



The Danish GCP Units guide - Submission of Annual Safety Report (ASR) in CTIS

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1 Abbreviations

ASR = Annual Safety Report

AR = Assessment Report

AxMP = Auxiliary Medicinal Products

CT = Clinical Trial

CTR = Clinical Trial Regulation

DLP = Data Lock Point

EMA = European Medicines Agency

IMPD = Investigational Medicinal Product Dossier

NCA = National Competent Authorities

MSC = Member States Concerned

RFI = Request for information

RMS = Reference member states

RSI = Reference Safety Information

SM = Substantial modification

SmPC = Summary of Product Characteristics

SAE = Serious Adverse Event

SAR = Serious Adverse Reaction

saMS = safety assessing Member States

2 Introduction

2.1 The Annual Safety Report

The Annual Safety Report (ASR) is a document provided to the authorities regarding the monitoring and evaluation of the evolving safety profile of the Investigational Medicinal Product (IMP) and the mitigation of potential risks. Sponsors must each year submit a report on the safety of each IMP or a combination of IMPs used in a clinical trial. This obligation starts with the first authorisation of the trial and finalises with the end of the trial. ASR submission is not required if the trial period is shorter than one year.

The ASR must conclude and evaluate the risk/benefit of the trial, based on all SAEs and SARs observed in the period of reporting, and must include a line listing of any SARs observed.

A single ASR for the trial can be prepared for multi-drug therapy using authorised/marketed products as IMP combination. See also section 2.5 of the [ICH E2F](#).

A separate ASR of the Auxiliary Medicinal Products (AxMPs) is not required either. However, any information relating to (authorised or non-authorised) AxMPs which are relevant for the IMP may be included in the ASR. All SARs to a non-authorised AxMP(s) should be included in the line listing of SARs.

A template for an ASR and line listing of SARs can be found on the GCP unit's Danish webpage: [Hændelser og bivirkninger vejledninger og skabeloner - GCP-Enhederne](#)

For multinational trials approved under the CTR, the Sponsor is required to use the simplified CTCTG ASR template (a template created for non-commercial sponsors with multinational trials under CTR). The template is available on CTCTG webpage (Under KEY DOCUMENTS LIST -> Clinical Trial Safety): <https://www.hma.eu/about-hma/working-groups/clinical-trials-coordination-group.html>

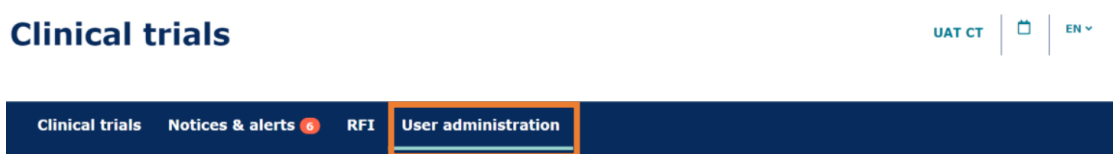
2.2 How to assign the business role; ASR submitter

The CT Admin can assign the ASR submitter business role for the specific trial. The CT Administrator user does not have ASR permissions to its role. In order to be able to perform ASR related activities; the CT Admin, should assign the ASR submitter role to him/herself.

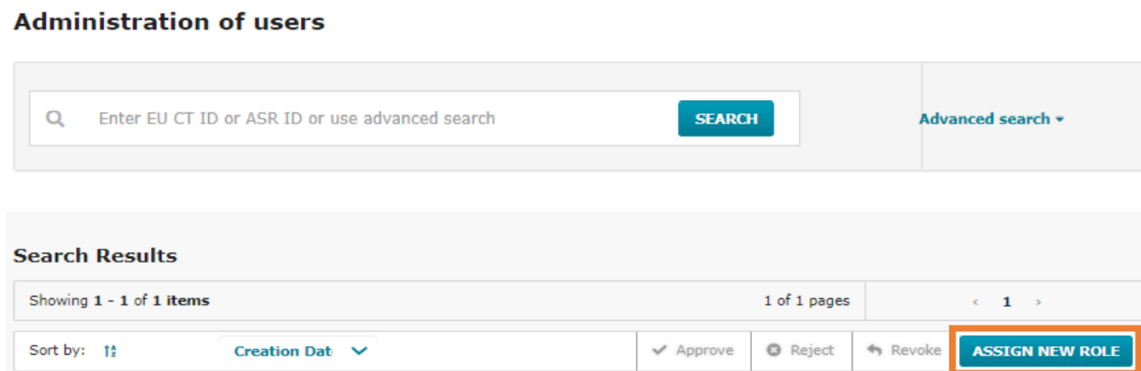
Info box:

For more detailed information please refer to "Roles and permissions matrix summary Sponsors Workspace CTIS Training Programme – Module 7" [Sponsor workspace - Roles and permissions summary \(europa.eu\)](#)

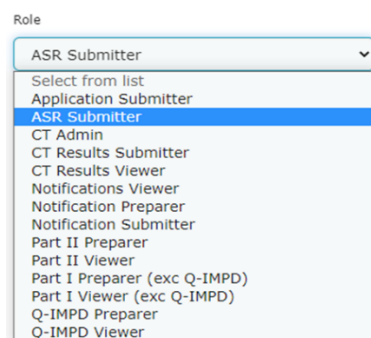
1. The CT Admin can log in to CTIS and click the User administration tab.



