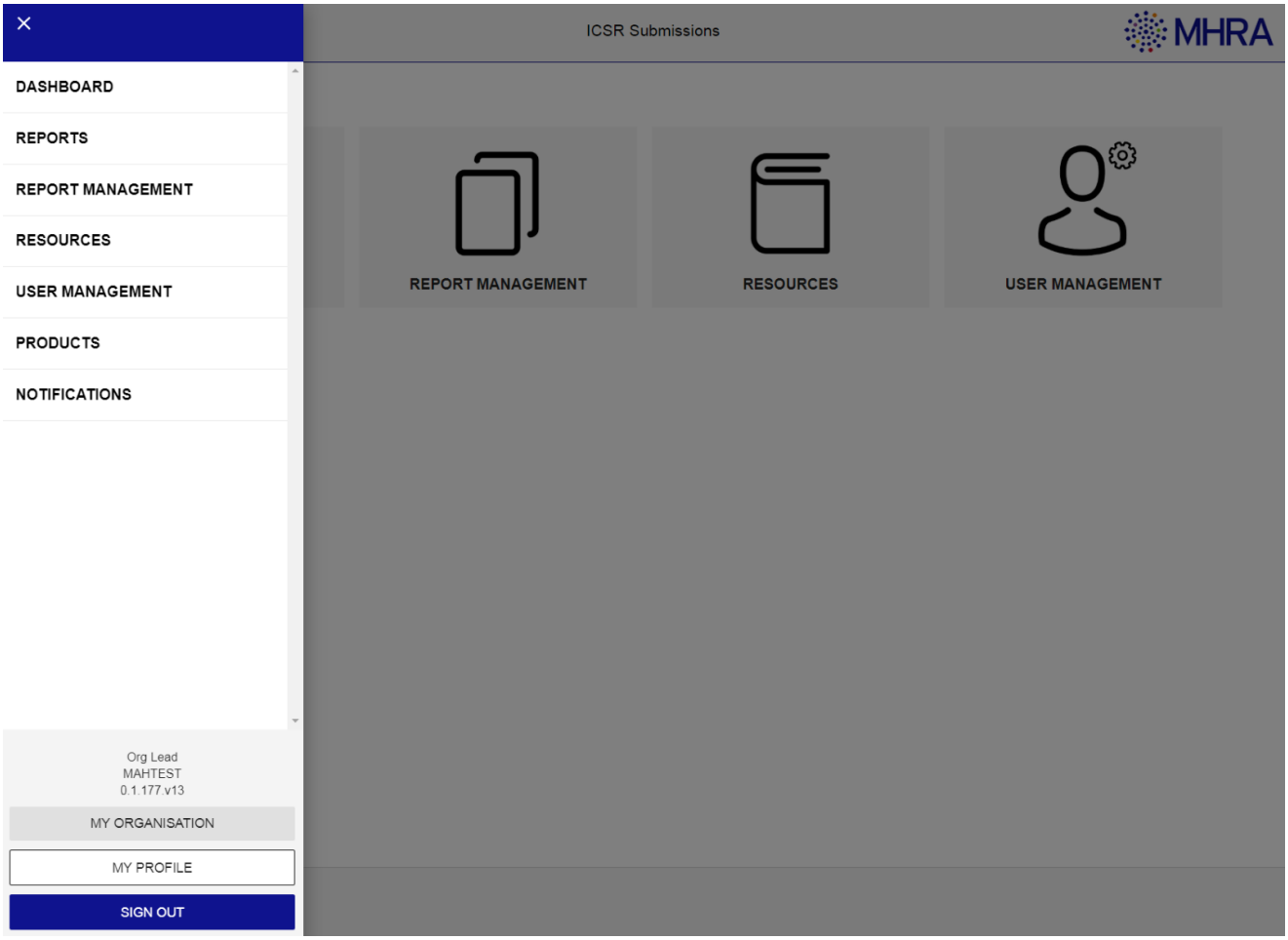
You can search for specific users using the ‘look up user’ search function.
You can filter users based on ‘organisation’ (if you are an organisation lead with access to multiple organisations), ‘role’ and ‘deactivated status’.



As an organisation lead you can view and edit user details including ‘personal details’, and ‘role and organisation’ by selecting the user.



You can view your own details either by selecting yourself from the ‘User Management screen’ or by selecting ‘My Profile’ from the burger menu. If you wish to edit your personal details, you should either contact your organisation lead (if you are a standard user) or email ICSRtesting@mhra.gov.uk.



Creating New Users

If you are an ‘organisation lead’, you are responsible for creating user accounts for others in your organisation(s) who require access to ICSR submissions.

You can create new users by selecting ‘Add new user’ and entering their details. Personal details are required including their email address which they will use to login to the system.

When creating users, you must select their role from either ‘Organisation Lead’ or ‘Standard’, depending on the access required.

Organisation leads can create new users whereas standard users cannot.

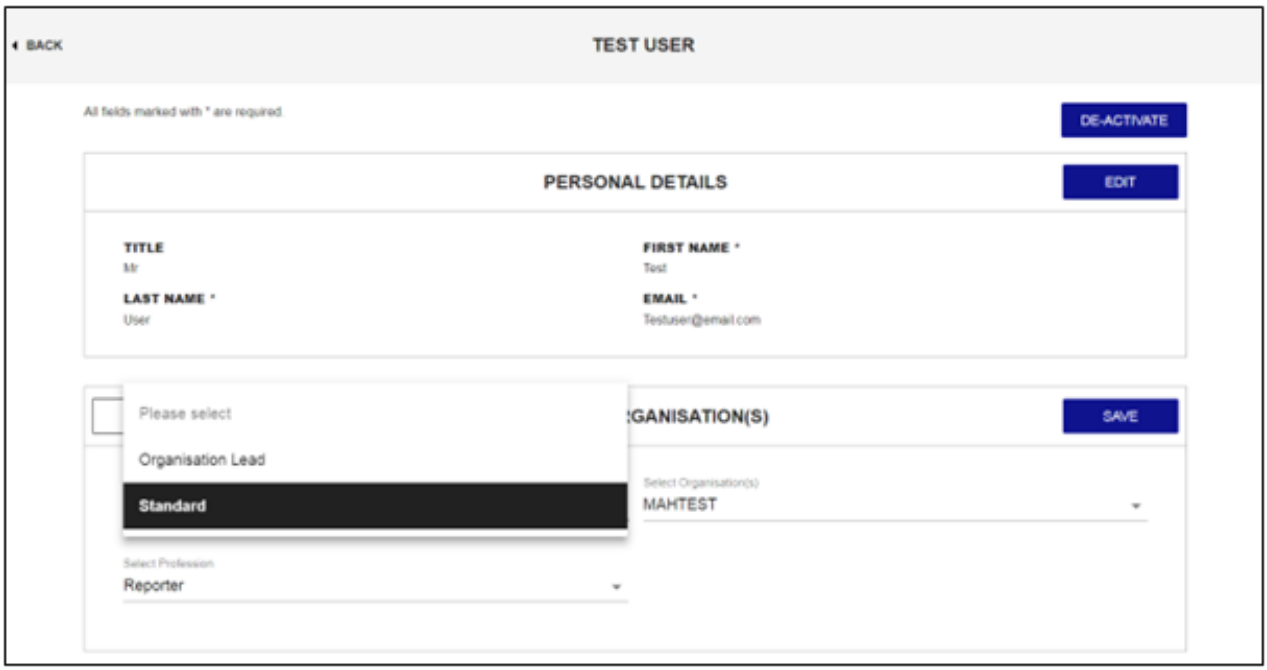
You must also create a password for the user. Passwords must have at least one capital letter, have at least one numeric character, and be at least 9 characters.