2. Click on the 'Assign new role' button.



3. Select the ASR submitter role to be assigned to the CT Administrator or other users within the organisation.



Select 'Specific trial' in the 'Scope' field, fill in EU CT number and click on the 'Assign' button.

Assign role(s) ✕

User Id:
 EU CT number:

Organisation name:
 Organisation Id:

Role:
 Scope:

Authorised date:

3 Create and submit an Annual Safety Report (ASR)

For more detailed information please refer to section 4.13 in Sponsors Handbook available on [Clinical Trials Information System \(CTIS\): training and support | European Medicines Agency \(EMA\)](#)

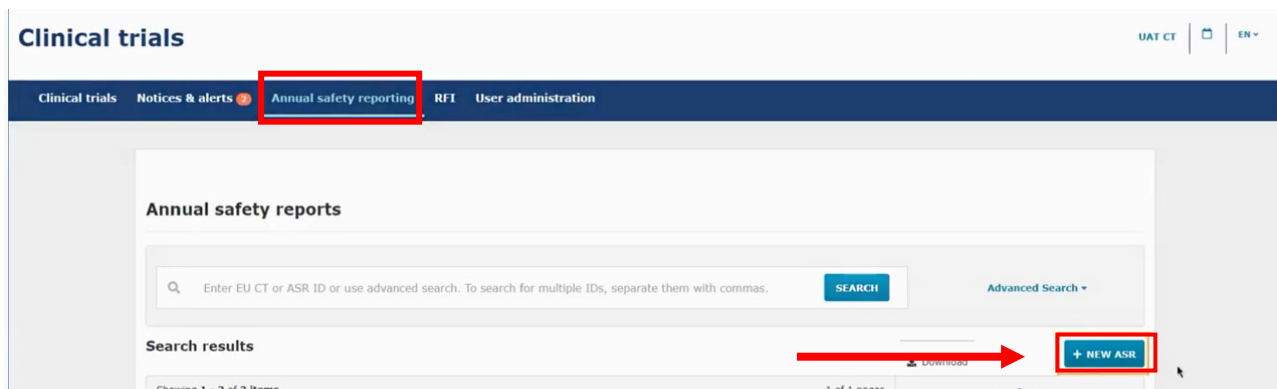
Info box:

Make sure to have the ASR document in PDF prepared before you start the completion of the ASR form.

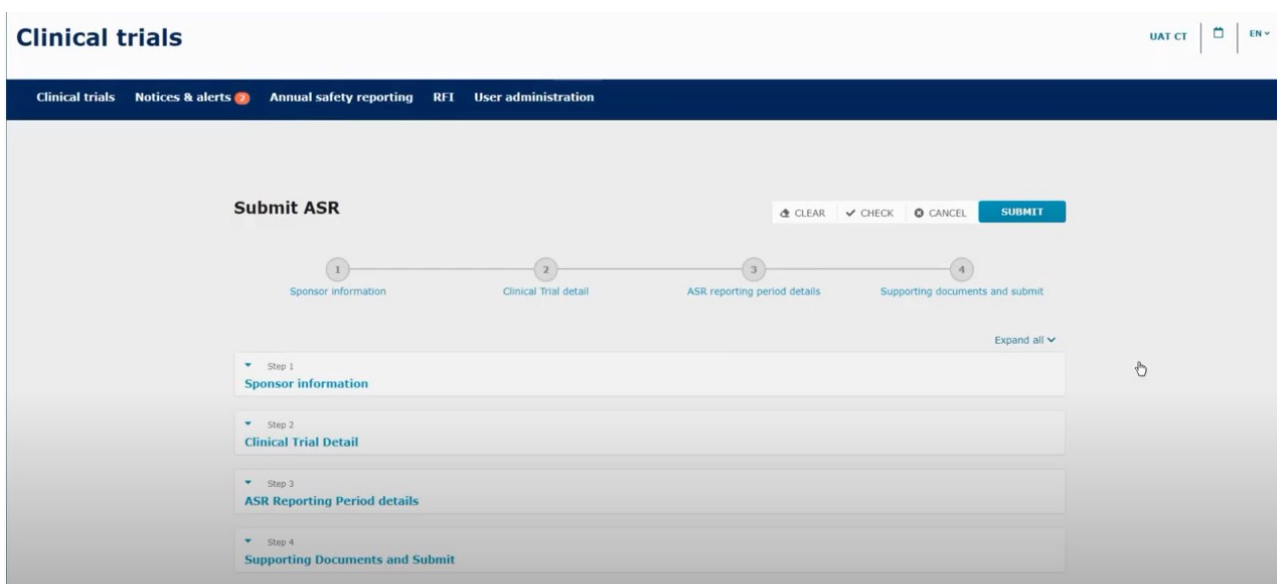
The ASR form cannot be saved, but has to be completed and submitted in one go!