Once all details are filled in you should select ‘Create User’.

Once the user is created, you will need to provide them with their login details (email and password).

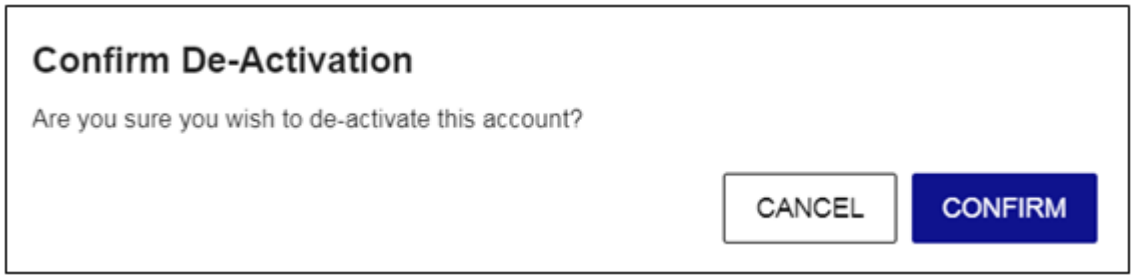
New users should be encouraged to update their password when logging in for security purposes.

Organisations can have more than one organisation lead. As an organisation lead, you can upgrade standard users to organisation lead by editing their profile.

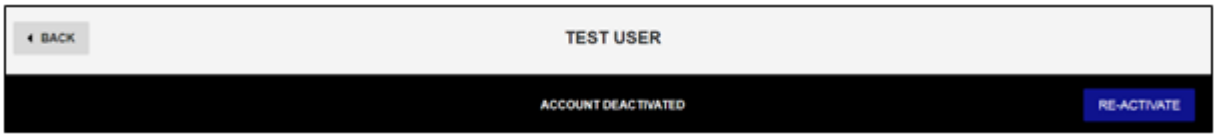


Deactivating Users

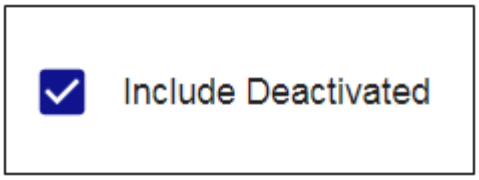
As an organisation lead, if you wish to deactivate standard users who have left your organisation, you can do so by choosing the desired user and selecting ‘De-activate’. If you require the deactivation of an organisation lead account, please contact ICSRtesting@mhra.gov.uk with the email address of the account you wish to deactivate.

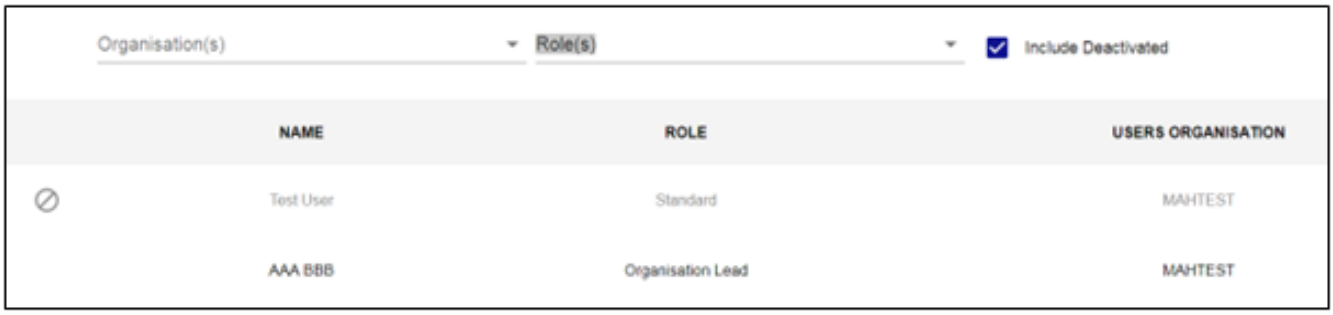


Users can be reactivated if desired by selecting ‘re-activate’.



Deactivated users can be viewed in the ‘user management’ screen by selecting ‘Include deactivated’. Deactivated users will appear greyed out, with a ‘Ø’ symbol to the left of their name.





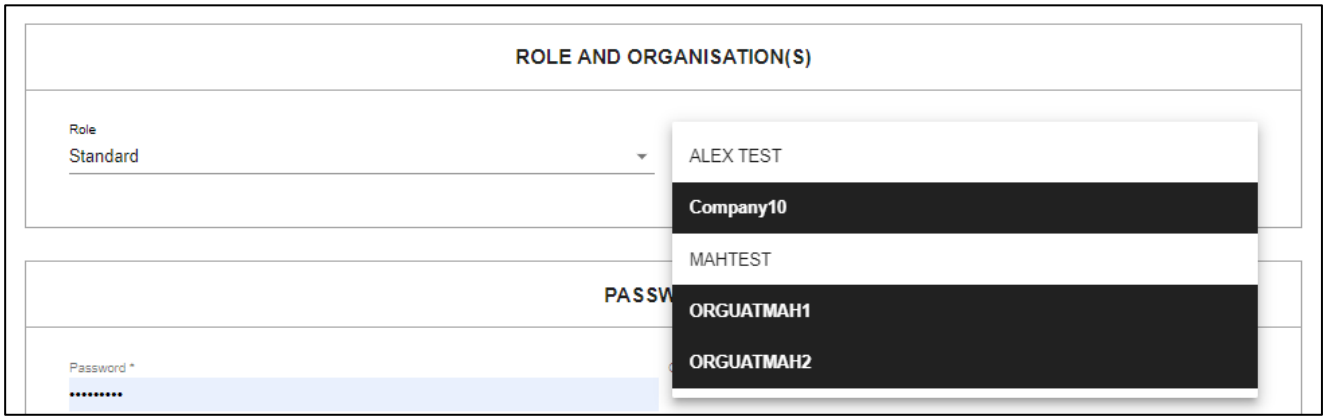
User accounts which are not used for 6 months are automatically deactivated. It is not possible to reactivate these accounts with an Organisation Lead account. To reactivate these accounts please contact ICSRtesting@mhra.gov.uk and quote the email address you wish to reactivate along with the organisation(s) associated with that account.

Section 6: Associating Users to Multiple Organisations

Users can be associated with multiple organisations in order to submit and receive reports on behalf of multiple organisations. For example, this can be used by Contract Research Organisations (CROs) or third-party users. Once a user is registered to multiple organisations, they can choose which organisation they wish to log in as by selecting from the drop-down list once they have entered their user email and password.

Organisation leads can add users to some or all organisations that they are associated with. When setting up a new user, to add a user to more than one organisation you can simply click on all the required organisations from the 'Organisation(s)' drop-down. To edit a user from one associated organisation and add them to another associated organisation you can click on the user in 'User Management' and edit their 'Role and Organisation(s)' section.

In ICSR Submissions 'organisations' refer to individual Sponsors. Therefore, for a CRO to report on behalf of several Sponsors, CRO users need to each be associated to the Sponsor organisation/s they are reporting for. Upon logging in, the user can then select which organisation they are reporting for, and the reports will be submitted under the Sponsors 'organisation' account, where they can also be viewed.



If an 'organisation lead' wishes to add a user that was initially set up by an organisation lead from another organisation they will need to contact ICSRtesting@mhra.gov.uk in order for one of our team to add this user to your organisation.

Contact Details

If you are experiencing issues with ICSR submissions, or have any questions, please email details of your questions to ICSRtesting@mhra.gov.uk.

For issues relating to missing or failed Acks and missing ASPRs please contact E2B.Support@mhra.gov.uk.