You also need to have all the relevant information ready (e.g. Reference Safety Information on Investigational medicinal products, relevant events that occurred (incl. SAR line listing), reporting period, etc.) before you start.

In the 'Annual safety reporting' tab, users of the sponsor workspace with the role of 'ASR submitter', are able to open 'the Annual Safety Reporting form' by clicking on the **'+New ASR' button** and to complete and submit new ASRs. Other sponsor users can only view ASRs for the clinical trials they have a role in.

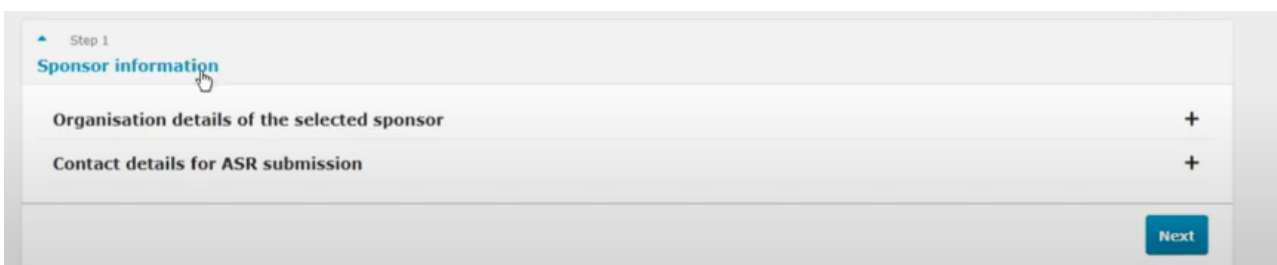


An ASR form opens:



Fill in the information for the four steps (**Sponsor information**, **Clinical Trial Detail**, **ASR Reporting Period details** and **Supporting Documents**) and submit by clicking the 'Submit' button.

Step 1: Sponsor information



Fill in Organisation details of the sponsor and contact details for the person responsible for the submission and can be contacted with an email address and a phone number. Click 'Next'.

Step 2: Clinical trial details

Search for the Clinical Trial (CT) to which you want to submit an ASR. You search for clinical trials that are authorised for the sponsor organisation and select the trial for which you want to submit an ASR.

Search for clinical trials

Clinical trial results based on your search criteria

← Try another search

	CT for training test	Decision date	Sponsor	MS
☒	EU CT number 2021-501398-35-00	20/05/2021	Test organisation	Austria Germany
☐	EU CT number 2021-501535-14-00	01/06/2021	Test organisation	Germany

Showing 1 - 2 of 2 items 1 of 1 pages < 1 >

✓ Add to ASR

When the form opens you click on the related IMP or IMP's for the clinical trial you want to submit an ASR.

Step 3: ASR reporting period details

ASR Reporting Period details

Is this the sponsor's first ASR for any of the IMP(s) selected? ☐ Yes ☒ No

If yes, indicate which IMPs

Paracetamol 500 mg Soluble Tablets

Data lock point

28/04/2021

ASR reporting period *

01/04/2020 30/04/2021

RSI Updated during the reporting period * ☐ Yes ☒ No

Substantial modification on RSI submitted and approved during the reporting period * ☐ Yes ☒ No

During the reporting period ASR includes *

Select

- Novel novel combination
- New combination
- First in class product/IMP(in EU)
- Advanced therapy medicinal product (ATMP)
- New signals or concerns or risk for the product
- Temporary halt or suspension of any trial due to safety reason
- Premature ended trial/s

Step 4

Supporting Documents and Submit

In this section you need to select and fill in the **data lock point (DLP)**. This is the cut-off date of selecting data for the ASR. The DLP must be as close as possible to the approval date.

If this is the first ASR in the clinical trial the **ASR reporting period** starts with the date where the clinical trial is first authorised and ends with the selected DLP (approximately after one year).

The deadline for the annual submission of ASR is 60 calendar days after the selected DLP.

The following must be answered:

- Has the RSI (reference safety information) been updated during the reporting period?
- Has a Substantial modification on the RSI been submitted and approved during the reporting period?

In most cases the answers would be **No**.

'During the reporting period the ASR includes' must be answered by selection of one or more items from the drop down menu.

Step 4: Supporting documents and submit

Supporting Documents and Submit

ASR Document *	
SmPC (if the SmPC includes RSI and not submitted as part of the ASR document)	
Investigator's Brochure (if the Investigator's Brochure includes RSI and not submitted as part of the ASR document)	
Other	

Submit

I, on behalf of the sponsor, confirm that the:

- Information provided is complete
- Attached documents contain an accurate account of the information available
- The Sponsor, , declares that the Annual Safety Report is prepared and hereby submitted to the Agency in accordance with Article 43 of Regulation (EU) No 536/2014 and all other applicable legal provisions.

☐ * RSI Document/.s (Old and new version where applicable)

☐ * I agree with the above statements

In step 4 you add the ASR report document and you can also add other supporting documents. The ASR report should be uploaded as a PDF.

Now scroll to the top of the form and check if all information is valid or anything is missing by using the **'Check' button** and submit the ASR by clicking the **'Submit' button**.

Once submitted you see this page where all the information that was populated will appear.

ASR-2021-00183

Test organisation
IMP: Paracetamol 500 mg Soluble Tablets
Submitted: 11/06/2021

MSC
AT, DE

saMS

ASR reporting period
01/04/2020 - 30/04/2021

Submitted
11/06/2021

ASR Submission Assessment

SPONSOR DETAILS

ORGANISATION DETAILS FOR SPONSOR
Test organisation
Dun Karm Street, 2 Floor, Orange Point Building, BKR 9037, Birkirkara, Malta

CONTACT FOR ASR SUBMISSION
Full name test
Test organisation
Dun Karm Street, 2 Floor, Orange Point Building, BKR 9037, Birkirkara, Malta
123123123
testmail@mail.com

Requests for information (RFI) can be created during the safety assessing Member States (saMS) evaluation. The ASR Submitter needs to proactively monitor the 'Notices & alerts' tab on a daily basis after submitting an ASR until the report is *finalised* and marked as such by the authorities. In addition, the due date of the ASR RFI should be noticed. Access for the ASR RFIs are gained either through the 'Annual safety reporting' tab, the 'RFI' tab or the 'Notices & alerts' tab. Note the ASR Submitter is the only role that can view an ASR RFI and reply to it (not even the CT Admin can see if an RFI was submitted on one of their trial's ASRs).

4 After submission of Annual Safety Report (ASR)

The ASR will not be available in the public CTIS database.

After submission you will get a screen showing "*in progress*" and eventually "*finalised*", which you can save/print (as a screen shot) and use as documentation for your Trial Master File (TMF). See example of screen shot below.

Clinical trials

Clinical trials Notices & alerts 0 Annual safety reporting RFI User administration

ASR-2023-

Submitted: 01/06/2023

ASR Submission () Assessment ()

SPONSOR DETAILS

ORGANISATION DETAILS FOR SPONSOR

CONTACT FOR ASR SUBMISSION

MSC
DK

saMS
Denmark

ASR reporting period
In progress
01/06/2023

CLINICAL TRIAL DETAILS Expand all

"Titel of trial"

IMP1: , injektionsvæske, suspension i fyldt injektionssprøjte / Role: Comparator ()

IMP2: injektionsvæske, suspension i fyldt injektionssprøjte / Role: Test ()

Annual safety report details

This is the first sponsor's ASR for any of the IMP(s) selected Yes

If yes, indicate which IMPs , injektionsvæske, suspension i fyldt injektionssprøjte, injektionsvæske, suspension i fyldt injektionssprøjte

Data lock point /2023

ASR reporting period /2023

RSI Updated during the reporting period No

Substantial modification on RSI submitted and approved during the reporting period No

During the reporting period ASR includes None

Submission documents

Annual safety report season 1
English · ASR Document · System version 1.00
Submission date 01/06/2023
Version 1 · 01/06/2023

SmPC
English · Summary of Product Characteristics (SmPC) · System version 1.00
Submission date 01/06/2023
Version 1 · 01/06/2023

SmPC
English · Summary of Product Characteristics (SmPC) · System version 1.00
Submission date 01/06/2023
Version 1 · 01/06/2023

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☐ RSI Document/s (Old and new version where applicable)

☐ I agree with the above statements

5 Changes log

Version 1.0

Version 1.2: Updated with section 4.

Version 2.0: Information added regarding simplified CTEG ASR template in section 2.1. Links and information regarding RFI in section 3 updated.